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Theoretical investigations of proton and hydrogen atom transfer in the condensed phase

M V Basilevsky, M V Vener

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Abstract. Theoretical studies of the dynamics and kinetics of proton and hydrogen atom transfer processes occupy a special place in the kinetics of chemical reactions. The transition state theory is often inapplicable to these processes due to substantial quantum effects. Different approaches to the description of these reactions are discussed and compared. Calculations for a number of particular condensed-phase reactions involving proton or hydrogen atom transfer are analysed. Data of calculations of potential energy surfaces for the considered systems and the results of experimental kinetic and spectroscopic studies are presented. The bibliography includes 469 references.

I. Introduction

Proton transfer (PT) and hydrogen atom transfer (HAT) deserve special consideration in the study of chemical reactions. Due to substantial quantum effects, the transition state (TS) theory — which today forms the basis for investigations of reaction kinetics and mechanisms — is often inapplicable in these cases. The existing numerous theories of PT and HAT are complicated and diverse. This review is an attempt to consider and compare, from a unified standpoint, various approaches to the theoretical description of PT and HAT and to identify the common points and the scopes of applicability of these approaches. Without pretending to an exhaustive consideration, we endeavoured to provide a concerned reader with the main ideas and trends in the development of the research in this field. More comprehensive formulation of the outlined approaches can be found in the key references.

It should be noted that the difference between PT and HAT is largely conventional. In the limiting case, PT is an ionic heterolytic process in which the influence of the medium is crucial, whereas HAT is a radical homolytic process depending only slightly on the medium. In reality, all types of intermediate situations are encountered and it is difficult to adhere to a consistent terminology. In some cases, the use of a particular term can be contested;

however, in our opinion, this discussion does not deserve much attention.

Two factors, namely, tunnelling and effect of the medium, restrict the applicability of the TS theory and account for the exceptional position of the PT and HAT processes in the theory of chemical reactions. For consistent treatment of tunnelling, one should consider (or, more precisely, calculate) the quantum-dynamic evolution of the reaction subsystem on a multidimensional potential energy surface (PES). The reaction rate constant is obtained by statistical averaging of the results of this calculation. An adequate allowance for the medium implies that a very large number (hundreds or even thousands) of degrees of freedom for particles surrounding the reaction subsystem should be included in this dynamic investigation. Taking into account simultaneously both factors mentioned above constitutes the essence of the dynamic theory of chemical reactions in the condensed phase as a modern line of research in theoretical chemical physics.

In practice, the stringent requirements outlined above can be markedly released, in particular, by using simplified models for tunnelling transitions and by decreasing the number of additional degrees of freedom interacting with the tunnelling coordinate to tens or even less. Nevertheless, in recent years, record-breaking computations have been carried out (they are described in this review) which attempted to minimise the simplifying assumptions and their consequences. However, real objects (*e.g.*, reactions in enzymes) are so complicated that even these calculations are simplified models.

In any case, the major requirement of explicit inclusion of the tunnelling dynamics into the mechanism of the elementary process remains valid. This feature distinguishes the studies discussed in this review from the numerous studies whose authors attempted to consider the PT and HAT reactions on the basis of the traditional TS theory, *i.e.*, using a quasi-equilibrium statistical rate constant. As the premise, we accepted the statement that interpretation of the kinetics and the mechanism of these reactions based only on the language of the energetic and topographic characteristics of PES such as the height of the potential barrier and the reaction coordinate is inadequate and recedes to the background.

The material presented here is arranged in the following way. First, the main concepts of the PT and HAT dynamics in the condensed phase are considered. They were formulated in the 1970s–1980s and they are still being developed and refined. This is followed by applications of the theory to calculations of particular systems carried out during the last 10–15 years. Many of the publications cited present also original theoretical

M V Basilevsky, M V Vener State Scientific Centre of Russian Federation 'L Ya Karpov Institute of Physical Chemistry',
ul. Vorontsovo Pole 10, 105064 Moscow, Russian Federation.
Fax (7 095) 975 24 50. Tel. (7 095) 917 39 03.

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developments; therefore, the subdivision into ‘theory’ and ‘applications’ is not fully consistent.

Simpler gas-phase reactions have been investigated much more extensively than reactions in the condensed phase. The relevant studies are not covered systematically but references to earlier reviews and monographs are given. However, since the understanding of the tunnelling dynamics of gas-phase reactions should precede any discussion of tunnelling in the liquid or solid phase or in biological objects, the key studies dealing with the theory of gas-phase PT and HAT are considered as examples.

Since we selected studies focused on the dynamics of an elementary process, the quantum-chemical calculations of PES (even the highest-level ones) are not of interest by themselves in this context. A summary of such calculations (the most significant in our opinion) is included as reference data together with experimental results. The experimental works presented in brief represent mainly investigations of the kinetics and mechanisms of PT and HAT by spectroscopy (NMR, UV, IR, radiospectroscopy, *etc.*). These studies provide the factual information necessary for the development and testing of the theoretical models discussed in the review.

II. Methods for the theoretical description of proton and hydrogen atom transfer

1. Potential energy surfaces

a. Reaction centre

Let us consider the reaction centre for PT or HAT in a simple two-mode linear model.



Here A_1 and A_2 are ‘heavy’ molecular fragments; their internal structure is not specified in detail now. The centres of gravity of particles A_1 , A_2 and H lie on the same straight line; this type of reaction is called collinear.

The dynamic behaviour of system (1) is fully described by variations of two coordinates, namely, the proton coordinate (s) measured from the centre of gravity of the whole complex (1) and the distance (R) between the heavy fragments. Figure 1 presents a typical PES $V(s, R)$ in these coordinates and cross-sections $V(s|R)$ of this surface along the coordinate s , which parametrically depend on R . For a symmetrical system ($\text{A}_1 = \text{A}_2$), the cross-sections are symmetrical. As R decreases, the double-well profiles become more gently sloping, which is accompanied by equalisation of the proton (hydrogen atom) bonds with fragments A_1 and A_2 . At the critical point R_c , the double-well potential profile turns into a single-well one. This PES topography determines the key characteristics of a PT or HAT reaction. Since one of the two equilibrium configurations of complex (1) is the initial state, either a PES with potential barriers with different heights (if $R_e > R_c$) or a barrierless PES (if $R_e < R_c$) appear, depending on the equilibrium distance R_e . In the former case, the initial equilibrium configuration is markedly asymmetrical ($\text{A}_1 - \text{H} \cdots \text{A}_2$), while in the latter case, it is nearly symmetrical ($\text{A}_1 \cdots \text{H} \cdots \text{A}_2$), even when the fragments A_1 and A_2 are different. In symmetrical systems, a combination of asymmetrical configurations of the reactants and products gives rise to a symmetrical double-well profile. The position of the top of the barrier, *i.e.*, TS (designated by $R^\ddagger$ in the axis R) cannot be smaller than R_c ($R^\ddagger \geq R_c$). The R_e and R_c values substantially depend on the nature of fragments A_1 and A_2 , most of all, their terminal atoms, which are linked to the proton or hydrogen atom that is transferred.¹ The distance between the terminal atoms (rather than between the centres of gravity of fragments A_1 and A_2) is usually taken as the coordinate R . For bimolecular reactions of non-polar reactants in the gas phase (for example, $\text{C} \cdots \text{H} \cdots \text{C}$), the R_e distance is great, $R_e \gg R_c$ (which corresponds to a van der Waals complex) and the barrier is usually

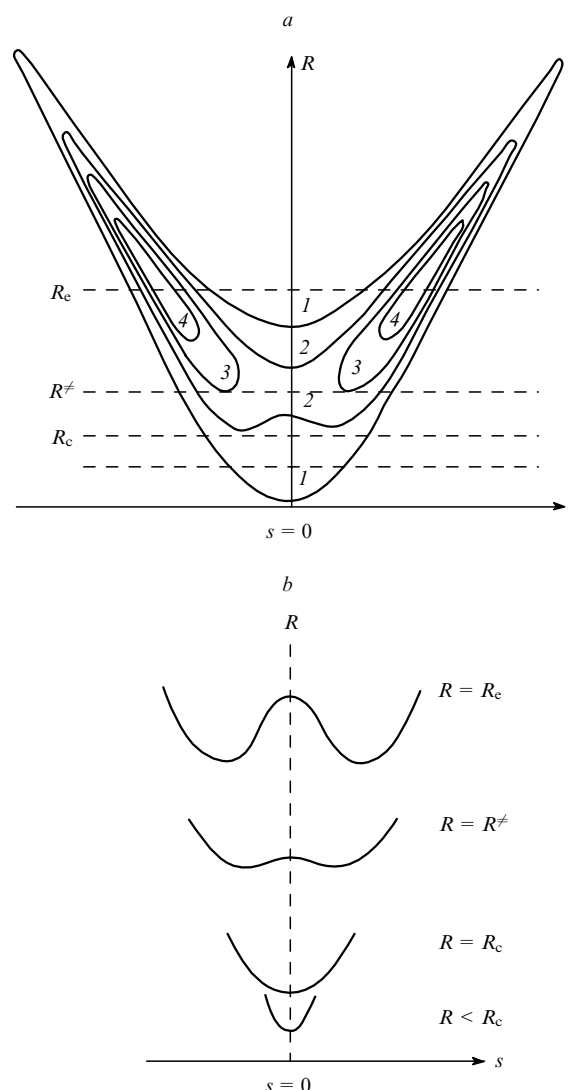


Figure 1. Typical symmetrical PES for PT or HAT reaction in the simplest two-mode collinear model;

(a) general view of the PES with isoenergy contour lines; closed loops (1–4) are isoenergy contour lines in arbitrary units; (b) PES cross-sections along the coordinate s for different R values; $R = R_e$ (reactants and products), $R = R^\ddagger$ (transition state) and $R = R_c$ (critical point). In the given case, $R_e < R^\ddagger$. The projections of the cross-sections on the R, s plane are shown by a dashed line in Fig. 1a.

rather high. Conversely, in the case of systems which tend to form strong and medium-strength hydrogen bonds (for example, the $\text{O} \cdots \text{H} \cdots \text{O}$ bonds in the condensed phase), the inequality $R_e < R_c$ usually holds, and the PES is often a single two-dimensional potential well. In this case, one cannot speak about a PT or HAT reaction. Particular examples of different possible situations are presented in Table 1. They mainly refer to electrically neutral systems; charged systems (FHF^- , H_3O_2^+ , *etc.*) with hydrogen bonds normally tend to form single-well PES.¹¹

In unimolecular processes, the reaction centre (1) is a fragment of an integrated, more or less rigid molecular structure. The equilibrium distance R_e stipulated by the structure is usually shorter than the R_e value between the reaction centres of the same type in bimolecular reactions. This is due to the fact that the $\text{A}_1 \cdots \text{H} \cdots \text{A}_2$ fragment in systems with intramolecular hydrogen bonds is non-linear. A typical example of the latter type is a *cis*-enol form of a β -dicarbonyl compound, for example, malonaldehyde or acetylacetone,^{12,13} which are six-membered chelate rings with an intramolecular hydrogen bond. The R_e values for these

Table 1. Typical R_e and R_c values in PT and HAT reactions for the $A_1-H\cdots A_2$ reaction sites.

Fragment	Process	$R_e/\text{\AA}$	Determination method	$R_c \approx R^\ddagger/\text{\AA}$ (see ^a)	Note	Ref. (see ^b)
O—H $\cdots$ O	PT and double PT in a symmetrical double-well potential	2.64	X-ray diffraction analysis of the benzoic acid crystal	2.40	the O $\cdots$ O distance in the TS for systems with a symmetrical two-well potential	2, 3
N—H $\cdots$ O	double PT in an asymmetrical double-well potential	2.95	X-ray diffraction analysis of the formamide cyclic dimer	2.55	the distance in the TS structure [B-LYP/6-311 + + G(d,p) calculations]	4, 5
N—H $\cdots$ N	double PT in a symmetrical double-well potential	2.93	the calculation (HF/3-21G) for the amidine dimer	2.53	the N $\cdots$ N distance in the TS structure for systems with a symmetrical double-well potential	6, 7
{C—H/C} [−]	PT in a symmetrical double-well potential	3.71	the calculation [MP2/6-31 + G(d,p)] for the CH ₄ /CH ₃ [−] ion–molecular complex	2.86	the C $\cdots$ C distance in the TS structure [MP2/6-31 + G(d,p) calculation]	8
{C—H/C} [•]	HAT in an asymmetrical double-well potential	3.35	spectroscopic and structural data on H abstraction from ethanol by the methyl radical in glasses	2.68	the C $\cdots$ C distance in the TS structure of the CH ₃ /CH ₃ OH system (MP2/6-31G calculation)	9, 10

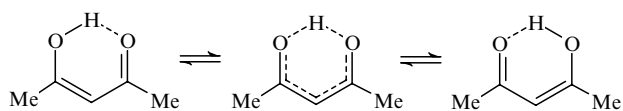
Note. Systems with intramolecular PT or HAT were not considered because in this case, the triatomic $A_1-H\cdots A_2$ fragment is essentially non-linear. ^a No direct estimate for the R_c value is known; therefore, the corresponding $R^\ddagger$ values are given, which are close to R_c . ^b The R_c value was taken from the first reference and R_e is from the second reference.

systems are much shorter than the corresponding value for the O—H $\cdots$ O fragment presented in Table 1. The rigid structure of the environment ('cage effect') is probably responsible for acceleration of enzymic PT reactions.^{14,15} In this case, the structure of the reaction centre is dictated by the architecture of the protein globule of the enzyme, while R_e is sufficiently small to lower the reaction barrier to a plausible value.

Thus, the potential relief depends appreciably on the distance between the chemically non-bonded heavy atoms, which accounts for stringent requirements to the accuracy of quantum-chemical methods used to calculate the PES. Slight errors in the estimation of R_e can change the calculated height of the potential barrier (defined as the difference between the energies of the saddle point and the reactant minimum on the PES) and can appreciably distort the potential relief that controls the reaction event.¹⁶ On the other hand, in constructing semiempirical PES, it is expedient to consider the R_e value as a control parameter whose variation allows one to reproduce a required potential relief.¹⁷

b. Rearrangement of the medium and classification of modes

Intramolecular and intermolecular relaxation. In most cases, the simplest two-mode model (1) does not provide an adequate description of PT. As an example, we consider the PT in acetylacetone molecule.



Here $R_e = 2.535 \text{ \AA}$ (see Ref. 18). According to the above simplest model, this geometry is expected to produce a single-well symmetrical equilibrium configuration of the O $\cdots$ H $\cdots$ O hydrogen bond. In reality, acetylacetone is an example of a system having a potential barrier, although it is relatively low: $\Delta V^\ddagger = 2.5 \text{ kcal mol}^{-1}$ (see Ref. 19). This 'classical' barrier disappears when the quantum zero-point vibrations of the H atom are taken into account.¹⁹ The tendency for the formation of an asymmetrical structure by the molecule is enhanced by rearrangement of its bond lengths and bond angles around the reaction centre caused by the variation of the proton coordinate s (Table 2). In the literature, this effect is often referred to as 'environment reorgan-

Table 2. Bond lengths (Å) and O $\cdots$ H—O angles (deg) for a fragment of the cyclic acetylacetone structure and the structure corresponding to the TS of the intramolecular PT reaction found by the Möller–Plesset *ab initio* calculations¹⁹ (MP2/D95 + + **).

Parameter	Cyclic enol form ^a	TS
C=C	1.376 (1.382)	1.410
C—C	1.452 (1.430)	1.410
C—O	1.338 (1.319)	1.295
C=O	1.259 (1.243)	1.295
O—H	1.004 (1.049)	1.201
O $\cdots$ H	1.626 (1.626)	1.201
O $\cdots$ O	2.549 (2.512)	2.363
O $\cdots$ H—O	150.6 (137.0)	159.1

^a The values in parentheses are experimental data.¹⁸

isation'; this term has been borrowed from electron transfer theory. In this particular case, an intramolecular reorganisation is involved.

When the PT process is accompanied by a substantial change in the charge distribution and takes place in a polar solvent, there exists an alternative mechanism for stabilisation of asymmetrical structures due to solvent reorganisation: the solvation shell is adjusted to the charge distributions, which are different for the reactants and the reaction products. This situation is referred to as the 'medium reorganisation'. Proton transfer in electrically neutral systems, for example, in a conjugate acid–base system usually does not occur in the gas phase,²⁰ but readily proceeds in polar solvents,²¹ which is due to medium reorganisation.

It can be seen from the above examples that reorganisation of the surrounding of the reaction centre (both intramolecular reorganisation and that of the environment) includes simultaneous change of many degrees of freedom, *i.e.*, it is a multimodal process.

Harmonic double-well potential energy surface. The simplest pattern of multimode reorganisation corresponds to the model harmonic PES formed by two multi-dimensional paraboloids shifted relative to each other. The two-dimensional analogue of this PES is shown in Fig. 2. The reorganising modes Q are

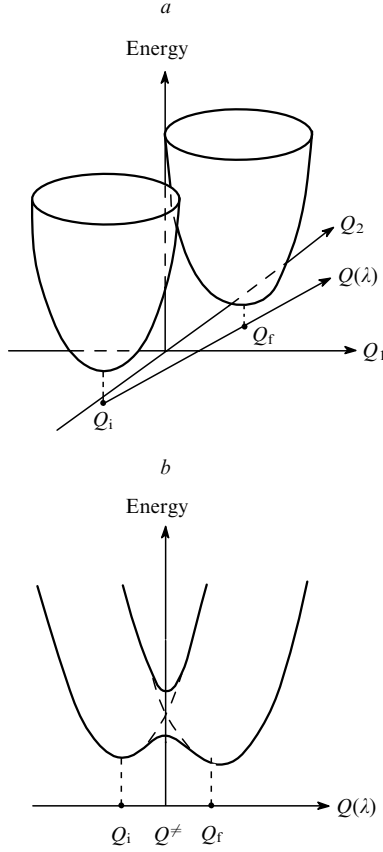


Figure 2. Two-dimensional scheme of the reaction transition between two paraboloids; (a) two-dimensional analogue of the model harmonic PES; the paraboloid minima are located at points Q_i and Q_f ; (b) energy profile of the reactive transition (shown by a dashed line in the intersection area of two parabolic potential curves corresponding to the PES cross-section along the straight line $Q_i Q_f$). The continuous lines show splitting of two energy profiles due to anharmonic interactions.

numbered by using subscripts $v = 1, \dots, N$; for Fig. 2 a, N is equal to 2. Their equilibrium positions for the reactants (subscript i) and products (subscript f) will be denoted by Q_{iv} and Q_{fv} . The description is simplified if the paraboloids are identical, i.e., the reactants and the products are characterised by identical systems of vibration frequencies and forms of normal vibrations (modes).

Let us denote the vectors with the components Q_{iv} and Q_{fv} by (Q_i) and (Q_f) and then form the vector

$$[Q(\lambda)] = (Q_i) + \lambda[(Q_f) - (Q_i)]; 0 \leq \lambda \leq 1, \quad (2)$$

which describes the change of the modes along the straight line connecting the projections (Q_i) and (Q_f) of the minima of the two paraboloids onto the $Q_1 Q_2$ plane (Fig. 2 a). Then the parameter λ can be considered as the ‘reaction coordinate’. If the paraboloids are identical, they intersect along some straight line in the coordinate plane. In this straight line (or in a planar hypersurface if $N > 2$), the PES cross-section passes through a minimum, which is characterised by a set of coordinates: $Q^\# = (Q_1^\#, \dots, Q_N^\#)$, the point $Q^\#$ lies in straight line (2). The cross-section of the PES along the coordinate (2) is shown in Fig. 2 b. At the intersection point of the parabolic potential curves, the reaction coordinate is found as

$$\lambda = \frac{1}{2} \left(1 + \frac{\Delta V}{E_r} \right), \quad (3)$$

where ΔV is the difference between the energies corresponding to the reactant and product minima

$$\Delta V = V_f - V_i, \quad (4)$$

E_r is the reorganisation energy characterising the energy consumption for transition from the reactant minimum to the product minimum; E_r is an additive relative to the contributions of separate modes characterised by masses m_v and frequencies ω_v :

$$E_r = \sum_v E_{rv}, \quad (5)$$

$$E_{rv} = \frac{m_v \omega_v^2}{2} (Q_{fv} - Q_{iv})^2.$$

The height of the potential barrier in this PES obeys the Marcus formula

$$\Delta V^\# = \frac{(E_r + \Delta V)^2}{4E_r}. \quad (6)$$

This PES model underlies most of the theories of multimode processes. Although the model is idealised, it can be useful for a qualitative discussion. Real PES are highly anharmonic,^{22–24} and the contributions of separate modes to the potential barrier cannot be distinguished unambiguously, as would be the case according to relations (5) and (6). There exist semiempirical interpolation-type analytical formulae, which allow one to describe the anharmonic PES and the free energy surface (FES) for PT in terms of a set of characteristic parameters.^{25, 26}

Combination of reorganisation and promoting modes. It is of interest to analyse how the allowance for reorganisation modes modifies the two-mode model described in Section II.1 a.^{27–31} For this purpose, we consider three points, (Q_i) , $(Q^\#)$ and (Q_f) , on the reaction coordinate Q . Even for a symmetrical system ($A_1 = A_2$), by fixing (Q) at the points (Q_i) and (Q_f) , we obtain asymmetrical potential energy profiles along the proton coordinate s (here we do not consider the dependence on R). This is shown schematically in Fig. 3. When $(Q) = (Q^\#)$, the $V(s)$ profile is symmetrical or nearly symmetrical even for the systems with dissimilar heavy fragments A_1 and A_2 . As noted above, in a two-mode double-well symmetrical system, the potential barrier is often relatively low and

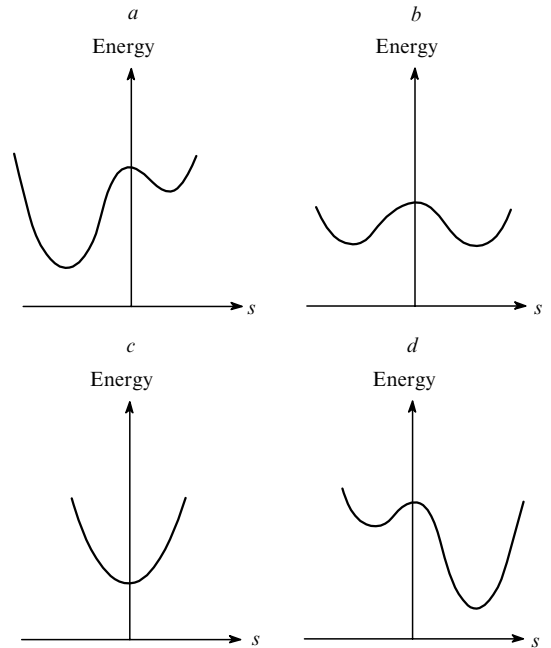


Figure 3. Potential curves of the reaction system along the proton coordinate s with allowance for reorganisation modes; (a, d) reactant and product regions, respectively; (b, c) TS region.

transitions between the wells occur rapidly. The asymmetry brought about by the relaxation of reorganisation modes hinders the transitions and thus contributes to fixing of the reactant and product configurations. In the case of bimolecular gas-phase reactions, this fixing is possible even in a two-mode model due to the spatial separation of the reactants and products along the reaction coordinate R . In the condensed phase, the reactants and products are in relatively close contact [the R_e distance is about the van der Waals distance in complex (1)]. Therefore, stabilisation of the initial and final states owing to relaxation of the environment modes acquires a crucial role.

In view of the foregoing, the following, frequently used classification of inter- and intramolecular degrees of freedom involved in PT processes can be proposed. First, the proton coordinate s is considered, which is called the reaction mode. Second, those modes are considered that do not change (or almost do not change) in the initial and final states but appreciably change in the TS and thus modify the height of the potential barrier. There modes are called promoting. A typical example is the R coordinate; other promoting modes are discussed below. Finally, some modes change their equilibrium positions on passing from the reactant configuration to the product configuration. They are referred to as reorganisation modes.

Naturally, this classification is not universal. However, it often reflects adequately the essential features of the PT process and is widely used in model considerations. Note that the term ‘reaction mode’, introduced above for the coordinate s does not necessarily mean the ‘reaction coordinate’. For real anharmonic PES, the mode s interacts with other reaction modes and, generally, it is not an independent motion in the region of the TS, as it would be the case for a strictly defined reaction coordinate. The mode s may be identified with the reaction coordinate only in terms of the simplest models; this terminology is often encountered in the literature and below it is used in some cases without special reservations.

In reality, the reaction mode for PT and HAT is always a combination of several simple modes. This is illustrated, in particular, by the following examples. According to the data of femtosecond spectroscopy, the rate of PT for the lower singlet electronically excited state of methyl salicylate, 2-(2'-hydroxyphenyl)benzothiazole and 1,8-dihydroxyanthraquinone is 50–60 fs⁻¹ in the gas phase^{32–34} and 170 fs⁻¹ in aprotic solvents.³⁵ The reaction coordinate for the PT includes, as a first approximation, the coordinate of the OH stretching vibrations and the coordinate of the O...H...O out-of-plane vibration.³² The periods of vibration are 13 fs for the OH bond and 190 fs for the O...H...O fragment. These vibration modes interact appreciably with one another, their relative contributions to the reaction mode being dependent on the process conditions. In systems with equivalent initial and final states, PT is manifested as tunnel splitting of the ground vibration state.^{36–38} The tunnel splittings have been measured for not only the ground state but for a number of vibrationally excited states for some systems in the lower singlet electronically excited state.^{39–42} A sharp increase in the tunnel splitting was observed upon selective excitation of particular low-frequency vibrations.^{39, 40} In the case of tropolone, this active vibrational mode was the displacement of heavy atoms of the O...H...O fragment,⁴¹ and in the case of azaindole dimer, an intermolecular stretching vibration.³⁹ Data of *ab initio* calculations of the PES for intra- and intermolecular PT in various systems^{22–24, 43} confirm the experimental results.

2. Dynamics and kinetics

a. Reactions with a low potential barrier

Quantisation of the reaction mode. A key feature of PT reactions is a quantal nature of, at least, one essential mode, namely, the reaction mode s . Let ω_0 be the characteristic frequency of the mode s and $\hbar\omega_0/k_B T \gg 1$. In this case, the traditional description of the kinetics using the classical TS theory is inapplicable. Due to this fact, theoretical description of PT is a difficult task. Never-

theless, the classical approach can be used in the modified form if the height of the barrier $\Delta V^\ddagger$ on the PES is sufficiently low for the reactant well to contain only one quantum level with a frequency close to ω_0 :

$$\frac{\hbar\omega_0}{\Delta V^\ddagger} \lesssim 1. \quad (7)$$

The quantum motion along s occurs much faster than along other modes ($\omega_0 \gg \omega_i$, where ω_i are other eigenfrequencies of the system); this allows one to use the double (along both the electronic and proton coordinates) adiabatic approximation. Different modifications of this model with a classical description of the promoting mode R have been discussed.^{29–31} The Schrödinger equation for the mode s has the form

$$h_s \varphi_n(s) = \varepsilon_n \varphi_n(s), \quad (8)$$

where h_s is a Hamiltonian,

$$h_s = -\frac{\hbar^2}{2m_0} \frac{\partial^2}{\partial s^2} + V(s|R, Q). \quad (9)$$

Here, m_0 is the corresponding mass, and the potential coincides with the full PES $V(s, R, Q)$. The notation of this function in Eqn (9) emphasises that it follows a parametric dependence on the R, Q coordinates of the heavy atoms. The eigenvalues and eigenfunctions in Eqn (8) depend on R and Q . In particular, the energies $\varepsilon_n(R, Q)$ are the PES (electron–proton PES) for the coordinates R, Q . In the adiabatic limit, it is sufficient to consider the ground state ($n = 1$), i.e., the PES $\varepsilon_1(R, Q)$. In many cases, the motion of heavy atoms in such a potential can be regarded to be classical and described using the TS theory in one or another variant.

A similar approximation is widely used in hydrogen bond spectroscopy.^{44, 45} It is called the Born–Oppenheimer separation of motions of light and heavy nuclei⁴⁶ or the adiabatic separation of vibrational variables.⁴⁷ A significant feature of the calculations of the vibrational spectrum of the $A_1-H\cdots A_2$ fragment is the quantum description of the promoting mode R .^{48–53}

Evolution of heavy modes. The specificity of using the double adiabatic approximation lies in the fact that the reaction coordinate s , natural for a chemist, is excluded from dynamic consideration. The role of the reaction coordinate is played by one of the reorganisation modes Q . For example, for low-barrier PT in polar media, the collective variable $Q = y$, describing the behaviour of the medium, is used as the new reaction coordinate. According to this model, the motion along y determines the reaction dynamics and kinetics. In the simplest case, the mode R is excluded from consideration, and the equation of motion reduces to the diffusion equation for the distribution function $n(y, t)$, which determines the probability density for realisation of various y values, depending on time t

$$\frac{\partial n}{\partial t} = D \frac{\partial^2 n}{\partial y^2} - \frac{D}{k_B T} \frac{\partial}{\partial y} \left(n \frac{\partial U_a}{\partial y} \right), \quad (10)$$

where D is the corresponding diffusion coefficient, and the potential profile $U_a(y)$ should be regarded as the cross-section of the electron–proton PES (Fig. 4).[†] The subscript ‘a’ means that the potential is adiabatic, i.e., double-well. (Further, an alternative description using diabatic, single-well potentials is also discussed.) The rate constant for PT can be estimated in terms of the Kramers approximation.^{54, 55}

$$k = A \exp \left(-\frac{\Delta U^\ddagger}{k_B T} \right), \quad (11)$$

[†] From here on, one-dimensional potential profiles present in the diffusion equations are denoted by the letter U .

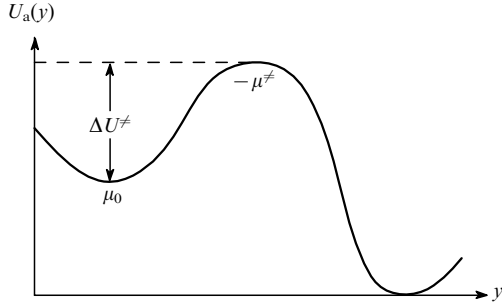


Figure 4. Adiabatic potential profile $U_a(y)$ obtained as a cross-section of the electron-proton PES and used in the Kramers equation.

where

$$A = \frac{(\mu_0 \mu^\#)^{1/2}}{\pi \gamma},$$

$\Delta U^\#$ is the height of the potential barrier on the electron–proton PES, μ_0 and $-\mu^\#$ are the force constants of the potential $U_a(y)$ in the bottom of the reactant well and on the top of the barrier. The friction coefficient γ is related to the diffusion coefficient D by the Einstein relation

$$D = \frac{k_B T}{\gamma}. \quad (12)$$

The Arrhenius dependence (11) with an activation energy equal to the height of the potential barrier is an immutable indication of the classical equilibrium kinetics. In more complex cases, the expression for the pre-exponential factor is modified depending on the particular dynamic model accepted for description of heavy modes instead of the simplest diffusion equation (10). For example, the common one-dimensional Kramers stochastic model proceeds from the Langevin equation

$$m_y \ddot{y} + \gamma \dot{y} + \frac{\partial U_a}{\partial y} = \text{GRF}, \quad (13)$$

where m_y is the mass corresponding to the collective mode of the medium, and GRF stands for the Gaussian random force, which gives rise to fluctuations of the variable y and is responsible for its diffusion motion. If the γ/m_y ratio is not very low, Eqn (13) corresponds to the Arrhenius rate constant (11) with the pre-exponential factor

$$A = \left\{ \left[\left(\frac{\gamma}{2m_y} \right)^2 + (\omega^\#)^2 \right]^{1/2} - \frac{\gamma}{2m_y} \right\} \left(\frac{\mu_0}{\mu^\#} \right)^{1/2}, \quad (14)$$

where $\omega^\#$ is a characteristic frequency on the top of the barrier [that is, $i\omega^\#$ is the decay frequency, $m_y(\omega^\#)^2 = \mu^\#$]. This well-known Kramers formula provides the pre-exponential factor in Eqn (11) if $\gamma/(2m_y\omega^\#) \gg 1$, i.e., in the limiting case of great friction. Further correction of the dynamic description results in a stochastic equation with a time-dependent friction coefficient (generalised Langevin equation). This equation is applicable to multimodal systems. The rate constant is calculated in terms of the Kramers–Grote–Hynes approximation (KGH).^{54–56} This procedure is briefly described in Supplement I. The standard multidimensional TS theory can also be used; with allowance made consistently for the medium modes, it is equivalent to the KGH theory.^{54–60} Finally, direct calculation of the reaction rate constant by classical molecular dynamics (MD) is also possible,^{61,62} for example, by the reaction flux method.⁵⁵

Electron–proton PES.^{63–65} A typical electron–proton PES depending on two heavy coordinates, the medium coordinate y and the promoting mode R , is shown in Fig. 5. The direction of the reaction coordinate at the saddle point coincides with the direction of the mode y . The rate constant can be estimated within the framework of the multi-dimensional KGH theory. Estimation of

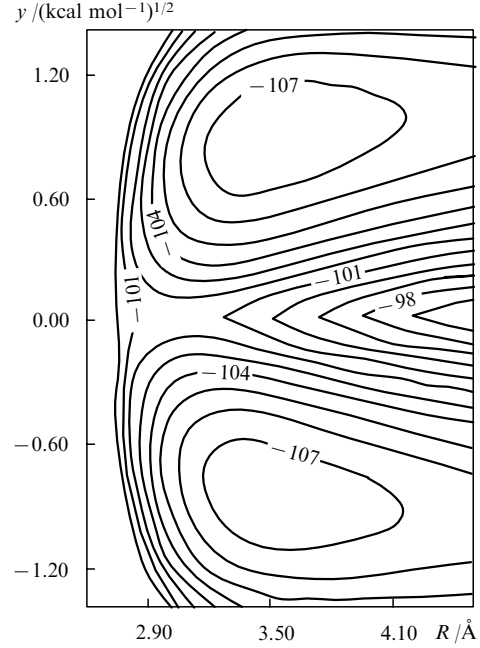


Figure 5. Electron-proton PES $\varepsilon_1(y, R)$ for the ground state of the reaction system $\text{ACH}_3 + ^-\text{CH}_2\text{A} \rightarrow \text{ACH}_2^- + \text{CH}_3\text{A}$; $\text{A} = \text{C}_6\text{H}_5$.⁶⁴ Isoenergy contour lines are spaced by 1 kcal mol^{−1}. The reactant and product minima correspond to the energy −107.3 kcal mol^{−1}.

the rate constant in terms of the stochastic (or the equivalent diffusion) theory requires the knowledge of dynamic characteristics of the solvent collective mode y such as the mass m_y , the friction or diffusion coefficient, *etc.* They can be found using semiempirical continuum models of the solvent.^{65–69} The most consistent and direct way of calculating these values is based on MD.^{61–63}

To conclude, note that the classical description of the promoting mode R accepted in the multidimensional TS theory, KGH theory and classical MD calculations is an approximation which often does not correspond to the real situation.^{70–77} The quantum treatment of R is discussed in Section II.4.c.

b. Proton tunnelling as a non-adiabatic transition

Adiabatic and non-adiabatic models of reaction transitions. Section II.2.a considered the adiabatic PT model. In this context, the term ‘adiabatic’ means that a double-well potential V appears in the Schrödinger equation (8). It corresponds to the lower electronic adiabatic PES; in more detailed notation,

$$V = V_{a1}(s, R, Q).$$

The next PES $V_{a2}(s, R, Q)$ corresponds to the first electronically excited state of the system. This is a single-well surface, its minimum being close to the top of the barrier of the lower PES, which corresponds to the ground state. The profiles of these two adiabatic PES are shown in Fig. 2 b by continuous lines.

In an alternative description, the potentials V_{a1} and V_{a2} are considered as combinations of the potentials V_{d1} and V_{d2} , corresponding to single-well surfaces, which are called ‘diabatic’. The theory of this transformation was outlined in several publications.^{78–81} The diabatic and adiabatic PES are sketched in Fig. 2 b. They almost coincide near the minima. The error of the diabatic description is the highest near the TS, i.e., near the barrier top of the lower adiabatic surface or, what is the same, around the intersection of the diabatic surfaces (shown by dashed lines).

Equations (8) and (9) describe the transition from the electronic PES $V_{a1}(s, R, Q)$ to the electron–proton PES $\varepsilon_1(R, Q)$. In the same way, by substituting $V_{a2}(s, R, Q)$ into Hamiltonian (9), one can obtain the electron–proton PES $\varepsilon_2(R, Q)$ for the electron–

proton excited state. Like the initial electronic PES, ε_1 has two wells, while ε_2 has one well. These surfaces are adiabatic, and they can be transformed into two single-well diabatic electron – proton PES, which we designated by $e_1(R, Q)$ and $e_2(R, Q)$. By substituting diabatic electronic potentials, instead of V , into Hamiltonian (9), we obtain two diabatic Schrödinger equations similar to Eqn (8). The surfaces e_1 and e_2 correspond to their eigenvalues. The corresponding eigenfunctions, which we designate by $\chi_1(s)$ and $\chi_2(s)$, are referred to as diabatic states. Unlike adiabatic states $\varphi_n(s)$ ($n = 1, 2$) in Eqn (8), these are always localised in their diabatic potential wells. The difference between the lower adiabatic potential and the combination of low-energy fragments of diabatic potentials (which is substantial near the TS) is considered to be responsible for the transitions between the diabatic states χ_1 and χ_2 . These transitions, called non-adiabatic, are identified with a PT or HAT process. For reactions with high barriers, splitting of

the adiabatic potentials is extremely small (Fig. 6) and the intensity of the transitions is very low.

Two-level kinetic equation. The scenario of a PT reaction described in Section II.2.a corresponds to the situation shown in Fig. 6a. For a low-barrier potential V_{a1} , the lower adiabatic level ε_1 is located near the top of the barrier and the next adiabatic level ε_2 is located much higher [$\Delta > 1000 \text{ cm}^{-1}$ (see Ref. 82)], therefore, its population is negligibly low. In this case, it is sufficient to consider the PES $\varepsilon_1(R, Q)$.

The alternative situation shown in Fig. 6b with a high barrier and a clearly defined double-well-potential relief requires a different description. Despite the fact that the proton motion in the wells remains fast, the probability of the inter-well tunnelling transition P_{12} is low: $P_{12} \ll 1$. If it is low enough, the transition between the diabatic states $\chi_1(s)$ and $\chi_2(s)$ becomes the rate-determining step of the process. In the two-level approximation, the localised diabatic wave functions $\chi_1(s)$ and $\chi_2(s)$ are linear combinations of the adiabatic functions φ_1, φ_2 . The variable s becomes the reaction coordinate, although of the quantum type. It is represented by two diabatic states with the PES $e_1(R, y)$ and $e_2(R, y)$ (we have replaced Q by y) and their cross-sections $U_{d1}(y)$ and $U_{d2}(y)$.

The limiting cases illustrated in Fig. 6 correspond to two limiting mechanisms of PT, namely, the classical motion of heavy atoms over the adiabatic surface $\varepsilon_1(R, y)$ with the cross-section $U_{a1}(y)$ and a quantum non-adiabatic transition between the PES $e_1(R, y)$ and $e_2(R, y)$ with the cross-sections $U_{d1}(y)$ and $U_{d2}(y)$. Now we consider the competition between these reaction mechanisms at a qualitative level using a simple one-dimensional model ($Q = y$ is the medium coordinate, and promoting mode R is excluded from consideration). The equations of motion for the populations $n_1(y, t)$ and $n_2(y, t)$ of the diabatic states have the form

$$\frac{\partial n_1}{\partial t} = D \left[\frac{\partial^2 n_1}{\partial y^2} - \frac{1}{k_B T} \frac{\partial}{\partial y} \left(n_1 \frac{\partial U_{d1}}{\partial y} \right) \right] + \langle \omega \rangle (n_2 - n_1), \quad (15)$$

$$\frac{\partial n_2}{\partial t} = D \left[\frac{\partial^2 n_2}{\partial y^2} - \frac{1}{k_B T} \frac{\partial}{\partial y} \left(n_2 \frac{\partial U_{d2}}{\partial y} \right) \right] + \langle \omega \rangle (n_1 - n_2),$$

where $\langle \omega \rangle$ is the average frequency of interlevel transitions. In the standard theory of non-adiabatic transitions with a linear approximation of the diabatic energy levels (terms) in the region of their intersection (see Fig. 6b), it is usually assumed that^{83–87}

$$\langle \omega \rangle = \frac{2\pi V_{12}^2}{\hbar |\Delta F|} \delta(y - y_0), \quad (16)$$

where V_{12} is the matrix element of the interaction between terms; $\Delta F = F_2 - F_1$, where $F_n = -\partial U_{dn}/\partial y$, ($n = 1, 2$) are forces acting on the system at the intersection point $y = y_0$; $\delta(y - y_0)$ designates the Dirac δ -function.

According to this (local) transition model, the expression for the probability of transition between the terms is formally similar to the Landau–Zener approximation⁸⁸

$$P_{12} = \frac{2\pi V_{12}^2}{\hbar |\Delta F| \dot{y}}. \quad (17)$$

The value

$$j_{\text{na}} = \frac{2\pi V_{12}^2}{\hbar |\Delta F|} \exp\left(-\frac{U_c - U_e}{k_B T}\right) = |y| P_{12} \exp\left(-\frac{U_c - U_e}{k_B T}\right) \quad (18)$$

is a non-adiabatic diffusion flux at the point y_0 ,⁸⁹ $U_c = U_{d1}(y_0) = U_{d2}(y_0)$, and U_e is the energy in the reactant minimum.

Turning back to the adiabatic description in terms of the diffusion equation (10), we can express an analogous adiabatic flux near the top of the barrier of the lower PES U_{a1} (see Fig. 4). For the case where the barrier $\Delta U^\ddagger$ on the initial electronic PES is

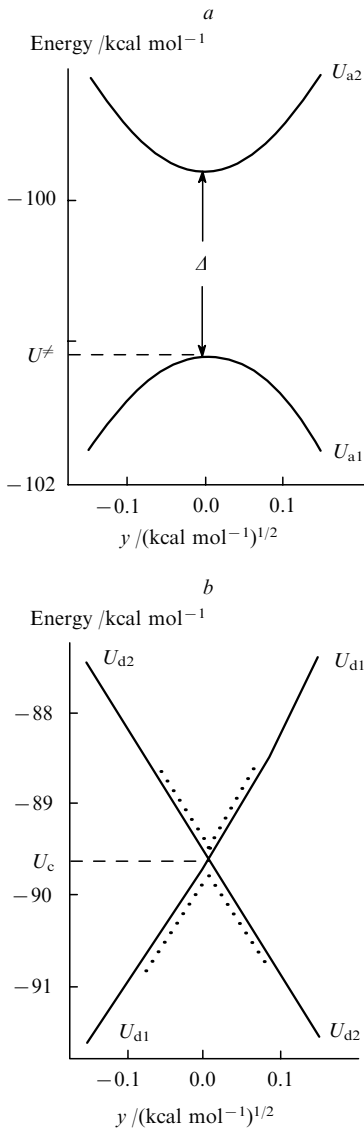


Figure 6. Double-well potential profiles for the two limiting mechanisms of PT and HAT reactions; only the TS region is given; (a) adiabatic energy profiles for a low-barrier reaction, see Fig. 5 ($A = \text{C}_6\text{H}_5$); $U^\ddagger$ is the saddle-point energy for the ground state of the reaction system, Δ is the splitting of PES in the saddle point; (b) diabatic energy profiles for a high-barrier reaction, $A = \text{C}_{13}\text{H}_9$ (fluorenyl);⁶⁵ U_c is the level intersection point; the abscissa y_0 of this point is taken to have the coordinate 0.0. The lower and upper broken lines consisting of two diabatic ‘rays’ can be regarded as two adiabatic potential profiles (shown by dots). The splitting of PES is very small; therefore, $U_c = U^\ddagger$.

high and the splitting Δ is small (see Fig. 6b), this potential profile corresponds to a triangular potential barrier (shown by dots). For such PES, the adiabatic flux equals⁸⁹

$$j_a = \frac{D}{k_B T} \frac{|F_1||F_2|}{|F_1| + |F_2|} \exp\left(-\frac{U_c - U_e}{k_B T}\right). \quad (19)$$

A different adiabatic flux corresponds to Kramers' result (11), (14). The difference is due to the fact that the potential shown by dots in Fig 6b has a singularity (cusp) on the top and the potential in Fig. 4 is smooth. Fluxes (18) and (19) are found by solution of diffusion equation (15) in the limiting cases of weak and strong coupling between the levels. In the intermediate kinetic regime, the flux j can be expressed as the ratio of the non-adiabatic to adiabatic fluxes⁸⁹

$$j = \frac{j_{na}}{(1 + j_{na}/j_a)}. \quad (20)$$

The corresponding rate constant is found from Eqn (20) by division by the partition function of the reaction system calculated within the reactant well.

The ratio j_{na}/j_a can be estimated by taking into account the fact that, within the model of non-adiabatic transition with linear intersecting diabatic energy levels,^{65, 79–81}

$$V_{12} = \frac{1}{2} \Delta; \quad (21)$$

$$|\Delta F| = |J| \Delta.$$

Here Δ and J are characteristics of adiabatic levels:

$$\Delta = \varepsilon_2(y_0) - \varepsilon_1(y_0),$$

$$J = \left\langle \varphi_2 \left| \frac{\partial}{\partial R} \right| \varphi_1 \right\rangle_{y_0} = \Delta^{-1} \left\langle \varphi_2 \left| \frac{\partial \varepsilon_1}{\partial y} \right| \varphi_1 \right\rangle_{y_0}, \quad (22)$$

i.e., Δ is the minimum splitting of the adiabatic levels and J is the measure of their interaction calculated for $y = y_0$. If the signs of the forces F_1 and F_2 are opposite, then

$$|\Delta F| = |F_2| + |F_1|.$$

Thus,

$$\frac{j_{na}}{j_a} = \frac{2\pi}{\hbar} \frac{\Delta^2}{|F_1||F_2|} \frac{k_B T}{4D} \simeq \frac{2\pi}{\hbar} \frac{k_B T}{DJ^2}. \quad (23)$$

The above approximate equality corresponds to the symmetrical case

$$|F_1| = |F_2| = \frac{1}{2} |F_1 - F_2|.$$

Competition between adiabatic and non-adiabatic mechanisms of proton transfer. It follows from Eqns (20)–(23) than the non-adiabatic kinetic mechanism of PT takes place when the splitting of the adiabatic levels is small (in this case, $U_c = U_e$). Small Δ values are typical of double-well potential profiles of the ground electronic state with a sharp relief. They give rise to electron–proton profiles with a cusp at the intersection (see Fig. 6b). For these electronic PES, tunnelling is observed, the model of non-adiabatic transitions on the electron–proton PES being a way of describing the tunnelling phenomenon. Equation (23) expresses the relative intensities of the tunnelling (non-adiabatic flux j_{na}) and activation (adiabatic flux j_a) mechanisms of proton transition. According to (23), they depend on the temperature. At the critical temperature $T = T_c$ where $j_{na}/j_a = 1$, the reaction mechanism switches. Thus, the flux ratio (23) is the key control parameter of the simplest expression for the rate constant taking into account both PT mechanisms.⁸⁷

The inclusion of the promoting mode R substantially complicates the PT description. In this case, the cross-section profile of the reaction PES depends on R (see Fig. 1a): the barrier is relatively low in the TS region ($R = R^\ddagger$); when $R \gg R^\ddagger$, the product and reactant wells become deeper, which disturbs the adiabaticity criterion (7). Hence, according to criterion (23), the transition is either adiabatic (activated, $j_{na}/j_a \gg 1$) or non-adiabatic (tunnelling, $j_{na}/j_a \ll 1$), depending on R and the temperature. In many cases, both mechanisms occur simultaneously on the same PES.⁹⁰ If the equilibrium position R_e is close to $R^\ddagger$ and (or) the temperature is relatively high, the reaction dynamics will mainly be classical. In the case of a sharp relief of the PES cross-section along the coordinate s and (or) low temperature, the reaction mainly follows the tunnelling mechanism.

3. The principles of description of the tunnelling kinetics

a. One-dimensional and quasi-one-dimensional tunnelling

Bimolecular rate constant. The character of tunnelling transitions is substantially different for the three different types of PES cross-sections $V(s)$ (Fig. 7). In the one-dimensional model of the bimolecular reaction, the states in the reactant and product regions belong to a continuum spectrum (Fig. 7a). In a quasi-classical approximation, the rate constant for this reaction is as follows:^{55, 91–94}

$$k(T) = \frac{1}{2\pi\hbar Z(T)} \int_0^\infty \exp\left(-\frac{E}{k_B T}\right) P(E) dE, \quad (24)$$

where E is the energy referred to the threshold (a minimum in the reactant region) and $P(E)$ is the quasi-classical coefficient for barrier penetration

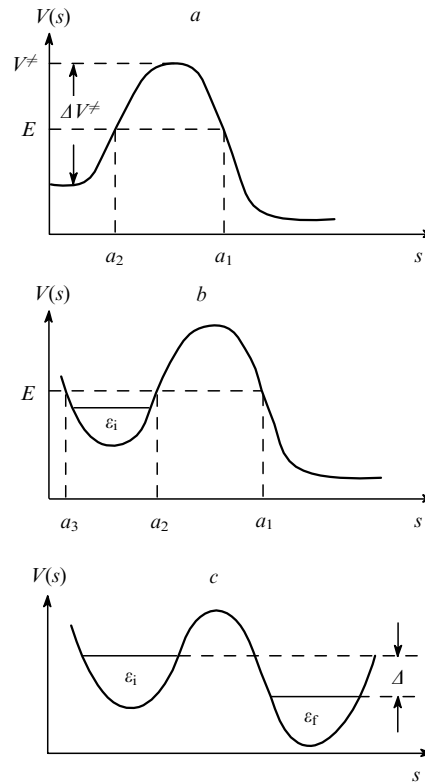


Figure 7. Three different types (a–c) of PES cross-sections $V(s)$ for the one-dimensional reaction scheme.

The turning points a_2, a_1 bound the classically inaccessible region, while points a_3, a_2 confine the classically accessible region; ε_i is the reactant energy level, ε_f is the product energy level, Δ is the resonance misfit.

$$P(E) = \frac{1}{1 + \exp[2W(E)]}, \quad (25)$$

$$W(E) = \frac{1}{\hbar} \int_{a_2}^{a_1} \{2m_0[V(s) - E]\}^{1/2} ds.$$

The turning points a_1 , a_2 depend on the energy E and confine the under-barrier area inaccessible for classical motion. In this case, the partition function $Z(T)$ corresponds to one-dimensional translational motion; as a result, the bimolecular rate constant has the dimensionality $(\text{time})^{-1}(\text{length})^{-1}$. In the classical limit, $P(E)$ is replaced by a stepwise function

$$P(E) = \begin{cases} 0, & (E < \Delta V^\ddagger) \\ 1, & (E > \Delta V^\ddagger), \end{cases} \quad (26)$$

where $V^\ddagger$ is the height of the potential barrier. In this case, relation (24) provides the standard result of the one-dimensional classical transition state theory, TST.

$$k_{\text{TST}}(T) = \frac{1}{2\pi\hbar Z(T)} \exp\left(-\frac{\Delta V^\ddagger}{k_B T}\right). \quad (27)$$

Relations (24)–(27) can be recommended for application to real three-dimensional PT processes if a ‘one-dimensional’ transmission coefficient

$$\kappa = \frac{k(T)}{k_{\text{TST}}(T)} \quad (28)$$

is introduced and used as a correction factor, *i.e.*, the rate constant for a real three-dimensional reaction obtained by the standard TS method is multiplied by this factor.

Decay kinetics of single-well systems. In the decomposition reaction with a potential profile shown in Fig 7b, the states of reactants are quantised, while those in the product region belong to a continuum spectrum. By designating the energies of the reactant level by ε_v and the partial decay rates by $(1/\hbar)\Gamma_v$ (Γ_v is the width of the level), we obtain the rate constant

$$k(T) = \sum_v \frac{\exp(-\varepsilon_v/k_B T)}{Z(T)} \frac{\Gamma(\varepsilon_v)}{\hbar}. \quad (29)$$

In the quasi-classical approximation,⁹⁵

$$\Gamma(E) = \frac{\hbar\omega(E)}{2\pi} \exp[-2W(E)], \quad (30)$$

where the under-barrier action integral $W(E)$ is defined in the same way as in Eqn (25); however, now $V(s)$ has the form shown in Fig. 7b. The decay frequency $\omega(E)$ is expressed in terms of the action integral $\theta(E)$, which is calculated in the region of classical motion confined by the turning points a_3 and a_2 ,

$$\theta(E) = \frac{1}{\hbar} \int_{a_3}^{a_2} ds [2m_0(E - V(s))]^{1/2}; \quad (31)$$

$$\omega(E) = \frac{\pi}{\hbar(\partial\theta/\partial E)}.$$

When the interaction of the coordinate s with the environment modes is taken into account, these relations are modified in the following way. The interaction makes the levels ε_v diffuse; in this case, it is expedient to introduce the distribution function $\rho_v(E)$ for a level v

$$\int_0^\infty \rho_v(E) dE = 1, \quad (32)$$

and the density of states

$$\rho(E) = \sum_v \rho_v(E). \quad (33)$$

The $N(E)$ value, called the ‘cumulative transition probability’,^{92–94} is defined as follows:

$$N(E) = 2\pi\rho(E)\Gamma(E). \quad (34)$$

Then the expression for rate constant (29) is reduced to the form

$$k(T) = \frac{1}{2\pi\hbar Z(T)} \int_0^\infty \exp\left(-\frac{E}{k_B T}\right) N(E) dE. \quad (35)$$

This expression formally coincides with expression (24) for the rate constant of the bimolecular reaction, the difference being in the interpretation of the partition function. The $Z(T)$ value now includes the states located in the reactant well; taking account of the level broadening due to interaction, it is found as

$$Z(T) = \int_0^\infty \exp\left(-\frac{E}{k_B T}\right) \rho(E) dE. \quad (36)$$

The quasi-classical expression for the cumulative probability (34) is similar to expression (25)^{55, 92–94}

$$N(E) = \frac{1}{1 + \exp[2W(E)]} \quad (37)$$

with an action integral defined in the under-barrier region (see Fig. 7b). This description of decay processes is almost identical to the quasi-one-dimensional theory of bimolecular reactions. However, a consistent definition of the decay model should take into account the interaction of the reaction centre with its environment not only in the reactant region but also for tunnelling under the barrier.^{55, 96} The calculation of the action integral is modified by introduction of a non-local potential brought about by the interaction. The corresponding theory^{55, 96–98} is a quantum generalisation of the classical stochastic scheme based on the Langevin equation (13) for the tunnelling coordinate s . The friction coefficient γ is a parameter of the interaction intensity; it is present in the final quantum expression for the rate constant.

The activation and tunnelling mechanisms. The classical and quantum dynamic effects are manifested in the chemical reaction kinetics as a competition between the activation (classical) and tunnelling (quantum) mechanisms of the reactive transition. This was described above within the framework of a non-adiabatic diffusion model. Now it will be considered using an alternative tunnelling dynamics language.

As in the previous case, in the simplest one-dimensional scheme, there exists a critical temperature T_c (see several studies^{55, 97–99}) such that the activation mechanism with the Arrhenius temperature dependence of the rate constant predominates above this temperature. At temperatures below T_c , the reaction mainly follows a tunnelling mechanism and in the limit $T/T_c \ll 1$, the reaction rate does not depend on the temperature. This low-temperature limit differs from zero when the reactant region is a potential well; it corresponds to transition from the ground vibrational level of the reactants. Systematic analysis of the ratio of the tunnelling and activated transitions is reduced to investigation of the integral over energy in Eqns (24) and (35). The theory can be reformulated using the language of classical dynamics, which describes the motion in the ‘inverted’ potential $\bar{V}(s)$ [$\bar{V}(s) = -V(s)$] for the total energy E .^{55, 97} In this potential, a cyclic classical trajectory with the period $\iota(E)$ is formed. The energy corresponding to the highest contribution of the integrand to integral (35) satisfies the equation

$$t(E) = \frac{\hbar}{k_B T}. \quad (38)$$

Its solution determines the energy corresponding to the cyclic trajectory as a function of temperature. This consideration underlies the calculation of integral (35) by the stationary phase method.^{97, 100, 101} The temperature-dependent extremal trajectory that satisfies condition (38) is called instanton. There exists a critical temperature above which Eqn (38) has no solution. It can be identified with the above-mentioned T_c value. Then the maximum contribution to the integral is determined by the energy near the top of the barrier, and formula (35) reduces to the result of the TS theory with slight quantum corrections. In the stochastic tunnelling model, which takes into account the interaction with the environment based on the Langevin equation, the Kramers equation for the rate constant, similar to relation (11) but with allowance for (14), is obtained in the classical limit.^{102–104} Thus, the relationship between two theories, the non-adiabatic and the tunnelling, is established; the tunnelling probability is determined in the latter case by the value of action on the instanton trajectory. The simplest equation for the critical temperature obtained for a parabolic barrier $V(s)$ with the decay frequency $\omega^\ddagger$ has the form^{99, 105}

$$T_c = \frac{\hbar \omega^\ddagger}{2\pi k_B}. \quad (39)$$

Tunnelling in a double-well potential. The calculation of tunnelling is complicated on passing to a double-well potential where it is necessary to take account of the quantisation of energy levels in both wells. Transitions between two levels take place only in the presence of interaction between the coordinate s and other degrees of freedom. Even where the levels are in resonance, *i.e.*, very close or coinciding, as in symmetrical systems, the interaction with the environment is required to ensure energy dissipation and destruction of the transition coherence, which are necessary conditions for irreversibility. Only due to these factors, can the system be fixed in the product region and a stationary flux for the two wells can be formed. In asymmetric systems, the interaction with the environment is also necessary in order to compensate for the resonance misfit (*i.e.*, the energy difference between the levels between which the transition takes place) by means of the intermode energy exchange.

Thus, double-well transitions are, in essence, multidimensional even in the case where the PES structure seems to allow the reaction mode to be considered as an independent variable. The intermode interactions, which ensure the energy exchange and phase relaxation (the latter term is equivalent to the term ‘coherence destruction’), can be small within the scale of the energy variation on the PES, but only consistent allowance for these interactions provides the possibility of correct description of the tunnelling dynamics.

b. Collinear model of simple gas-phase reactions

Quantum computation scheme. Let us consider a two-dimensional quantum problem for collinear model (1) of a PT with two coordinates s, R and the corresponding reduced masses m_0 and M . After conversion to a mass-weighted coordinates $s' = s(m_0)^{1/2}$ and $R' = R(M)^{1/2}$, it is expedient to introduce polar coordinates

$$y = [(s')^2 + (R')^2]^{1/2}, \quad (40)$$

$$\alpha = \arctan \frac{s'}{R'}.$$

The potential energy surface in these coordinates is shown in Fig. 8. The two valleys stretched along y correspond to the translational motion in the asymptotic regions, as we consider a gas-phase bimolecular reaction. This PES is confined within the angle

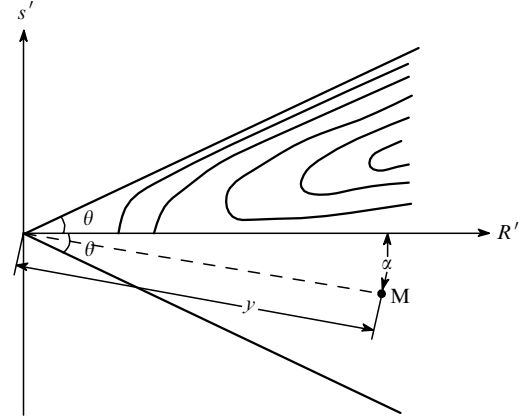


Figure 8. Potential energy surface of the gas-phase PT and HAT reaction in the polar coordinates.

The isoenergy contour lines of PES are shown only for the product valley ($\alpha > 0$). The potential energy in the reactant valley ($\alpha < 0$) has the same form. The point M has the polar coordinates y, α .

$$2\theta = \arctan \left(m_H \frac{m_{A_1} + m_{A_2} + m_H}{m_{A_1} m_{A_2}} \right)^{1/2}, \quad (41)$$

where m_H, m_{A_1}, m_{A_2} are the masses of the H atom and the heavy fragments A_1 and A_2 , respectively. The reduced masses m_0 and M are related to these masses in the usual way. The Hamiltonian for this problem has the form

$$H = -\frac{\hbar^2}{2} \left(\frac{\partial^2}{\partial y^2} + \frac{1}{y} \frac{\partial}{\partial y} \right) + h_\alpha, \quad (42)$$

$$h_\alpha = -\frac{\hbar^2}{2y^2} \frac{\partial^2}{\partial \alpha^2} + V(\alpha|y),$$

where the operator h_α depends parametrically on y . When y is constant, variation of the mode α is described by the Schrödinger equation

$$h_\alpha \varphi_n(\alpha|y) = \varepsilon_n(y) \varphi_n(\alpha|y). \quad (43)$$

Equations (42) and (43) are similar to Eqns (8), (9) for the coordinate s and are converted into the latter (to within a mass factor) after the substitution

$$s = y\alpha. \quad (44)$$

As a result of the coordinate scaling performed, the major dynamic feature of PT reactions, *i.e.*, the fact that the ratios

$$\frac{m_H}{m_{A_1}} \ll 1, \quad \frac{m_H}{m_{A_2}} \ll 1$$

are small, is manifested in the PES relief, in particular, the angle θ becomes a small parameter in this description

$$\theta \ll 1. \quad (45)$$

It can be seen in Fig. 8 that in this case, the reactant and product valleys are nearly parallel, the barrier separating them being narrow. This accounts for the specific features of process dynamics (1), the possibility of tunnelling along the variable α being the most important of them.

In numerical dynamic studies of system (1), the solutions $\varphi_n(\alpha)$ of Eqn (43) are used as the basis functions. The two-dimensional Schrödinger equation (43) is reduced to a set of one-dimensional coupled equations for the motion along the translational coordinate y . The solution of this set of equations provides the probabilities $P_{mn}(E)$ of reactive transitions from the reactant valley to the product valley and the probabilities $R_{mn}(E)$ of reflection in the reactant valley. The transition takes place between the states φ_m and φ_n at a given total energy E . The

procedure of such calculations has been well developed^{106, 107} and extended to the description of reaction in a real 3D space, which takes into account the interaction of the internal degrees of freedom with the rotational motion.¹⁰⁸ The results of numerical studies are reported in several reviews.^{109–112} The potential in Eqn (43) has a complex form. Depending on y , it can be either double-well (large y) or single-well (small y). For non-symmetric reactions, the potential is asymmetric. It should be emphasized that the use of eigenfunctions of the Hamiltonian h_x with this complex potential as the basis functions has a crucial impact on the success of calculations.^{106, 107} The convergence of the solution of Eqn (43) with oscillatory basis functions proved to be unsatisfactory.

The results of calculations showed that the reactions in symmetrical systems are adiabatic, *i.e.*,

$$\frac{P_{mn}(E)}{[P_{mm}(E)P_{nn}(E)]^{1/2}} \ll 1. \quad (46)$$

In the case of asymmetric reactions, transitions between the vibrational levels of the reactants ε_{im} and the products ε_{fn} characterised by the smallest in magnitude resonance misfits

$$\Delta_{mn} = \varepsilon_{fn} - \varepsilon_{im}$$

sharply predominate. This is a natural consequence of inequality (45). The small parameter θ is a measure of dynamic interaction between the coordinates α and y . Since the interaction is weak, transformation of the resonance defect energy into the energy of translational motion is unlikely and resonance or nearly resonance processes predominate.

Study of the collinear dynamics at a qualitative level. When analysing studies of the collinear dynamics at a qualitative level, we restrict ourselves to the discussion of HAT reactions that have rather high potential barriers ($V \geq 10$ kcal mol⁻¹) and can be expected to proceed in the tunnelling regime even at high temperature ($T \geq 300$ K). The early studies of these systems^{113, 114} were performed using a multi-dimensional quasi-classical approximation,^{115, 116} whose one-dimensional version is considered in Section II.3.a. Extension to multidimensional (two-dimensional, for a collinear reaction) case brings about a procedural difficulty: it is necessary to match the trajectories of a multidimensional classical motion at the boundary of classically allowed (reactant and product valleys) and classically forbidden (under-barrier region) PES sections. A rigorous solution of this problem is extremely unwieldy. It is more convenient to proceed directly from quantum equations of motion which do not face the matching problem.

The quantum interpretation becomes simple for those regions of PES where the cross-sections along the coordinate α have a rather sharp double-well profile. This is not the case in the vicinity of the saddle point, which imposes restrictions on the conditions under which the HAT process can be calculated; it is assumed to proceed in the tunnelling regime, the classical activated transitions being suppressed. In this situation, there exist diabatic states well localised in the reactant $\chi_{im}(\alpha)$ and product $\chi_{fn}(\alpha)$ regions. They can be regarded as eigenfunctions of two different one-dimensional Hamiltonians h_i and h_f :

$$h_i \chi_{im}(\alpha) = e_{im} \chi_{im}(\alpha), \quad (47)$$

$$h_f \chi_{fn}(\alpha) = e_{fn} \chi_{fn}(\alpha).$$

Single-well potentials in the Hamiltonians h_i and h_f are distorted with respect to the true double-well profile $V(\alpha|y)$ [see Eqn (42)] in such a way as to ensure localisation of eigenfunctions. In Fig. 9a, the continuous line shows the double-well adiabatic profile $V(\alpha)$ for a given value y . The diabatic potentials coincide with it in the region of one of the wells and are continued by dots to the region of the neighbouring well. As noted above, it is legitimate for considering the transitions between two diabatic states closest in energy. Let energies of these states be e_{im} and e_{fn} . This corresponds to the two-level model in which the designations can be simplified: $\chi_{im} \rightarrow \chi_i$, $e_{im} \rightarrow e_i$, $\chi_{fn} \rightarrow \chi_f$, $e_{fn} \rightarrow e_f$. The solu-

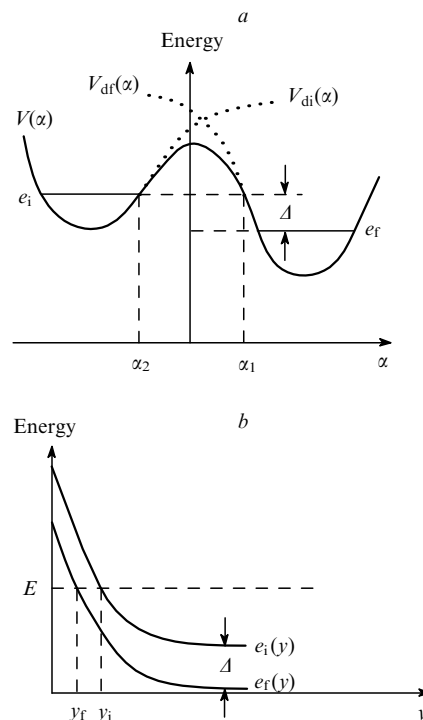


Figure 9. Model of a two-dimensional tunnelling transition for the PES shown in Fig. 8 (asymmetric case); (a) adiabatic [$V(\alpha)$] and diabatic [$V_{di}(\alpha)$ and $V_{df}(\alpha)$] energy profiles along the coordinate α ; (b) pattern of the translational motion along the coordinate y in the reactant and product valleys. The difference in the diabatic potentials $e_i(y) - e_f(y) = \Delta$ is constant. The turning points y_i , y_f correspond to the energy E .

tions of the complete Schrödinger equation (43) designated by φ_n are adiabatic states; in the two-level model, they are linear combinations of two functions, χ_i and χ_f . For symmetrical systems, $e_i = e_f = e$ and adiabatic functions possess definite symmetry properties, one of them being symmetric and the other, antisymmetric

$$\varphi_s(\alpha) = \frac{1}{[2(1 + \sigma)]^{1/2}} [\chi_i(\alpha) + \chi_f(\alpha)], \quad (48)$$

$$\varphi_a(\alpha) = \frac{1}{[2(1 - \sigma)]^{1/2}} [\chi_i(\alpha) - \chi_f(\alpha)],$$

where σ is the overlap integral of diabatic functions.

When the potential $V(\alpha, y)$ is substantially asymmetric, one of the adiabatic functions is mainly composed of function χ_i with a small portion of function χ_f , while the other, mainly of the function χ_f . Then the adiabatic states are labelled by the same subscripts i and f . In the tunnelling regime, the adiabatic energy levels ε_i , ε_f differ little from the diabatic energies e_i , e_f . In this case, the resonance misfit

$$\Delta_{if} = \varepsilon_f - \varepsilon_i \approx e_f - e_i \quad (49)$$

becomes an important dynamic parameter.

Within the framework of the model with two coordinates α and y , the potential profiles shown in Fig. 9a depend on y . Diabatic levels become the functions of y and their energies play the role of repulsive potentials $e_i(y)$ and $e_f(y)$ in the reactant and product channels, as shown in Fig. 9b. More complex potential profiles along y (with a well near the saddle point) can arise in special cases;^{106, 107, 117} however, for reactions with high potential barriers considered here, these situations are unlikely. Each vibrational state of the reaction system or ‘reaction channel’ (i and f , or s and a for a symmetrical reaction) is matched by its own potential.

Due to the small magnitude of the θ parameter [see inequality (45)], the interaction of a given pair of closest channels with other channels is negligibly small. This simplification has been suggested by the experience of full multichannel computations. In an approximation that takes into account only transitions between two reactant and product channels closest in energy, we will consider analytical expressions for the probability of reactive transitions for different limiting situations.

In the case of a symmetrical system, channels s and a also split. By solving a one-dimensional Schrödinger equation for the coordinate y for each of them, one can get the following expression for the probability of the reaction transition between the diabatic states i and f :¹¹⁸

$$P_{if}(E) = \sin^2(\xi_s - \xi_a), \quad (50)$$

where ξ_s and ξ_a are the shifts of scattering phases in the channels s and a . Quasi-classical estimate gives

$$\sin(\xi_s - \xi_a) \approx \xi_s - \xi_a \approx \frac{2}{\pi} \int_{y_0}^{\infty} \frac{e_i(y)}{p_i(y)} \exp[-W_i(y)] dy. \quad (51)$$

Here

$$e_i(y) = e_f(y),$$

$p_i(y)$ is the momentum for the translational motion along the coordinate y

$$p_i(y) = \{2[E - e_i(y)]\}^{1/2},$$

$W_i(y)$ is the under-barrier action integral calculated between the turning points α_2 and α_1 [the symmetrical variant is considered (see Fig. 9 a)].

Expression (51) can be simplified by expanding in a series near the $y_0(E)$ turning point in which $p_i(y) = 0$ (see Fig. 9 b).^{113, 114, 119–121}

In the case of an asymmetric potential profile, the transition probabilities $P_{if}(E)$ can be estimated only in terms of the perturbation theory ('golden rule'), whose applicability is ensured by low values of these probabilities ($P_{if} \ll 1$) and, finally, by the smallness of the PES parameter θ . It is convenient to accept an exponential form of diabatic repulsive potentials in channels i and f (see Fig. 9 b):

$$\begin{aligned} e_i(y) &= e_0 \exp(-cy), \\ e_f(y) &= e_0 \exp(-cy) + A, \end{aligned} \quad (52)$$

where c is the potential parameter, $A = A_{if}$ is the resonance misfit [see Eqn (49)].

For energy E , the potentials have turning points $y_i(E)$ and $y_f(E)$. When the resonance misfit $|A|$ is small, the following expression was obtained:^{119–121}

$$P_{if}(E) = P_{sif}(E) \exp\left(-\frac{A^2}{2cF}\right), \quad (53)$$

where $P_{sif}(E)$ is the probability of non-adiabatic transition [see Eqn (50)] for a symmetrical potential profile (see Fig. 9 a),

$$F = -\frac{\partial e}{\partial y} \Big|_{y_0(E)},$$

F is the force for the average potential

$$e = \frac{1}{2} [e_i(y) + e_f(y)]$$

at the turning point $y_0(E)$.

Relation (53) is valid when $|A/E| \ll 1$ and some additional conditions are met.

If $|A/E| \gg 1$, a different asymptotic estimate follows¹²²

$$\begin{aligned} P_{if}(E) &= \frac{6}{\pi^2 c |A| [(E+A)^{1/2} - E^{1/2}]} \left[\left(\frac{d \ln A}{dy} \right) A \right]^2 \times \\ &\times \exp \left\{ -\frac{2\pi}{c} [(E+A)^{1/2} - E^{1/2}] \right\}. \end{aligned} \quad (54)$$

Here $A = A(y)$ is a matrix element for the transition along the vibrational coordinate (the tunnelling transition amplitude)

$$A(y) = \int \chi_i(\alpha|y) \left[H - \frac{1}{2}(e_i + e_f) \right] \chi_f(\alpha|y) d\alpha, \quad (55)$$

where H is a two-dimensional Hamiltonian [see Eqn (42)]. The amplitude $A(y)$ is calculated at the turning point for function χ_i . The dependence of the matrix transition element along the translational coordinate y plays an important role in HAT reactions [the probability $P_{if}(E)$ vanishes if this dependence is missing].

Equations (53)–(55) reflect the main features of energy transfer between vibrational and translational degrees of freedom in collinear HAT reactions. The main parameters that determine the probability of transfer include the resonance misfit (A), characteristics of adiabatic translational potentials (c , F), the amplitude of the tunnelling transition, and its dependence on the translational coordinate.

4. Tunnelling in a multidimensional double-well potential a. Specific features of the reactive transition dynamics in double-well systems

Continuum spectrum of vibration frequencies. Up to here, the discussion has been concerned with reactions for which the states of the reactants or the products (or both) have a continuum spectrum of eigenvalues. The reactions in double-well systems where all the energy levels are discrete require a specific approach. They can proceed only due to interactions with the environment, which is assumed to be a macroscopic system and, hence, has a continuum energy spectrum. However, the continuum spectrum of the medium differs from the one-dimensional continuum spectrum inherent in the translational degrees of freedom of the reaction system. The medium can consist of subsystems, each having a discrete energy spectrum: in the simplest case, the medium can be considered as an ensemble ('reservoir') of harmonic oscillators. The continuous nature of the general spectrum of the medium is ensured by the fact that the number of its degrees of freedom is infinite, *i.e.*, we are dealing with a continuum spectrum of vibration frequencies.

The interaction of the reaction mode with the oscillator reservoir having a continuum spectrum of frequencies, as well as the interaction with the translational degree of freedom (see Section II.3.b) ensures transfer of the resonance misfit energy and destruction of the transition coherence — *i.e.*, two conditions needed for a chemical reaction to proceed. As a result of this interaction, the reservoir oscillators rearrange (*i.e.*, change equilibrium positions) and are involved in the reaction. Thus, the chemical reaction in a double-well reaction system is an essentially multimode process that includes rearrangement of the states of the medium with a continuum spectrum of frequencies.

The simplest pattern of quantum rearrangement. The theory of quantum rearrangement processes has been developed for a model in which the reaction transition occurs between two multidimensional paraboloids with shifted minima which describe the PES of the reactants and the products (see Fig. 2).^{123–129} We restrict ourselves to the case where the normal modes of the reaction system and their frequencies do not change during the transition (a more general theory is extremely cumbersome, although it still can be formulated^{123, 127}). The straight line connecting the minima of the paraboloids (see Fig. 2 a), *i.e.*, the reaction coordinate, is a linear combination of the normal modes of the reactants and the products. The change in the distance along this straight line is

measured using the scalar parameter λ [see Eqn (3)]. Let one normal mode with the frequency ω_0 be quantum

$$\frac{\hbar\omega_0}{k_B T} \gg 1. \quad (56)$$

First, this is the high-frequency proton mode; as in Sections II.1 and II.2, we designate it by s . On the harmonic PES that we consider, each mode makes its individual contribution to the height of the potential barrier; the contribution of the mode s equals

$$\Delta V_s^\# = \frac{m_0\omega_0^2}{2}(\lambda^\#)^2(s_f - s_i)^2, \quad (57)$$

where m_0 is the mass corresponding to this coordinate, $\lambda^\#$ is the value of the reaction coordinate at the point of quasi-intersection of diabatic PES (this is a minimum on their intersection hypersurface),

$$\lambda^\# = \frac{1}{2} \left(1 + \frac{\Delta V}{E_r} \right),$$

$\Delta V = V_f - V_i$ is the energy difference between the minima of the diabatic parabolooids, *i.e.*, the heat of the reaction; E_r is the reorganisation energy, s_f and s_i are the values of the coordinate s at the minima. The other modes ω_v will be considered classical

$$\frac{\hbar\omega_v}{k_B T} \ll 1. \quad (58)$$

The frequencies ω_v form continuum spectra. Then one can expect that the reaction rate constant would have the form

$$k = k_s \exp \left(- \frac{\Delta V_1^\#}{k_B T} \right), \quad (59)$$

where k_s is the one-dimensional tunnelling rate constant in a double-well potential profile that corresponds to the PES cross-section along the mode s , $\Delta V_1^\#$ is the contribution of classical modes to the height of the potential barrier. It is significant that the partial height of the barrier determined by formula (57) is much smaller than the total value $V^\#$, which is given by the Marcus formula (6) with allowance for (5).

This qualitative discussion has been extended to the case of a larger number of quantum modes.^{126–129} The quantum modes that satisfy criterion (56) form altogether the tunnelling pre-exponential factor of the rate constant, which depends only slightly on the temperature. Classical modes are responsible for the Arrhenius exponential factor in which the activation energy is equal to their contributions to the barrier height.

Turning back to the classification of modes introduced in Section II.1.b, one can state that formula (59) reflects the situation where all the rearranging modes Q_v ($v = 1, 2, \dots$) are classical in conformity with criterion (58). As the temperature decreases, condition (58) starts to be violated for some of these modes. They become quantum modes and form the tunnelling pre-exponential factor, whereas those modes that still remain classical form the ever decreasing reaction barrier. This idealised pattern is valid only for a double-well harmonic potential. In PT reactions, the PES anharmonicity is substantial and the separation of variables throughout the whole path along the reaction coordinate (*i.e.*, along the curve connecting the potential minima *via* the saddle point) is impossible. However, at a qualitative level, the idea of more or less independent contributions of the proton (s) and rearrangement (Q_v) modes to the potential barrier remains valid.

Comparison of different ways of description of the reaction transition. Let us discuss in more detail how the theory formulated in terms of normal modes (non-interacting degrees of free-

dom)^{124–129} can be correlated with the statement according to which one or several reaction modes interact with an ensemble of harmonic oscillators of the medium.^{130, 131} We have in view the following. The discrete coordinates of the reaction system are considered oscillatory in each of the two diabatic regions (those of the reactants and the products). In each of these regions, their interaction with the medium oscillators is assumed to be bilinear and is excluded by diagonalisation of the corresponding diabatic oscillatory Hamiltonian. The normal modes thus found are those used in the double-well transition model. The allowance for the interaction results in renormalisation of the initial oscillator frequencies (both discrete and medium oscillators), shift of their equilibrium positions and the change in the form of vibrations. The assumption that normal vibration frequencies and forms are the same in both diabatic regions is actually made for the system of modes resulting from the diagonalisation mentioned above. The oscillator modes of the medium change most appreciably. Their interaction with the reaction system leads to a shift in the equilibrium of the reservoir oscillators, which are different for the reactants and the products.

Thus, the chemical reaction is accompanied by reorganisation of the medium, which is a necessary item of the theory we consider. Two limiting cases are analysed below. In the first case, the promoting mode R is ignored and the reaction dynamics is entirely determined by the medium reorganisation (electron transfer). Conversely, in the second case, the role of the medium is minimised and the main dynamic features of the reaction system are determined by the interaction between the proton (s) and promoting (R) modes (HAT in non-polar media). The promoting mode is usually assumed to be classical.

b. Electron transfer as an example of multimode tunnelling

Calculation technique. We will consider multimode transitions between the reactant and product states in which the quantum numbers of oscillators in the reactant well ($im_1, im_2, \dots$) are replaced by oscillator quantum numbers in the product well ($fn_1, fn_2, \dots$); the first character implies the belonging to either the reactants or the products, while the second one is the number of the level of the corresponding oscillator. To simplify the designations, we replace the set of characters in the parentheses by a single letter (a or b) and write down the transition probability per unit time as T_{ab} (it is measured in s^{-1}). In a deep tunnelling regime, the probabilities of individual transitions are low. They can be calculated using the perturbation theory (in terms of the golden rule)

$$T_{ab} = \frac{2\pi}{\hbar} A_{ab}^2 \delta(E_b - E_a). \quad (60)$$

Here, A_{ab} is the transition amplitude

$$A_{ab} = \langle \chi_b | H - E_a | \chi_a \rangle, \quad (61)$$

where χ_a and χ_b are the wave functions of multimode diabatic states, which are the products of oscillatory functions; H is the total double-well Hamiltonian; E_a and E_b are the energies of diabatic multimode states in the reactant a and product b wells, respectively; they are the sums of energies of the levels $e_{m_1}, e_{m_2}, \dots$ and $e_{n_1}, e_{n_2}, \dots$ for separate oscillators

$$\begin{aligned} E_a &= e_{m_1} + e_{m_2} + \dots; \\ E_b &= e_{n_1} + e_{n_2} + \dots \end{aligned} \quad (62)$$

As in the one-dimensional formulation (see Section II.3.b), χ_a and χ_b are not eigenstates of H : the oscillatory functions corresponding to them are localised in the reactant and product wells and, hence, they are the eigenfunctions of two different diabatic Hamiltonians, so that the corresponding off-diagonal matrix element H_{ab} does not vanish. According to the perturbation theory, the probabilities T_{ab} are additive, and the resultant thermal rate constant for the reaction equals^{99, 124, 125}

$$k = \frac{2\pi}{\hbar} \sum_{a,b} \exp\left(-\frac{E_a}{k_B T}\right) A_{ab}^2 \delta(E_b - E_a). \quad (63)$$

In Eqns (60) and (63), the delta-function expresses the energy conservation law for the multimode transition, which is accompanied by the intermode energy exchange. The summation is carried out over all combinations of the oscillatory functions, *i.e.*, multipliers in the multimode product functions χ_a, χ_b . The use of the delta-function provides the possibility of counting all combinations that ensure energy conservation.

Like any other relation containing the delta-function, expression (63) acquires a definite meaning and can be really calculated only if the sums appearing in it contain a continuum frequency spectrum and can be reduced to integrals. Reactions in the condensed phase represent an appropriate object for the application of this calculation procedure. In the harmonic model of the medium, a continuum frequency spectrum is specified using the spectral function $J(\omega)$ (spectral density, see Supplement II).^{96, 130–132}

Let us consider the case where there is only one quantum reaction mode (with the frequency ω_0), while the other modes (modes of the medium) are reorganisation modes with a continuum frequency spectrum. Then the function $J(\omega)$ gives the frequency distribution for the intensity of interaction between the reaction mode and the medium modes

$$J(\omega) = \text{const } \Delta Q(\omega) \rho(\omega), \quad (64)$$

where $\Delta Q(\omega)$ is the shift of the equilibrium position of the medium reorganisation mode Q with the frequency ω , which is induced by this interaction and can serve as its measure; the function $\rho(\omega)$ characterises the density of oscillator levels with the frequency ω ; it is different for different condensed media; the constant in the equation does not depend on ω .

The description of the continuum frequency spectrum by means of the spectral density is considered in more detail in Supplement II.

Expression for the rate constant.^{124, 125, 127, 131} Now we list once again the key assumptions made in the model of multidimensional tunnelling transition in a medium consisting of a continuum ensemble of harmonic oscillators.

First, the reaction system is described by a single reaction mode s with the frequency ω_0 . This is a quantum mode [see criterion (56)] related to the medium modes Q_v , which are characterised by frequencies ω_v and masses m_v . All modes of the medium are reorganisation modes. In the continuum limit, $Q_v \rightarrow Q(\omega)$. This limiting transition gives rise to the spectral function $J(\omega)$ as a characteristic of the interaction between the reaction mode and the medium.

Second, the tunnelling reaction does not change the frequency spectrum of the medium [*i.e.*, the function $J(\omega)$] or the forms of normal vibrations Q_v [or $Q(\omega)$]. This assumption is not fundamental but it allows one to represent the results of the theory in a rather simple form.

Finally, one special assumption concerning the form of the amplitude of the tunnelling transition is also required

$$A_{ab} = A_0 \langle \bar{\chi}_a | \bar{\chi}_b \rangle, \quad (65)$$

$$A_0 = \left\langle \chi_i \left| H - \frac{1}{2}(e_i + e_f) \right| \chi_f \right\rangle.$$

Here, the diabatic functions are represented by the products

$$\chi_a = \chi_i \bar{\chi}_a, \quad \chi_b = \chi_f \bar{\chi}_b,$$

where χ_i and χ_f are the eigenfunctions for the reaction mode s , corresponding to the energies e_i and e_f , while $\bar{\chi}_a$ and $\bar{\chi}_b$ are the products of the wave functions of the medium oscillators. The functions $\bar{\chi}_a$ and $\bar{\chi}_b$ correspond to the energies

$$\bar{E}_a = E_a - e_i, \quad \bar{E}_b = E_b - e_f.$$

These relations follow from the energy conservation law. The overlap integral $\langle \bar{\chi}_a | \bar{\chi}_b \rangle$ is equal to the product of the overlap integrals for the shifted oscillators of each of the medium modes; it is called the multidimensional Frank–Condon factor.

Equations (65) represent the Condon approximation according to which the dependence of the matrix element A_0 on the oscillatory coordinates is not taken into account. This approximation is justified provided that the frequency ω_0 is much greater than the medium frequencies. In this case, the A_0 value is calculated for those medium coordinates that make the greatest contribution to the full transition amplitude.

When these assumptions are taken into account, the reaction rate constant given by relation (63) is transformed in the following way:^{127, 133–137}

$$k = \frac{A_0^2}{\hbar^2} \int_{-\infty}^{\infty} C(t) \exp\left(-\frac{it\Delta V}{\hbar}\right) dt, \quad (66)$$

$$C(t) = \exp\left[-\frac{1}{\pi\hbar} \times \int_0^{\infty} \frac{J(\omega)}{\omega^2} \frac{\text{ch}(\hbar\omega/2k_B T)(1 - \cos\omega t) + i\text{sh}(\hbar\omega/2k_B T)\sin\omega t}{\text{sh}(\hbar\omega/2k_B T)} d\omega\right].$$

Here, t is time; $\Delta V = V_f - V_i$ is the difference between the energies of the diabatic PES at their minima [see Eqn (4)].

Relation (66) is a typical result of the multimode oscillatory perturbation theory. It is widely used in the theory of electron transfer in polar solvents.^{127, 129, 133–137} In this case, s is the electron coordinate and the function $J(\omega)$ is proportional to the reorganisation energy of the modes of the medium, *i.e.*, the energy evolved upon the shift of the equilibrium positions of the oscillatory modes. The frequency dependence of $J(\omega)$ is determined by the function $\text{Im}\{\epsilon(\omega)/|\epsilon(\omega)|^2\}$, where $\epsilon(\omega)$ is the frequency-dependent complex dielectric constant, which is the key phenomenological characteristic of the dynamic properties of the dielectric medium. This representation of the spectral density is valid for any reactions with charge redistribution in polar disordered media. The parametrisation of $J(\omega)$ can be quite different for reactions in non-polar media or in molecular crystals (see Supplement II).

Equation (66), which seems to be complicated, holds for a broad range of temperatures including the lowest ones and describes the reorganisation dynamics for both classical and quantum modes of the medium. More precisely, this theory is valid as long as the key expression of the golden rule (60) holds. There is always a lower temperature limit depending on the resonance misfit and on the spectral density,^{130, 131} beyond which the steady-state regime (which ensures the existence of exponential decay and the rate constant) is violated and quantum beats appear, *i.e.*, coherent periodic transitions of the reaction system from the reactant well to the product well and back. This lower temperature limit is commonly considered to arise in the extremely low-temperature region.

If all modes of the medium are considered to be classical in conformity with criterion (58), expression (66) is reduced to the usual Arrhenius law (59), which was postulated above relying on intuitive considerations:

$$k = \frac{A_0^2}{\hbar} \left(\frac{\pi}{E_r k_B T}\right)^{1/2} \exp\left[-\frac{(E_r + \Delta V)^2}{4E_r k_B T}\right]. \quad (67)$$

Here, the activation energy coincides with the potential barrier (6).

Thus, in the high-temperature limit, the electron transfer kinetics is mainly determined by three key reaction parameters, namely, the transition amplitude for the reaction mode, the medium reorganisation energy E_r , and the heat of the reaction ΔV . The dependence of the rate constant on details of the frequency spectrum of the medium is manifested only in the low-

temperature quantum regime. Various approximations of expression (66) are possible, which are valid in more or less broad temperature ranges.^{99, 138–141} One of them is given below.

c. Hydrogen atom transfer in the liquid and solid phase

Reaction model. The PT and HAT reactions in the condensed phase have been considered in a number of early studies using relation (66).^{27–31, 142–147} The proton coordinate was used as the only quantum coordinate s . It can be seen from the above consideration that this approximation is inadequate and that the promoting mode R is to be taken into account.¹⁴⁸ The simplest plausible model should explicitly include the modes s , R and the medium modes Q_v .^{30, 148–151} This model is formulated as follows.^{99, 148} The interaction of modes s and R is introduced through the dependence of the proton transition amplitude A_{if} on R (recall that this dependence plays a crucial role in the energy exchange in gas-phase hydrogen atom abstraction). A convenient approximation is

$$A_{if}(R) = \bar{A}_0 \exp[-\alpha(R - R_e) - \gamma(R - R_e)^2], \quad (68)$$

where R_e is the equilibrium R value.

The second term in brackets rapidly decreases both for positive and negative values of the $R - R_e$ difference. It is necessary for providing the convergence of the perturbation theory integrals with the continuum spectrum. Then it is sufficient to assume that only the low-frequency mode R interacts with the medium oscillators. The corresponding frequency and mass will be designated by ω_R and m_R . This mode is not a reorganisation mode, *i.e.*, its equilibrium position does not change upon the reaction. Correspondingly, the modes of the medium do not change equilibrium positions and remain exclusively promoting modes. The full expression for the rate constant in this model⁹⁹ is cumbersome and unwieldy. A rather simple expression can be obtained by neglecting the squared dependence on R in the exponent in Eqn (68) and taking that $\gamma = 0$. Then

$$k = \frac{\bar{A}_0^2}{\hbar^2} \int_{-\infty}^{\infty} C(t) \exp\left(-\frac{it\Delta V}{\hbar}\right) dt, \quad (69)$$

$$C(t) = \exp\left[\frac{(\hbar\alpha)^2}{\pi\hbar} \times \int_0^{\infty} J(\omega) \frac{\text{ch}(\hbar\omega/2k_B T) (1 + \cos\omega t) - \text{ish}(\hbar\omega/2k_B T) \sin\omega t}{\text{sh}(\hbar\omega/2k_B T)} d\omega\right].$$

Here the spectral density $J(\omega)$ describes the expansion of the promoting mode R over the normal modes of the full system comprising the reaction subsystem and the medium. In the discrete representation,

$$R - R_e = \sum_v C_v Q_v.$$

The methods for the transition to the continual representation that allow one to obtain expressions (66) and (69) are considered in Supplement II.

Temperature dependence of the rate constant. One can expect that there exists, at least, one localised normal mode that makes a substantial (perhaps, the major) contribution to the coordinate R . Therefore, the expansion

$$J(\omega) = \text{const} \delta(\omega - \omega_R) + J_{\text{cont}}(\omega), \quad (70)$$

where ω_R is the frequency of the localised normal mode, can be an appropriate approximation.

The second (continuum) term remains, as usual, a smooth spectral function. Therefore, using relation (70), the factor^{99, 148, 152}

$$k \sim \exp\left\{\text{const} \left[\frac{(\hbar\alpha)^2}{\pi\hbar} \text{cth} \frac{\hbar\omega_R}{2k_B T}\right]\right\}, \quad (71)$$

which determines the temperature dependence of the rate constant in the temperature range where

$$\frac{\hbar\omega_R}{2k_B T} \lesssim 1, \quad (72)$$

can be separated in the rate constant.

This dependence is well fulfilled for photochemical elimination of a hydrogen atom by the singlet excited acridine impurity in the molecular crystal of fluorene (Fig. 10). Condition (72) determines the position of inflection point on the temperature kinetic curve; this is used to determine the resonance frequency ω_R . The value found in this way coincided with the frequency of the promoting mode ($\omega_R = 130 \text{ cm}^{-1}$) found by an independent procedure using the vibrational spectrum of the fluorene crystal.^{153, 154}

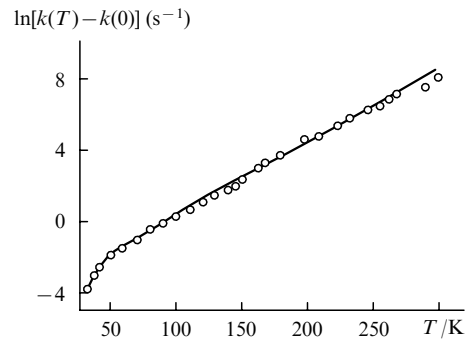


Figure 10. Temperature dependence of the rate constant for a photochemical reaction of HAT in a fluorene molecular crystal doped with acridine.

Experimental data are shown by dots.¹⁵³ The continuous line was calculated using relation (71) for $\omega_R = 131 \text{ cm}^{-1}$ (see Ref. 152).

The factor (71) can also be distinguished in the equation for the rate constant of the reaction with medium reorganisation [see Eqn (66)]. The correlation (71) cannot be extended to a too broad temperature range. With an increase in temperature, one should take into account the Gaussian exponential component in the transition amplitude (68),⁹⁹ which is ignored in expression (69). The corresponding temperature factor for $\hbar\omega_R/k_B T \ll 1$ (when the promoting mode becomes classical) has the form

$$k \sim \exp\left(\frac{1}{2} \frac{\alpha^2 l_R^2}{2l_R^2 \gamma' + \hbar\omega_R/4k_B T}\right), \quad (73)$$

where l_R is the amplitude of zero-point vibrations along the coordinate R

$$l_R = \left(\frac{\hbar}{m_R \omega_R}\right)^{1/2}.$$

This factor can be derived using simple quasi-classical consideration.¹⁴⁸ Provided that

$$2l_R^2 \gamma \ll \frac{\hbar\omega_R}{4k_B T}$$

this leads to a linear dependence of $\ln k$ on T , which was observed in many experiments. As the temperature further increases, the dependence becomes more gentle. The linear section can be clearly seen in Fig. 10. At very low temperatures ($\hbar\omega_R/k_B T \gg 1$), the continuum spectrum component $J(\omega)$ should be taken into account. The factor (71) becomes constant at this temperature. The corresponding temperature dependence, which follows from relation (69), has the form

$$\ln k \sim T^n,$$

the power n ($2 < n < 4$) being determined by the spectral density $J(\omega)$ of the condensed medium.^{99, 155} This conclusion, however, is not fully unambiguous due to the presence of a lower temperature limit below which the concept of rate constant becomes invalid in terms of the harmonic oscillatory model of the medium, and the energy exchange proceeds by an anharmonic mechanism.

The above analysis of the temperature dependence of the rate constant is wholly determined by the dynamics of the promoting mode, which interacts with the modes of the continuous spectrum, according to the accepted model [in the derivation of formula (69), it is expanded over normal vibrations of the overall system composed of the promoting mode and the medium coordinates]. The coordinate R does not pass across a potential barrier; therefore, the usual Arrhenius dependence such as (59) is not observed at all. Within the framework of a classical consideration of the coordinate R , this dependence could arise only due to the reaction mode s , but this is a quantum mode at any temperature that may be of interest and, hence, it does not make a significant contribution to the temperature dependence of the reaction rate.

III. Calculations for particular systems

1. Multidimensional quasi-classical calculations

a. Problem definition

Quasi-classical calculations are based on the quasi-one-dimensional model of tunnelling (see Section II.3.a). In the space of active coordinates of the reaction system, the reaction path curve connects the regions of reactants and products. Let us consider one-dimensional tunnelling on the energy profile along this curve and calculate the quasi-classical action $W(E)$ [see Eqn (25)] in the region under the potential barrier, which determines the amplitude of the tunnelling transition. Selection of the reaction path is the key problem in this procedure. For a rigorous definition of the problem, the curve should ensure a classical action extremum for motion of the system in the inverted potential (the potential barrier becomes a potential well, and the reactant and product minima become top points of the potential relief). The classical trajectory with specified initial and end points is calculated in the inverted potential. The trajectory depends on the initial and final quantum states between which the transition takes place. Boltzmann averaging of the initial states gives rise to a dependence of the reaction path on temperature. The paths are different for low-temperature (tunnelling predominates) and high-temperature (tunnelling effects are slight) processes; its optimisation ensures a smooth transition between these kinetic regimes. However, in practice, such advanced scheme has never been applied to particular HAT or PT reactions. Actually, calculations are always carried out for a fixed trajectory chosen by some procedure.

The equation for the rate constant in a multidimensional case has the form:^{156, 157}

$$k = A \exp[-W(E)].$$

The pre-exponential factor A can be conveniently calculated in a special coordinate system, which is usually referred to the reaction path curve, also called the reference curve. One of the coordinates (the reaction coordinate) is measured as an arc length along the reference curve. A local system of Cartesian transverse coordinates is specified at every point of the reference curve; usually, the coordinates are modelled as harmonic oscillators. In these ‘natural reaction coordinates’,^{158, 159} the PES is a multidimensional valley stretched along the reaction path and the expression for kinetic energy has a complex form depending on the curvature of the reference curve.^{158–161} The corresponding multidimensional Hamiltonian is called the reaction path Hamiltonian.¹⁶⁰ The minimum potential energy route is normally used as the reference curve: in this curve, the PES cross-sections along the transverse coordinates have minima.¹⁶¹ This path connects the TS, *i.e.*, the saddle point on the PES, with the reactant and product minima, although the action for transverse coordinates rather

than the potential cross-section profile should have a minimum on the reference curve in a consistent theory.¹⁵⁷

b. The variational transition state theory

In the variational approach, the standard minimum potential energy route on the PES is chosen as the reaction path (in some cases, insignificant modifications are made).^{162–164} The theory remains classical in this respect. The expression for the rate constant derived in terms of the classical TS theory by the variational method is used.^{91, 165} The critical point in the reaction coordinate at which the reaction flux is calculated (*i.e.*, the TS) does not coincide with the top of the barrier. According to the variational theory, it is determined by minimising the expression for the rate constant with respect to the position of the TS in the reaction coordinate. At the final stage, a transmission factor (28), determined by tunnelling along a curvilinear reaction trajectory, is introduced to the rate equation.

This method was used to study HAT reactions in the gas phase^{166–168} and in solutions^{169–172} and PT and hydride ion transfer in enzymes.^{173, 174} The calculation of a model collinear reaction (see Section II.3.a) in the presence of 250 solvent (methyl chloride) molecules is notable from the procedural standpoint.¹⁷⁵ The classical minimum energy path was calculated taking into account all degrees of freedom of the system. As noted above, the variational TS theory was implemented to calculate the transmission factor.

It is clear that this approach cannot be extended to the region of low-temperature kinetics.

c. Low-temperature instanton method

In the low-temperature instanton approach,¹⁷⁶ the reaction path corresponds to a classical action minimum on the under-barrier trajectory in the inverted potential. The start of the trajectory is chosen in the reactant minimum on the real (rather than inverted) PES. This is valid for $T = 0$ K. The classical action is calculated along such trajectory and a correction for the interaction with transverse vibrational degrees of freedom is introduced into the resulting expression (in terms of the perturbation theory).^{177–180}

The use of this method is currently restricted to the study of tunnel splittings in the microwave spectra of non-rigid molecules. The calculations of splittings have been carried out for both the ground state and the vibrationally excited states. Systems with intra- and intermolecular hydrogen bonds, namely, malondialdehyde and formic acid dimer, have been considered. Two-proton tunnelling transfer in the porphyrin molecule has been discussed.¹⁸¹ A study of splittings in the malondialdehyde molecule with 21 degrees of freedom is the utmost achievement in this series of studies.¹⁸²

d. The model instanton method

The model instanton approach¹⁵¹ employs the classical reaction path with a classical TS at the PES saddle point. This is an attempt to take into account the influence of all the other (transverse) vibration modes without resorting to the perturbation theory. This is indeed possible for a model two-dimensional PES formed by two paraboloids (see Fig. 2a).¹⁸³ Extrapolation of this model to a multidimensional situation gave the equation^{184, 185}

$$W = \frac{W_0}{1 + \sum_s \delta_s(T)} + \alpha_s \sum_a \delta_a(T), \quad (74)$$

where W is the dimensional action, unlike the dimensionless action $(1/\hbar)W$ [see, for example, relation (25)]. The action W_0 is calculated along the standard classical reaction path. The transverse degrees of freedom are separated into symmetrical (the subscript s) and antisymmetrical (the subscript a); the symmetry is determined at the point of classical TS. ‘Symmetrical’ and ‘antisymmetrical’ are synonyms for ‘reorganisation’ and ‘promoting’ modes. The corrections they introduce to the action are additive. The δ_s , α_s and δ_a values can be explicitly calculated

from a specified multidimensional PES. Expression (74) is an empirical prescription, which provides physically reasonable estimates in some limiting situations. Of interest is the appearance of a typical temperature dependence of the action

$$\delta_s(T) = \delta_s \Big|_{T=0} \text{cth} \frac{\hbar \omega_s}{2k_B T},$$

where ω_s is the frequency of the corresponding symmetrical vibration. The reaction rate constant is calculated in terms of the standard instanton procedure

$$k(T) = A(T) \exp \left[-\frac{1}{\hbar} W(T) \right]. \quad (75)$$

As in standard instanton methods, the pre-exponential factor is replaced by an effective frequency, which characterises the system vibrations in the reactant potential well.

This method was applied to study the tunnel splittings for intramolecular PT (malondialdehyde,¹⁵¹ tropolone¹⁸⁶ and 9-hydroxyphenalenone¹⁸⁵). The rate constants have been calculated for many reactions^{187–191} including two-proton transfer in porphins.¹⁸⁵ The temperature dependences of the rate constants and the isotope effects were compared with experimental data.

The tunnel splittings for malondialdehyde have been calculated taking into account all the vibrational degrees of freedom and using various modifications of the instanton method.^{192–194}

2. Two-state model with the molecular description of the medium

a. Collective coordinate of the medium

The quantum theory of PT reactions with allowance for two electron–proton states is used fairly often (see Section II.2). A Hamiltonian depending on the variables s (proton coordinate) and R (symmetrical vibration of the A_1 and A_2 fragments, promoting mode) is written down for a three-particle $A_1 \cdots H \cdots A_2$ model system. An ensemble of modes of the medium Q_v , which interact with s and R , is added to the system. The complete Hamiltonian depends on each of the variables. Quantisation of the coordinate s in the basis set of two diabatic functions $\varphi_n(s|R, Q_v)$, $n = 1, 2$, gives the matrix Hamiltonian

$$H = \begin{pmatrix} H_{11} & H_{12} \\ H_{21} & H_{22} \end{pmatrix}, \quad H_{12} = H_{21}. \quad (76)$$

The diagonal elements are the classical Hamiltonians for two electron–proton states

$$\begin{aligned} H_{11} &= T_R + T_Q + \varepsilon_1(R, Q_v), \\ H_{22} &= T_R + T_Q + \varepsilon_2(R, Q_v), \end{aligned} \quad (77)$$

where T_R and T_Q are the kinetic energies for the mode R and the medium coordinate Q ; ε_1 and ε_2 are the corresponding FES, which are found by solving the Schrödinger equation for the coordinate s

$$h_s \varphi_n(s|R, Q_v) = \varepsilon_n(R, Q) \varphi_n(s|R, Q_v), \quad n = 1, 2. \quad (78)$$

The proton Hamiltonian h_s is specified by Eqn (9). The potential in this case is the full PES in the coordinates s , R and Q_v , in which R and Q_v are considered as parameters. The corresponding parametric dependence appears in the solution of Eqn (78), i.e., in the eigenvalues ε_n and eigenfunctions φ_n .

A remark concerning the designations is pertinent. In the key relations (8), (9) for quantisation of the proton coordinate s , the type of representation (either adiabatic or diabatic) is not specified; therefore, the potentials $V(s)$ and the eigenfunctions $\varphi_n(s)$ can be both adiabatic and non-adiabatic. In further consideration in Section II.2, the designation φ_n is used for functions of the adiabatic basis, whereas diabatic functions were designated by χ_n . Here, it is more convenient to use the common designation φ_n for both diabatic and adiabatic functions.

It should be noted that Hamiltonian (76) can be represented in the form

$$H = \begin{pmatrix} 0 & H_{12} \\ H_{21} & \Delta\varepsilon \end{pmatrix} + H_{11}, \quad (79)$$

$$\Delta\varepsilon = H_{22} - H_{11} = \varepsilon_2(R, Q_v) - \varepsilon_1(R, Q_v).$$

The dynamics and kinetics of the interlevel transition do not depend on the scalar (non-matrix) value H_{11} . The matrix element of the transition H_{12} (equal to H_{21}) is specified empirically. The energy gap $\Delta\varepsilon$ is the only significant variable; as can be seen from Eqn (79), the dependence on the particle velocity, present in Eqn (77), has disappeared because the classical kinetic energy is the same in the states φ_1 and φ_2 . The variable $\Delta\varepsilon$ is a typical collective coordinate; calculation procedures with the use of this variable are well developed (numerical modelling by the MD or Monte-Carlo methods). This investigation scheme was first applied by Warshel and coworkers;^{195–197} subsequently, various modifications of this scheme were applied by many authors.

b. Triatomic model of a proton transfer reaction in a model solvent. Calculations by molecular dynamics

A popular investigation object is the PT reaction (acid–base equilibrium) in the molecular complex



where PT is accompanied by pronounced polarisation of the heavy fragments A and B . In the calculations described above, the fragment A is represented by phenoxide $C_6H_5O^-$, while the fragment B is the amino group [trimethylamine $N(CH_3)_3$ is a typical example]. The reactants and products in reaction (80), described by the functions φ_n , which have served as the basis for constructing Hamiltonian (76), have dipole moments $\mu_1 \approx 2$ D (covalent complex) and $\mu_2 \approx (10–15)$ D (ion pair), respectively. The solvent particles are simulated in MD calculations by methyl chloride (CH_3Cl , $\mu = 2.15$ D).

The calculation starts with explicit solution of the Schrödinger equation (78) for the diabatic proton states. The single-well diabatic potentials $V(s|R, Q_v)$ appearing in the proton Hamiltonian h_s are modelled empirically by combining the LEPS (London–Eyring–Polanyi–Sato) type schemes for the internal variables s , R in the gas-phase reactions¹⁹⁸ with the MD parametrisation of the interactions involving the solvent particles.⁶³ With respect to the proton coordinate s , the functions $V(s|R, Q_v)$ are highly asymmetric single-well potentials (see Fig. 3). With these potentials, Eqn (78) can be solved numerically. This demonstrates the unique advantage of introducing the collective variable $\Delta\varepsilon(R, Q_v)$ [see Eqn (79)]. Equation (78) is solved for a one-dimensional set of values of the coordinate $\Delta\varepsilon$ rather than for the whole set of combinations of R and Q_v (which arise, for example, in a calculation with 256 solvent particles⁶³). This gives two diabatic FES, $\varepsilon_1(R, Q_v)$ and $\varepsilon_2(R, Q_v)$, in which the explicit dependence on the medium coordinate is included through $\Delta\varepsilon$. Diagonalisation of the Hamiltonian (79) gives two adiabatic FES

$$E_{1,2} = \frac{1}{2} \left[\varepsilon_1 + \varepsilon_2 \pm (\Delta\varepsilon^2 + 4H_{12}^2)^{1/2} \right]. \quad (81)$$

The free energy surface for the ground adiabatic state E_1 is double-well (see Fig. 2b). It is significant that in the TS region, the medium coordinate $\Delta\varepsilon$ is the reaction coordinate: the FES profile along $\Delta\varepsilon$ has a maximum at the saddle point.

The way for calculating the kinetics of reaction (80) is obvious in the adiabatic approximation where the transitions between surfaces E_1 and E_2 are ignored. In the simplest version, the coordinate R is considered to be classical (the medium coordinates Q_v are always classical in this model). The rate constant is then calculated using a standard MD procedure, namely, the steady-state reaction flux method.⁵⁵ It is reduced to the calculation of

k_{TST} , *i.e.*, the rate constant in the TS approximation, and the correcting classical transmission factor κ_c :

$$k = \kappa_c k_{\text{TST}}. \quad (82)$$

For determining κ_c , the correlation functions for the coordinate $\Delta\epsilon$ and its derivative with respect to time ($\Delta\dot{\epsilon}$) have to be calculated (by MD methods).^{63, 199, 200} When these functions are known, one can also determine the friction kernel in the generalised Langevin equation (see Supplement I) and calculate κ_c within the framework of the KGH stochastic theory.⁶³

In earlier studies of reaction (80), the promoting mode R was not taken into account.^{29, 200–203} The most comprehensive study was carried out for a two-dimensional model ($R, \Delta\epsilon$) with allowance for quantisation of R .⁶³ The transmission factor varied in the range of $0.4 < \kappa_c < 0.8$ depending on the parametrisation. The attempts to take into account the non-adiabatic transitions within the framework of this scheme are not quite consistent.^{63, 200} The transition probability for a one-dimensional potential profile along the coordinate $\Delta\epsilon$ has been calculated by the Landau–Zener method.⁸⁸ Then it was averaged with allowance for the statistical distribution of the $\Delta\epsilon$ values using the MD technique. The choice of parametrisation for the transition matrix element H_{12} is significant at this stage.

c. Quantum effects

According to the accepted terminology (see Section II.2.a), reaction (80) has a low barrier. The quantum effects involved are insignificant. Conversely, HAT reactions in systems containing hydrocarbon molecules have high barriers. The quantum transmission factors for them are low ($\kappa_q < 10^{-4}$ or lower^{166–168}). The golden rule procedure for their calculation is considered in Sections II.4.a and II.4.c. This line of research was initiated by early studies performed before the mid-1980s.^{126, 143, 148} Subsequently, this approach was modified by using advanced computer simulation procedures.^{27, 28, 30, 149} However, no calculations of this type for particular systems taking account of quantum effects have been reported so far.

A complete and consistent theory for describing the kinetics of reaction systems with multidimensional double-well FES taking into account the tunnelling and non-adiabatic transitions should cover the two above-mentioned limiting cases and intermediate kinetic regimes. No theory of this type has yet been developed. Some approximate approaches are considered in Section II.2.b. Calculations of the probabilities of non-adiabatic transitions in model one-dimensional multilevel systems are documented.^{204–206} In terms of the principles inherent in them, these calculations are related to calculations of two-level systems considered in this Section and to quantum-classical calculations of PT (see below, Section III.4).

3. Continuum models of the medium

a. Definition of the problem in the adiabatic representation

A two-state model of the reaction subsystem with explicit inclusion of the surrounding solvent particles is considered in Section III.2. An alternative problem formulation is possible on the basis of a continuum description of the medium.^{64, 65, 69}

The first stage is to construct the FES for the ground state of the system spanned by the coordinates s, R, X , where X is the collective coordinate of the medium. Its definition was borrowed from the theory of electron transfer.^{66, 87, 207, 208} The corresponding Hamiltonian has the form

$$H = T_s + T_R + S + W(s, R, X), \quad (83)$$

where T_s and T_R are the kinetic energies of modes s and R ; in the general case, these are quantum-mechanical operators; the value $S = X^2/2E_r$ is the self-energy of the polarisation field of the medium. Polarisation is induced by the electric charges of the chemical subsystem, which are calculated by quantum-chemical methods. The reorganisation energy E_r appearing in the expression for the self-energy is the key parameter of the electron transfer

theory (see Sections II.1.b and II.4.b); it is calculated within the framework of continuum models of the medium.^{209–212} The three-dimensional FES $W(s, R, X)$ is constructed in terms of the semi-empirical scheme combining the quantum-chemical calculation with calculation of the polarisation effects (dependence on X) in terms of continuum models.^{213, 214} This FES is a double-well surface on which the reaction transition takes place.

The proton coordinate s is excluded at the next stage. The numerical solution of the Schrödinger equation

$$[T_s + W(s, R, X)] \varphi_n(s|X, R) = \varepsilon_n(X, R) \varphi_n(s|X, R) \quad (84)$$

for different fixed X and R values gives the eigenvalues $\varepsilon_n(X, R)$ and the eigenfunctions $\varphi_n(s|X, R)$; $n = 1, 2$. They correspond to the adiabatic representation, because $W(s, R, X)$ in Eqn (84) is the total potential of a two-level system. (In this respect, this scheme differs from the diabatic one considered in Section III.2.b, although the diabatic definition is also possible in the continuum model of the medium.²¹⁵) Two two-dimensional FES, $\varepsilon_1(X, R)$ and $\varepsilon_2(X, R)$, obtained from Eqn (84) correspond to the ground and excited states of the proton subsystem. The dynamic description of the continuum variable X is performed using stochastic or diffusion models. Two-dimensional and two-level stochastic (or diffusion) equations of motion, whose one-dimensional versions are considered in Section II.2.b and in Supplement I, are found for these surfaces.

b. Non-adiabatic transitions

The matrix element which determines non-adiabatic transitions between the levels in the adiabatic representation is an imaginary quantity^{65, 69}

$$H_{12} = \frac{\hbar}{i} (v_R J_R + v_X J_X), \quad (85)$$

where v_R and v_X are the velocities corresponding to the coordinates R, X

$$J_R = \left\langle \varphi_2 \left| \frac{\partial}{\partial R} \right| \varphi_1 \right\rangle, \quad (86)$$

$$J_X = \left\langle \varphi_2 \left| \frac{\partial}{\partial X} \right| \varphi_1 \right\rangle.$$

The intensity of non-adiabatic transitions is determined by the parameter ξ

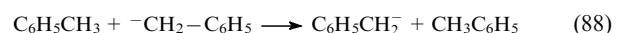
$$\xi = \frac{|\langle H_{12} \rangle_T|}{\varepsilon_2 - \varepsilon_1}, \quad (87)$$

$$\langle H_{12} \rangle_T = \hbar \left(\frac{2k_B T}{\pi} \right)^{1/2} \left(\frac{J_R}{\sqrt{m_R}} + \frac{J_X}{\sqrt{m_X}} \right).$$

Here, the averaging $\langle \dots \rangle_T$ takes place over the Maxwell velocity distribution; m_R and m_X are the masses corresponding to the coordinates R and X (m_X is estimated on the basis of generalised Langevin equation^{64, 69}). The ξ value is calculated at the point where the surfaces ε_2 and ε_1 approach each other most closely and the energy gap $\varepsilon_2 - \varepsilon_1$ is the smallest.

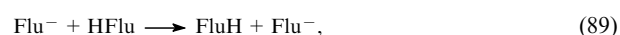
c. Systems with the C–H...C reaction centre

The free energy surface $\varepsilon_1(X, R)$ for the ground (proton) state of the reaction system



is shown in Fig. 5. It bears a strong resemblance to a similar double-well FES calculated in the molecular description of the medium.⁶³ The calculation of reaction (88) showed⁶⁴ that $\xi \ll 1$, *i.e.*, the reaction is adiabatic. This is a reaction with a low barrier. If non-adiabatic transitions are neglected, the classical reaction kinetics can be derived using the KGH theory.

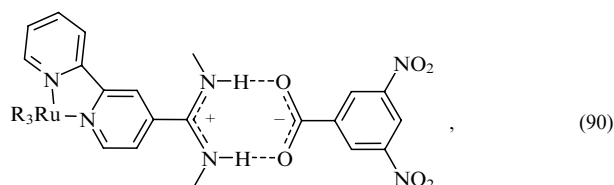
The opposite limiting case is represented by the reaction



where FluH is the fluorene molecule. This is a reaction with a high barrier, a very small energy gap $\varepsilon_2 - \varepsilon_1$ and $\xi \gg 1$, which complies with the non-adiabatic kinetics. The quantum transmission factor is estimated as $\kappa_q \approx 10^{-5} - 10^{-7}$ (see Ref. 65). This exceptionally low value corresponds to the deep tunnelling regime and is at variance with the insignificant isotope effect ($k_H/k_D \approx 10$) observed in the experiment. Apparently, this contradiction can be eliminated by noting that two internal coordinates s and R are inadequate for full description of the PES for reaction (89). It is necessary to take into account the dependence of PES on the reorganisation modes describing the change in the environment of the reaction centre. Their role is described in Section II.1.b. In view of this circumstance, it is possible to decrease the effective barrier to tunnelling²¹⁶ and to increase the quantum transmission factor by several orders of magnitude.

d. Coupled electron and proton transfer

The model described above was developed and applied for interpreting the features of coupled electron and proton transfer.^{215, 217–219} This type of process takes place in the system



where R is 3,3',4,4'-tetramethyl-2,2'-bipyridine. The synchronous transition of two protons is accompanied by substantial charge redistribution between fragments of system (90). For describing these effects one should circumvent the limitations of the two-level model of the reaction subsystem. A large number (4 or 8^{215, 218}) of electron–proton states corresponding to various basis structures of the valence bond method should be explicitly included into consideration. In the case of N states, a matrix ($N \times N$) Hamiltonian and N coordinates of the medium ($X_1, \dots, X_N$) appear. Before constructing the matrix Hamiltonian (*i.e.*, before excluding the coordinate s), one should proceed from the ground state Hamiltonian, similar to Hamiltonian (83) but depending on all the medium coordinates X_i , $i = 1, \dots, N$. The self-energy S of the medium polarisation field is^{208, 209}

$$S = \frac{1}{2} \sum_{ij} (T^{-1})_{ij} X_i X_j, \quad (91)$$

where T is the reorganisation matrix, which is calculated using techniques of the continuum theory of the medium.

When dealing with the given multilevel theory, non-adiabatic transitions between various pairs of basis states arise. They can be classified into transitions with electron transfer and transitions with PT. This calculation procedure has been developed in detail^{215, 220} and brought to the calculation of the rate constant in a kinetic regime such that the non-adiabatic electron transfer is treated in the usual way in terms of the golden rule and PT takes place on adiabatic FES without transitions between the FES.^{215, 219} The results provided an explanation for some features of the coupled electron and proton transfer for system (90) and other related systems. An alternative interpretation has been proposed in earlier theoretical studies,^{221, 222} but they appear less convincing.

e. Some conclusions

Little experience in using continuum models of the medium to calculate PT reactions has been accumulated so far. Apart from the studies described above, calculations of bimolecular and intramolecular PT in water should be mentioned.^{223, 224} The available material allows one to draw some conclusions concerning the prospects of the continuum method as applied to PT reactions.

First, the use of continuum models greatly facilitates the calculations compared to those done in terms of similar molecular models of the medium.

Second, description of the rearrangement of chemical subsystem in the basis set of two electron–proton states restricts the scope of the method. This is true not only for coupled electron and proton transfer where extension of the basis of quantum states is the key item of the theory.^{215, 218, 219} The calculations of FES for usual PT systems revealed characteristic situations in which the limitations of the two-level model result in serious inconsistencies.⁶⁹ The two-level approximation equally restricts the validity of calculations with the molecular description of the solvent.

Third, a substantial restriction follows from the usual two-coordinate model of PT, which takes into account only two internal degrees of freedom (coordinates s and R) of the reaction subsystem. The reorganisation of modes associated with the change in the close environment of the reaction centre is an important factor for many PT and HAT reactions with a high barrier.²¹⁶ It has a crucial influence on the kinetics of HAT reactions; when the changes in these modes are ignored, the tunnelling effect is substantially overestimated.

Fourth, it is necessary to note a serious problem of the continuum theory, which restricts its practical value. The problem lies in the basic concept of the cavity which incorporates the reaction subsystem in the continuum medium. The change in the cavity during the reaction is supposed to induce no substantial energy or dynamic effects. This hypothesis is applicable to intramolecular processes for which the change of the cavity can indeed be considered insignificant. In bimolecular systems with PT and HAT, the cavity changes during the reaction but no procedures for calculation of the concomitant effects are suggested by the continuum model of the medium. This problem does not arise in the case of molecular models of the medium; this forms the strategic advantage of the latter.

Thus, the existing continuum theories of the solvent are barely applicable to a detailed quantitative description of PT and HAT reactions, although they are attractive for a qualitative description due to their simplicity and clarity.

4. Numerical modelling of proton transfer reactions by molecular dynamics

a. Quantum-classical methods

The use of simplified structural and dynamic models for a reacting subsystem (see Sections III.2 and III.3) restricts the scope of investigation of real chemical objects. In this respect, of interest are attempts at direct computer simulation of PT dynamics based on microscopic (molecular–dynamic) description of the solvent without rigorous constraints on the form of quantum electron–proton states. These approaches consider joint dynamic evolution of quantum and classical degrees of freedom. The number of quantum variables is limited; usually, only a single proton coordinate s is considered. The list of classical variables includes several selected kinetically active coordinates of the reacting subsystem and the coordinates of several hundred of solvent particles. The general strategy for deriving the quantum–classical equations of motion is standard (the main principles are outlined in Sections II.2.a, II.2.b and III.2). The equations of motion along quantum coordinates (the Schrödinger equation for the wave function or the von Neumann equation for the density matrix) involve a parametric dependence on all the classical variables (*via* the interaction potential).

Further development of this approach includes explicit derivation of the time dependence of the classical variables by MD computation of their evolution. Substituting the resulting multidimensional classical trajectory into the quantum equation of motion, *i.e.*, expressing the parameters of the potential of a quantum variable as functions of time, gives a time-dependent Hamiltonian. It controls the quantum evolution, which is accompanied by transitions between the levels. This non-adiabatic multilevel dynamic set of equations contains, in principle, tunnel-

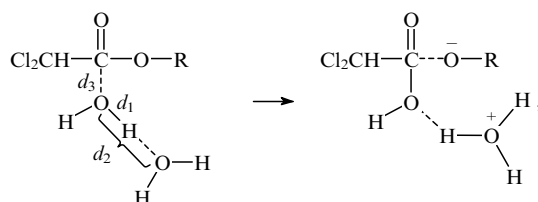
ling effects. The back influence of the quantum subsystem on the classical variables is taken into account using the generalised Hellmann–Feynman theorem; the corresponding classical forces are determined by differentiating the electron–proton PES along the classical coordinates. Since the total quantum state is time-dependent, *i.e.*, it contains several stationary adiabatic components with time-dependent coefficients, their contributions are averaged with time-dependent weights.

Thus, a classical MD computation gives non-pairwise multi-particle forces, which are added to the pairwise Lennard-Jones forces acting between the solvent molecules. As a result, one can obtain a closed self-consistent scheme for the calculation of combined dynamic evolution of quantum and classical coordinates adapted for the use of well-developed MD procedures. This is the main advantage of this scheme; however, the scope of its applicability is not entirely clear. The completeness and self-consistency is attained at the expense of several simplifying assumptions having no convincing substantiation. Moreover, no consistent algorithms for the calculation of reaction rate constants (similar to the reaction flux method in usual classical MD⁵⁵) have yet been formulated within the framework of this theory.

b. Some applications

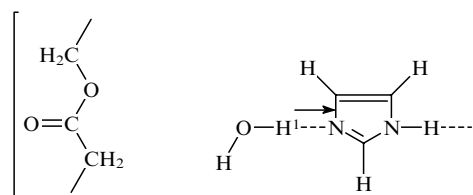
Without further dwelling on the principles of quantum-classical dynamics, we would like to note that there are several versions of its computational implementation, which have been described in reviews.^{225,226} The calculations are rather laborious; most often, they are applied to oversimplified model objects. We restrict our consideration to the studies attempting to apply these procedures to real chemical or even biochemical systems.

Ester hydrolysis. Hydrolysis of esters in a neutral aqueous medium has been studied.²²⁷ The reaction complex of a dichloroacetic acid ester includes two water molecules. The following mechanism was postulated:

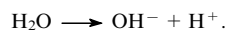


where R is the methoxyphenyl group. The distances d_1 (O–H, quantum variable), d_2 and d_3 (O···O and C···O, two classical variables) were included in the dynamic calculation, while the other coordinates within the complex were optimised. The PES was calculated by the AM1 semiempirical quantum-chemical method with the addition of the reactive field of the solvent to the electronic Hamiltonian. This system, together with 510 solvent (water) molecules, was included in the MD calculation. For the estimation of the rate constant, the procedure described in Section III.4.a was markedly simplified. A mechanism was postulated according to which the most probable pre-reaction configuration of the complex is formed initially and then fast PT takes place in this configuration. The structure of the pre-reaction configuration was also postulated; its formation was considered as a purely classical equilibrium process (as in the TS theory). The free energy change was calculated by the thermodynamic integration method, standard for MD. A temperature dependence of the rate constant (free activation energy is 10.7 kcal mol^{−1}) appears at this stage. The frequency of the quantum transition that contributes to the pre-exponential factor for the PT was then determined by solving the time-dependent Schrödinger equation.²²⁸ The primary result is the value of kinetic H/D isotope effect, equal to 3.9, which is consistent with experimental data.

Enzymic hydrolysis.^{229,230} The active site of the catalytic system of an enzyme (phospholipase A₂) can be represented in the form



During enzymic hydrolysis, dissociation of water molecules takes place



As a consequence, the H¹ atom moves to the imidazole fragment (shown by an arrow).

The system fragment represented in the picture was calculated by quantum-chemical methods (valence bond method calibrated against the data of *ab initio* calculations using the density functional theory). This fragment was inserted into the remaining part of the enzyme structure, which was calculated by molecular mechanics, while its dynamics was simulated by MD techniques. The coordinate of the H¹ proton was assumed to be a quantum one, while the other reaction centre coordinates were taken to be classical and were included in the MD calculation. The combined dynamic calculation of the evolution of the quantum variable and its classical environment was described in Section III.4.a; as has been noted, the reaction rate constant cannot be calculated in this way. Therefore, auxiliary characteristics of the reaction were extracted from the calculation which provided useful information for the understanding of the mechanism of catalysis.

Tentative conclusions. It can be seen from the above examples that model-free quantum-classical calculations still cannot be regarded as a routine tool for chemists. However, good prospects of this approach are beyond doubt. Its practical implementation requires higher computational facilities and development of new, more efficient and reliable calculation algorithms.

Note that in all systems studied by this method, the tunnelling effects were insignificant. They were also insignificant in the test calculations for simple systems that preceded the calculations described above {PT reactions in the [NH₃···H···NH₃]⁺ system,^{229,231} in protonated malonate ion,²²⁸ and in deprotonated water dimer [H–O–H···OH][−] (see Ref. 232) were studied}. The question of the possibility of reliable description of PT kinetics in a deep tunnelling regime in terms of the quantum-classical approach remains open. More promising in this respect is the theory in which the PT or HAT kinetics is considered on the basis of the quantum-mechanical perturbation theory, while the dynamic effect of the medium can be taken into account within the framework of classical MD.²³³ This advanced modification of the multimodal harmonic PT theory (see Section II.4) fully takes into account the anharmonic effects and removes restrictions on the shape of diabatic potentials of the reactants and products. However, practical application of this strategy to PT or HAT processes is still unknown.

IV. Experimental data and summary of calculations of the potential and free energy surfaces

Detailed description of PT and HAT kinetics in the gas phase and condensed media requires determination of the reaction rate constants and the isotope effects over a broad temperature range. These experimental data are, however, available for a small number of reactions, because the temperature range in a particular experiment is often limited due to the destruction of organic molecules and/or crystal melting. In the liquid phase, the temperature variation range is determined by the melting and boiling points of the solvent; in addition, the solubility of many substances sharply decreases with a decrease in temperature. Moreover, the reaction mechanism can change on passing from

one aggregate state to another. For example, many processes involving acids and bases do not proceed in the gas phase but easily occur in polar media;²¹ bimolecular HAT reactions which are barrierless in the gas phase are characterised by high barriers in organic crystals,^{234,235} and crystal field effects can result in asymmetric double-well PES for systems with symmetrical O–H...O fragments.²³⁶ Therefore, experimental data often cannot be interpreted unambiguously without invoking quantum-chemical calculations. In what follows, the conclusions drawn in experimental works are compared, whenever possible, with the data of calculations. Note in this connection that the applicability of quantum-chemical methods is restricted by many factors: the size of the hydrogen-bonded system (not more than 10 heavy atoms), the occurrence of PT or HAT in electronically excited states and the influence of solvation or crystal environment.

1. Gas phase

In descriptions of intramolecular PT in the lower singlet or triplet electronically excited states, the terms of PT and HAT are often used as synonyms. When intra- and intermolecular reactions are considered together and the principles outlined in the Introduction are taken into account, it is expedient to distinguish between these terms. Proton transfer usually involves a step of hydrogen bond formation.²³⁷ The PES for this process is characterised by the presence of a potential well (or two wells), whose depth can exceed the hydrogen bond energy (5–10 kcal mol^{−1}). Hydrogen atom transfer is a radical process; therefore only shallow minima can appear on the PES (about $k_B T$).

Let us consider, for example, two exothermic reactions²³⁸ for which the motion in the reactant and product valleys can be considered translational as a first approximation (see Section II.3.b). One of these reactions is HAT involving neutral molecules and radicals



The other process is an ion–molecular PT reaction



The PES profiles for these reactions are essentially dissimilar (Fig. 11). The PES (93) has a deep minimum [~ 14 kcal mol^{−1} (see Ref. 238)], which corresponds to the formation of the FHCl[−] complex. In addition, reaction (93) involves reactants with closed electronic shells and their electronically excited states lie very high (in $k_B T$ units). The radicals in reaction (92) can exist in different electronic states, F(²P_{3/2}) and F(²P_{1/2}); therefore, correct descrip-

tion of reaction (92) requires that at least two PES be considered.²³⁸

In the general case, HAT in the gas phase can be represented as follows:



where Y = H, D, F, Cl, O, CN; X = H, D, Cl, Br, I, *etc.*^{239,240}

The PT reaction in the gas phase can be described by several schemes:



(Y and X are the same as in the previous case²³⁹);



(Y is water, ammonia, *etc.*²⁴¹);



(YH⁺ is H₃O⁺, X is methylamine²⁴²);



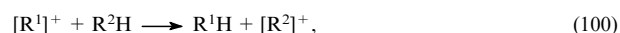
(A and B are either heteroatoms incorporated in the same molecule and linked by an intramolecular H-bond or terminal atoms in hydrogen-bonded dimers, trimers, *etc.*);



(AH and B designate a conjugate acid–base system).

Many HAT reactions [see Eqn (94)] and ion–molecular PT reactions [see Eqns (95)–(97)] are highly exothermic and readily proceed in the gas phase. The intramolecular PT process (98), where A = B (or the synchronous transfer of two protons in dimers with two hydrogen bonds), proceeds in a symmetrical double-well potential and is accompanied by simultaneous rearrangement of the system of double and single bonds. Finally, the gas-phase PT reaction between neutral molecules [see reaction (99)] is endothermic, the equilibrium being often appreciably shifted to the left.^{20,21}

A special type of reaction is represented by hydride ion H[−] transfer, for example



where $[\text{R}^1]^+ = \text{C}_2\text{H}_5^+$, *tert*-C₄H₉⁺ and so on, and R²H are hydrocarbons with 4–8 carbon atoms containing at least one quarternary carbon atom.²⁴³

a. Intermolecular hydrogen atom transfer

A large number of experimental and theoretical works on the intermolecular HAT in the gas phase have been published.^{109–112} The corresponding rate constants and their temperature dependences are systematically summarised and discussed in monographs and reviews.^{244–246} It has been noted above that this reaction follows a radical mechanism and that the pre- and post-reaction states in the gas phase have shallow minima on the PES (depths of about $k_B T$). Therefore, the scattering cross-section is a fundamental characteristic of the process and the methods of process investigation are based on the scattering theory, which describes transition from an unbound state of the reactants into an unbound state of the product (see Section II.3.b). An adequate description of HAT dynamics requires that at least two coordinates be taken into account. In the simplest case, these are the lengths of the breaking and forming bonds of the hydrogen atom. Considerable attention has been devoted to the reaction H₂ + X, where X = H, D, F, Cl, *etc.*^{247–253}

The PES of reaction (92) has a relatively low potential barrier [~ 1 kcal mol^{−1} (Ref. 254)].

The scattering in a system comprising three atoms, ‘heavy–light–heavy’, for example,



requires particular attention because many theoretical methods developed to describe this reaction^{49,255} are applicable to the

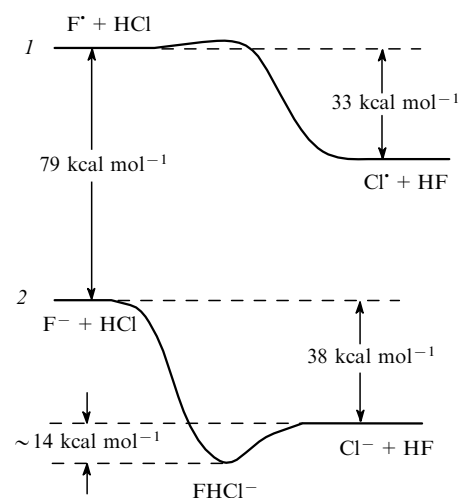
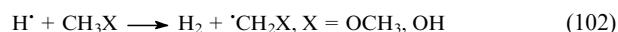


Figure 11. PES profiles for two bimolecular gas-phase reactions. (1) radical HAT reaction, (2) ion–molecular PT reaction.

description of intramolecular PT or synchronous transfer of two protons in dimers (98). The main conclusion of the theory is the possibility of formation of the metastable IHI complex in the PES region corresponding to the TS. The complex is of a dynamic nature. The minimum on the PES is not very deep, about 2 kcal mol⁻¹ (see Ref. 49). However, calculations show that several levels corresponding to symmetric vibrations of IHI may occur in the potential well.²⁵⁶ Experimental studies confirmed the existence of a metastable IHI complex.^{257, 258}

The bimolecular elimination of a hydrogen atom from methanol and dimethyl ether



has been studied both in the gas phase and in aqueous solutions. In the gas phase, this exothermic reaction ($\Delta H \sim -10$ kcal mol⁻¹) was studied over a broad temperature range (298 to 575 °C).²⁵⁹ The H/D-isotope effect is very small; the temperature dependence of the rate constant is well described by the Arrhenius equation. Therefore, it was concluded that no tunnelling effects are involved in reaction (102).²⁵⁹

b. Proton transfer in ion–molecular reactions

Gas-phase PT in ion–molecular reactions of type (95)–(97) have been extensively studied (see reviews^{239, 241, 242, 260}). Ion cyclotron resonance, high-pressure mass spectrometry and flowing after-glow technique were used most often in these studies. The principal results of these investigations include elucidation of gas-phase acidity scales,^{260–264} basicity and proton affinity scales^{242, 264–266} and a detailed description of solvation of the H₃O⁺ ion in the gas phase.²⁶⁷

A large array of kinetic data has been obtained for PT reaction (95) (see Table III in Ref. 239). Depending on the nature of the anion and the ‘acid’ molecule participating in the reaction, its exothermic effect varies from -0.68 to -2.82 eV and the rate constant ranges from 1.5×10^{-10} to 3.7×10^{-14} cm³ (molecule)⁻¹ s⁻¹. Comparison of the kinetic parameters of this reaction with similar data for HAT reactions [see reaction (94)] shows that, with exothermic effects being similar, the rate constant for PT is two or three orders of magnitude higher than the rate constant for the corresponding HAT reaction, which is due to the presence of a deep minimum on the PES of ion–molecular reactions (see Fig. 11).

c. Intramolecular proton transfer

The intramolecular PT and synchronous transfer of two protons in carboxylic acid dimers in the electronic ground state have been studied by radiospectroscopy and vibrational spectroscopy. Symmetrical reactions, *i.e.*, those with equivalent initial and final states, are usually considered. Proton transfer in these reactions shows itself as tunnel splitting of the ground vibrational state. The experimental value of splitting is ~ 21 cm⁻¹ for malondialdehyde,³⁷ varies from 1 to 5 cm⁻¹ for mixed carboxylic acid dimers,³⁶ or equals 1 cm⁻¹ for tropolone.³⁸ Due to procedural difficulties, virtually no data on the tunnel splitting for vibrationally excited states are available.^{36, 268, 269}

The influence of H/D isotope substitution on the tunnel splitting and on the geometric structure of H-bonded systems has been studied. The tunnel splitting for deuterium was found to be strongly reduced (by an order of magnitude). The equilibrium distance between hydrogen-bonded atoms usually increases by ~ 0.02 Å. This is the so-called Ubbelohde effect,²⁷⁰ whose theoretical interpretation is based on the assumption of strong interaction between the coordinate of the tunnelling particle and low-frequency vibrations of hydrogen-bonded heteroatoms.^{3, 78} Theoretical estimates of tunnel splitting are discussed in Sections III.1.c and III.1.d.

Vibration-rotational tunnelling spectroscopy seems to be a promising method for the study of systems with H-bonds in the ground electronic state.²⁷¹ However, this method has not yet been applied to PT reactions.

Numerous publications describe the use of spectroscopy to study PT in the lower singlet electronically excited state S₁ (see Refs 90 and 272). This is due to fast development of spectral methods with high temporal or space resolution based on the use of frequency-controlled lasers.^{42, 273, 274} The studies are usually carried out for large aromatic (pseudo-aromatic) molecules containing one or several functional groups which are linked by an intra- or intermolecular H-bond. The type of PES in the ground electronic state S₀ of the H-bond varies from a symmetric or asymmetric double-well surface to a highly asymmetric single-well one. Upon excitation to the S₁ state of the $\pi\pi^*$ type, the H-bond is usually retained; however, its potential markedly changes.

For systems with a symmetric double-well PES, the potential barrier separating two minima normally decreases along the effective PT coordinate (9-hydroxyphenalenone, tropolone, benzoic acid dimer), which results in a sharp increase in the tunnel splitting of the ground vibrational state.^{40, 275, 276} This is due to substantial shortening of the distance between the atoms linked by the hydrogen bond as a result of electronic excitation and is confirmed by *ab initio* calculations for malondialdehyde and tropolone in the S₀ and S₁ states.^{24, 277, 278}

Electronic excitation of systems with highly asymmetric intramolecular hydrogen bonds often results in an inversion of the H-bond potential.²⁷² The excitation causes a sharp change in the acid–base properties of the functional groups that form the H-bond.²⁷⁹ Proton transfer is accompanied by very fast rearrangement of the system of double and single bonds; therefore, the ‘classical’ keto form is formed in the S₁ state, instead of the zwitter-ion.⁹⁰ This is confirmed by the data of *ab initio* calculations of *o*-hydroxyacetophenone, 2-(2'-hydroxyphenyl)benzimidazole and salicylic acid in the S₀ and S₁ states.^{52, 280, 281} The intramolecular PT in the S₁ state usually proceeds in such systems without a barrier³² and can be regarded as intramolecular vibrational relaxation. This accounts for the very high rate of PT in the S₁ state (more than 10¹² s⁻¹),⁹⁰ typical of systems with hydrogen bonds. The absence of H/D isotope effect for the rate of PT supports the conclusion that the reaction is barrierless. 1,5-Dihydroxyanthraquinone is, apparently, the only system with a highly asymmetric H-bond for which the intramolecular PT was proved to proceed through tunnelling.²⁸²

Transfer of several protons in various hydrogen-bonded complexes in the S₀ state has been studied in a number of theoretical works. Carboxylic acid dimers,^{43, 283–286} hydrogen fluoride oligomers,²⁸⁷ water tetramers,²⁸⁸ methanol tetramers²⁸⁹ and mixed dimers¹⁹¹ have been considered. A synchronous PT mechanism was assumed for the most stable cyclic structures.^{290–292} Various dynamic methods were used to calculate the tunnel splittings on the basis of PES determined by *ab initio* calculations. Note that the magnitude of tunnel splitting is very sensitive to calculation details. Slight variations of the PES caused by the use of different basis sets²⁸³ or insignificant modifications of the dynamic calculation procedure²⁸⁸ can change the resulting value of tunnel splitting by two orders of magnitude. Experimental determination of the tunnel splitting in cyclic molecular complexes by microwave spectroscopy is difficult because of the absence of a permanent dipole moment. It was suggested that synchronous transfer of protons in methanol-based complexes takes place only in cyclic structures with an even number of molecules.²⁸⁹

d. Proton transfer in molecular clusters in the S₀ and S₁ states

Proton transfer in isolated 1:1 asymmetric complexes with one hydrogen bond in the S₀ state is usually not observed in the gas phase.^{293–296} In neutral weak acid–base complexes (FH:NH₃ and PhOH:NH₃), the proton is localised near the ‘acid’ heteroatom. The potential profile along the proton coordinate corresponding to stretching of the O–H bond is single-well and highly asymmetric.^{297, 298} As the strength of the acid increases, the proton moves to the base; the profile remains single-well but becomes

very smooth.²⁹⁸ The potential energy surface for charged 1:1 complexes also has one minimum.^{299,300}

When considering ROH:X_n type clusters where ROH is an 'acid' molecule (phenol, 1-naphthol, *etc.*) and X_n are *n* solvent molecules that interact with the 'acid' (and with each other) through H-bonds, note that most of experimental data correspond to the electronic state S₁. Ammonia or water are used most often as solvents. In the case where X_n = (H₂O)_n for *n* from 1 to 21, no PT was detected.³⁰¹ For X_n = (NH₃)_n, PT does take place in the S₁ state when *n* = 3 for 1-naphthol and *n* = 5 for phenol,^{301,302} because ammonia is a stronger base than water. Clusters consisting of several ammonia molecules, for example (NH₃)₅, are known to have a fairly high proton affinity.²⁰ Thus, the PES of phenol or 1-naphthol clusters with ammonia in the S₁ state can have two minima.

Experimental and theoretical data allow one to draw an important conclusion, namely, there exists a threshold number of solvent (ammonia) molecules starting from which PT is possible^{301–308} and an adequate description of the PT dynamics requires explicit consideration of the collective coordinate, which describes synchronous motion of molecules forming the first solvation shell^{309,310} and ensures favourable energy characteristics for the PT process.³¹¹

2. Liquid phase

The structure of the reaction site (and the whole reaction system) in the liquid phase depends on the properties of the solvent (polarity, proton-donor or proton-acceptor characteristics), reactant concentrations, temperature and impurities. Proton or hydrogen atom transfer is accompanied by the rearrangement of the solvation shell of the system,^{312–314} which sharply complicates the process description at the molecular level. During the last five decades, enormous experimental material on liquid-phase reactions has been accumulated; however, interpretation of the results is the underbelly of most studies. The key problem is the difficulty of experimental determination of the geometric structures of reaction products in the liquid phase. In many cases, the product structures are postulated in order to bring the experimental data in the correspondence with the model used. The model is usually based on representing the isolated reaction complex as A–H...B or on placing the reaction complex in a cavity surrounded by a dielectric.

Thus, the molecular structure of the solvent and the problems caused by the presence of impurities (traces of water), counter-ion, complexation, *etc.* are usually neglected in the interpretation of experimental data.

a. Proton transfer between neutral molecules in aprotic solvents

A number of terms are used in the literature to describe the PT in organic aprotic solvents:³¹⁵ proton exchange reactions, molecular exchange between H-bonded complexes, ion–molecular PT, and reversible PT in H-bonded complexes. The last-mentioned term appears the most appropriate for describing the PT between neutral molecules [see Eqn (99)]. Phenol and carboxylic acid derivatives are usually considered as acids, and pyridine derivatives, pyridine *N*-oxides and aliphatic amines are taken as bases. Halogen-substituted hydrocarbons and acetonitrile are the most typical solvents.

The proton transfer in H-bonded complexes is accompanied most often by a substantial increase in the dipole moment (to 10 D),³¹⁶ pointing to an appreciable change in the geometric and electronic structures of the complex induced by PT. The changes are detected by NMR, IR and UV spectroscopy and by measurement of dielectric properties. It is clear that in a 'strong base–weak acid' system, the equilibrium is shifted almost entirely to the left, while in a 'weak base–strong acid' system, it is shifted to the right. The degree of shifting of equilibrium (99) can be found from a plot where the value

$$\Delta pK_a = pK_a(\text{HB}^+) - pK_a(\text{AH}),$$

where *pK_a* (the proton affinity), is laid off along the *x*-axis, while the *y*-coordinate is an observed quantity (the change in the dipole moment,³¹⁷ the ¹H, ¹³C or ¹⁵N NMR chemical shift,³¹⁸ integral intensity of the A–H stretching vibration³¹⁹ or the centre of gravity of this band,³²⁰ *etc.*). Usually, this gives an S-shaped curve whose inflection point corresponds to a 50% degree of PT. A feature of these dependences is sharp change in the spectral characteristic over a small range of variation of ΔpK_a . The proton affinity,³²⁰ the enthalpy of formation of the H-bonded complex,³²¹ or another quantity can be used instead of ΔpK_a . The plots obtained in this case will have a break. A unified theory for explaining these dependences is missing. It was suggested³²² that a mobile equilibrium of the considered type exists in the liquid phase but this hypothesis provoked a lot of debate. According to another publication,³²³ only one complex is formed in each case in which the proton shifts from A[–] to B⁺ as the base becomes stronger and the acid becomes weaker. Nevertheless, in some cases, mobile equilibrium still does exist because the dependence under discussion does not have any break in systems without PT.³²⁴

Equilibrium (99) has been repeatedly studied by UV spectroscopy.^{21,325,326} It was shown that depending on the dielectric constant of the solvent³²⁷ or the solution pH,³²⁸ different complexes with H-bonds are formed, in particular the A[–]...H–B⁺ complex with the transferred proton. The UV absorption bands of these complexes markedly differ in frequency and intensity.

Most of the studies mentioned above give only qualitative characteristics of PT: the structure with the transferred proton is detected and the degree of PT is estimated. The reported equilibrium constants of the PT process (see, for example Refs 317 and 329) are often phenomenological (*i.e.*, they characterise a complex multistep process whose detailed mechanism is unknown). In the case of relatively weak acids and bases, the following reactions are most probable:^{330–333} dimerisation of carboxylic acids or polymerisation of phenols; dissociation of the structure with a transferred proton to give free ions; and self-association of complexes with a transferred proton.

With excess free acid or base, other side reactions can also proceed to give ions like (BHB)⁺, (AHA)[–], *etc.*^{334–336} A review of the literature published before 1968 dealing with the secondary processes that accompany PT in solutions can be found in Chapter 8 of the monograph (Ref. 337).

It follows from the foregoing that experimental determination of the rate constant for a PT reaction in the conjugate acid–base system in an aprotic solvent in the S₀ state is a rather complicated task. Quantitative estimates of the PT kinetics in aprotic solvents were obtained in a number of the most recent studies.^{338,339} The kinetic H/D-isotope effect in the reaction between 2,4,6-trinitrotoluene and 1,8-diazabicyclo[5.4.0]undec-7-ene in benzonitrile was found to change from 18.3 to 14.5 as the temperature rises from 288 to 308 K.³³⁸ The ratios of the pre-exponential factors (~2.5) and the difference between the activation energies (~2.1 kcal mol^{–1}) are also reported. In is suggested that these values point to a tunnelling mechanism of PT.

In a study of the PT in the complex of 2,4-dichlorophenol with triethylamine in chloroethane,³³⁹ measurement of the temperature dependence of the chemical shift of the bridging proton made it possible to establish thermodynamic and kinetic characteristics of the PT process. It was concluded that in this case, the FES is almost symmetrical and has two minima. The free activation energy of PT at 195 K is only 8.9 kcal mol^{–1} and the heat of the reaction is 0.2 kcal mol^{–1}. The rate constant of the forward PT reaction is 605 s^{–1}. The concentration dependences of these values were not studied in this publication;³³⁹ therefore, the assignment of these characteristics to the PT process is not validated. Rather high reactant concentrations were used, 0.2 mol litre^{–1} for phenol and 0.4–0.6 mol litre^{–1} for amine. At these concentrations, dissociation of aggregates with high-molecular masses to give kinetically active components rather than the PT is the rate-determining step of the process.³⁴⁰

Subsequently, the occurrence of a competing process, namely, the formation of a complex consisting of two 2,4-dichlorophenol molecules and one triethylamine molecule was discovered.³³¹

The PT kinetics in the S_1 state has been characterised more comprehensively than that for the S_0 state.^{341–346} Depending on experimental conditions (temperature and solvent) and the nature of the reactants, the rate of this reaction can be limited by either non-adiabatic transitions or diffusion processes.³⁴⁷

The results of some other studies are briefly considered below. Study of H-bonded complexes of 7-hydroxyquinoline and methanol by UV spectroscopy³⁴⁸ showed that PT takes place in the S_1 state of the 1:2 complex. The activation energy of this process equals $0.54 \text{ kcal mol}^{-1}$. The activation energy of the 'back' PT in the S_0 state is $4.2 \text{ kcal mol}^{-1}$ in CH_3OH and $5.5 \text{ kcal mol}^{-1}$ in CH_3OD .

The PT kinetics in the S_1 state of 2-(2'-hydroxyphenyl)benzothiazole in aprotic non-polar solvents has been studied by femtosecond spectroscopy.^{35,349,350} The formation of the keto-form upon PT was confirmed by the appearance of a spectral band corresponding to the N–H stretching vibrations.³⁴⁹ The characteristic time of the PT is equal to 170 fs.³⁵ In 2-(2'-hydroxyphenyl)benzothiazole derivatives, the PT time varies from 100 to 200 fs. These times correspond to the motion of a proton with a great vibration amplitude and a frequency varying from 100 to 200 cm^{-1} (see Ref. 350). A similar procedure has been used to estimate the rate constant for the PT in a 1-pyrenol–triethylamine complex using a number of organic solvents.³⁵¹ The characteristic time was equal to 1 ps and almost did not depend on the solvent polarity; the replacement of the bridging proton by deuterium also had only a slight influence on the rate constant.³⁵¹

The kinetics of PT in the lower triplet electronically excited state has been studied in a number of publications.^{352–355} The keto–enol tautomerism in the lower triplet state of 2-(2'-hydroxyphenyl)benzothiazole in hexane has been investigated.³⁵² It was found that the observed rate constant for PT almost does not depend on temperature below 70 K. The H/D-isotope effect is 30 at 200 K and more than 100 at 100 K. Proton transfer was concluded to follow a tunnelling mechanism.

Quantum-chemical calculations of the PES of a PT reaction in the S_1 state are usually carried out without explicit allowance for the presence of a solvent. High-level *ab initio* calculations^{278,356} are used when considering model photochemical systems, for instance, CIS calculations^{357–358} are used for real systems with intramolecular PT (1-hydroxy-2-acetophenone³⁵⁷) or double PT (7-azaindole dimer^{358,359}).

A number of kinetic data have been obtained for synchronous transfer of several protons in hydrogen-bonded complexes in the S_0 state. Proton exchange in formic acid and methanol clusters in perdeuterated tetrahydrofuran has been studied by NMR spectroscopy.³⁶⁰ The acid and methanol form 1:1 and 2:1 hydrogen-bonded complexes in which transfer of two or three protons (deuterons), respectively, takes place. The rate constant was measured in the temperature range from 255 to 335 K. No deviations from the linearity of the Arrhenius plots were found. The activation energy varies from 6.5 to 10 kcal mol^{-1} .

The PT reaction in the porphyrin ion³⁶¹ and the double proton transfer in the porphyrin molecule³⁶² in various aprotic solvents have also been studied by NMR. In these systems, one or two protons move in a four-well potential. The rate constants for hydrogen, deuterium and tritium transfer were determined over a broad temperature range. The Arrhenius dependence is clearly non-linear. The kinetic H/D-isotope effect equals 93(34) at $T = 240 \text{ K}$ and 16.5(11.4) at $T = 298 \text{ K}$; the values for the porphyrin molecule are given in parentheses.

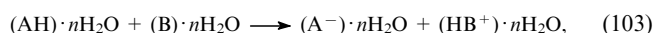
The mechanism of double PT in the formic acid dimer in the S_1 state in aprotic solvents has been studied in detail,³⁶³ although there is still no consensus about its nature.

The PT structure and dynamics in the H-complexes of the $\text{M–H}\cdots\text{H–OR}$ type, where M–H is the $(\text{PMe}_3)_2(\text{CO})_2$, $(\text{NO})\text{W–H}$ hydride ligand and H–OR is trifluoroacetic acid,

have been vigorously studied in the last decade.³⁶⁴ Low-temperature NMR and IR spectroscopy were used to obtain information on the PT kinetics and the activation barrier depending on the properties of $\text{H}\cdots\text{H}$ complexes, determined by the nature of the metal, the ligands and the medium (hexane, toluene and dichloroethane).^{365,366}

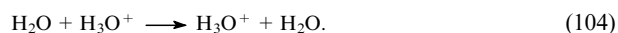
b. Proton transfer in protic solvents

Proton transfer in protic solvents (water, alcohols, *etc.*) requires special consideration because the reaction complex forms additional H-bonds with solvent molecules.³¹⁴ This complicates the PT and in some cases, also changes the reaction mechanism. Usually, four types of PT reactions in aqueous solutions are distinguished:³⁶⁷ neutralisation, protolysis, hydrolysis and PT in a conjugate acid–base system. The first three reactions are complex processes, in which one cannot distinguish the individual characteristics of an elementary PT step. The last-mentioned reaction can be described as follows



where n is the number of water molecules that interact with reacting molecules through the formation of H-bonds.

A large number of publications has been devoted to so-called abnormally high proton mobility in aqueous solutions. To interpret the obtained data, it is necessary to know the structure of the simplest stable proton hydrate. X-Ray diffraction and neutron diffraction methods as well as NMR provide little information due to the thermal motion of molecules in the liquid. Conclusions about the structure of the simplest proton solvate in aqueous solutions of acids are usually drawn by examining the vibrational spectra. It has been suggested initially that the simplest proton solvate is the hydroxonium ion, H_3O^+ (see Ref. 368). Thus, PT in the aqueous medium can be represented as



The PT process in water enriched in the ^{17}O isotope has been studied by NMR in the temperature range from 288 to 348°C .^{369,370} The rate constant was found from broadening of the spectral lines. The results were described by the Arrhenius equation in which the rate constant for the PT is

$$k = 6.0 \times 10^{11} \exp\left(-\frac{2.4}{RT}\right) \text{ litre mol}^{-1} \text{ s}^{-1}.$$

Thus, PT in water has a low activation energy. The lifetime of the simplest proton hydrate is 1 ps. (Most of modern theoretical studies rely on these experimental data; for example, see Ref. 371.) The hydroxonium ion really exists in solid and liquid systems if only one water molecule per acid proton is present.³⁶⁸ The existence of this ion, whose vibrations are both IR- and Raman-active, in dilute aqueous solutions of acids is not confirmed experimentally.^{372,373}

The IR spectra of all systems containing proton hydrates exhibit continuous intense absorption in the range from 3500 to 800 cm^{-1} (see Ref. 374). Studies devoted to this phenomenon are discussed in several reviews.^{45,375} According to Zundel's model,³⁷⁶ H_9O_4^+ is the most stable ion–molecular species whose vibrations can be observed in the IR spectrum of a solution. In this model, a special role is played by the extremely high polarisability of the hydrogen bond. This feature is postulated for the $\text{O–H}\cdots\text{O}$ fragment. The origin of the continuous absorption can be explained by assuming strong interaction of the bridging proton with the medium. This model is widely used in many theoretical and experimental works, despite the fact that continuous absorption is observed when the formation of the H_9O_4^+ ion is impossible and the solvation effects are minimised (aprotic low-field solvent).^{377,378} Thus, continuous absorption may be due not only to the influence of the medium but also to intrinsic properties of ions with a symmetrical hydrogen bond, the simplest of them being the H_5O_2^+ ion.³⁷⁹

A particular theory could, in principle, be validated by MD simulation of the IR spectra. However, applicability of MD techniques to the simulation of spectral properties of the proton in aqueous solutions is quite limited. The trajectory length found by so-called *ab initio* MD methods³¹² is several picoseconds; this is inadequate for calculating the IR spectrum of the solution.³⁸⁰ Molecular-dynamic approaches based on the valence bond method either make use of a linear approximation of the system dipole moment^{381, 382} or imply calculation of the vibrational spectrum by Fourier transform of the velocity autocorrelator.³⁸³ However, the linear approximation is inapplicable to the description of the dipole moment of the H_5O_2^+ ion^{379, 384} and the velocity autocorrelator was calculated for the Raman spectrum of this ion.³⁸⁴

Experimental data on PT reactions in protic solvents can be found in several reviews.^{385, 386} A widely used non-aqueous solvent is methanol, which makes it possible to measure the rate constant for the PT over a broad temperature range, from -97 to 64°C .³⁸⁷ The double PT in the $(\text{CH}_3)_3\text{NH}^+ + \text{CH}_3\text{OH} + \text{N}(\text{CH}_3)_3$ system in methanol has been studied by NMR spectroscopy.³⁸⁸ It was found that the activation energy decreases with an increase in the temperature: from $3.8 \text{ kcal mol}^{-1}$ at -97.8°C to $2.2 \text{ kcal mol}^{-1}$ at 25°C ; a tunnelling mechanism for double PT was proposed.

The influence of the solvent on the PT can be taken into account using the variational TS theory (see Section III.1.b), numerical MD or Monte Carlo modelling (see Section III.2.b), models in terms of the continual description of the medium (see Section III.3), or various quantum-classical methods (see Section III.4). Molecular dynamics methods have been successfully used to describe PT in acid–base equilibria¹⁹⁹ and in model systems²³¹ simulating ionisation of HCl in water³⁸⁹ and ester hydrolysis.²²⁷ Self-consistent reaction field methods were used to simulate the PT dynamics in systems with strong hydrogen bonds²²³ and in amino acids.²²⁴ Combined (hybrid) approaches were used to describe the solvation of the hydroxide ion,³⁹⁰ to model PT in systems with strong hydrogen bonds²³² and to calculate barriers to the PT reaction in water.³⁹¹

c. Hydrogen atom transfer in liquids

A large number of reactions involving HAT take place in liquids. In particular, HAT limits the chain termination during oxidation of organic compounds in the liquid phase.³⁹² Data on the rate constants for HAT and the influence of the H/D isotope effect on these constants are summarised and discussed in monographs and reviews (see, for example, Refs 393–395), although usually it is impossible to draw an unambiguous conclusion on the magnitude of the tunnelling effect on the basis of experimental data because no reliable data on the temperature dependence of the kinetic H/D-isotope effect in HAT are available.

The hydrogen atom transfer in the first step of oxidation of 4a,4b-dihydrophenanthrene with dioxygen in 2,2,4-trimethylpentane has been studied at $T = 191\text{--}263 \text{ K}$.³⁹⁶ In this case, the Arrhenius plot is essentially non-linear. The experimental H/D-isotope effect is 95 at 242 K .³⁹⁶ Arrhenius parameters were also found for the bimolecular elimination of a hydrogen atom from methanol in aqueous solutions in the temperature range from 283 to 359 K .³⁹⁷ The corresponding activation energy amounted to 30 kJ mol^{-1} and the observed rate constant at 25°C was $2.8 \times 10^6 \text{ litre mol}^{-1} \text{ s}^{-1}$. Comparison with the data for gas-phase reactions²⁵⁹ shows that the interaction with the solvent leads to some acceleration of the reaction ($\sim 25\%$).

A lot of data have been accumulated for intramolecular HAT.³⁹⁸ In most cases, the experimental values for the kinetic isotope effect do not exceed 3.³⁹⁸ The intramolecular HAT involved in the isomerisation of aryl radicals with bulky substituents has been characterised in sufficient detail.^{399, 400} Isomerisation of 2,4,6-tri-*tert*-butylphenyl into 3,5-di-*tert*-butylneophenyl in cyclopropane has been studied by EPR in the temperature range from 113 to 247 K . It was found that due to

steric hindrance, the abstraction of hydrogen from the solvent molecule is virtually impossible. Hydrogen atom transfer proceeds via a five-membered cyclic TS. The Arrhenius plot for the transfer of hydrogen and deuterium atoms is highly non-linear. The experimental kinetic H/D-isotope effect varies from 80 at 250 K to 13 000 at 120 K .

Various approaches are used for theoretical investigation of HAT reactions in the liquid phase. The variational TS theory is successfully used to calculate the temperature dependences of the reaction rate constant, H/D-isotope effect, the addition of a hydrogen atom to benzene⁴⁰¹ and elimination of a hydrogen atom from methanol⁴⁰² in aqueous solutions. Empirical models for the radical abstraction of hydrogen^{403, 404} are used to classify the results of analysis of the experimental rate constants and activation energies for HAT reactions.

d. Proton transfer in ion–molecular reactions in the liquid medium

A PT reaction results in highly reactive systems: carbanions, carbocations, carbenes and ylides, *etc.* Therefore, ion–molecular reactions involving PT play an important role in organic chemistry.^{405, 406} The rate and equilibrium constants for such reactions are determined by a variety of factors including the spatial and electronic structures of the reactants, their concentrations, the natures of the solvent and the catalyst and so on. Direct approach to the problem of elucidating the structure–reactivity relationship based on quantum chemistry and statistical physics techniques is seldom used for complex organic compounds. As a rule, methods of physical organic chemistry are used.^{337, 405–407} At this level, the mechanisms of chemical reactions are considered in terms of empirical and semiempirical rules. These rules can be formulated in a quantitative form as linear free energy relationships.³³⁷ Interpretation of the obtained results can be simplified by considering so-called intrinsic barriers (*i.e.*, barriers for symmetrical reactions²⁶) and the intrinsic rate constants for the PT in ion–molecular reactions.^{408, 409} From the kinetic standpoint, this situation occurs in the case where the rates of forward and back reactions are equal, and from the thermodynamic standpoint, where the reaction heat is zero irrespective of temperature and pressure. The use of intrinsic rate constants allows one to separate the thermodynamic effects from purely kinetic effects.

The dependences of the rate constant for PT on the nature of the solvent, the substituents and the strength of the base are studied most often.^{410–413} In the case of PT in carboxylic acids, this provides detailed characterisation for the relative contributions of the resonance and induction effects and the nature of the solvent to the increase in the CH acidity.^{411, 413} For PT reactions involving radical cations, negative activation energies and H/D-isotope effect values smaller than unity are often obtained.⁴¹² This may imply the existence of mechanisms alternative to the direct PT from the radical cation to the base. The H/D-isotope effects in the PT rate constant for the reaction of various methylarene radical cations and pyridine bases in dichloroethane have been estimated.⁴¹⁴ Depending on the structure of the reactants, they vary from 31 to 47. In the studies cited, the rate constants were usually determined at room temperature.

Numerous experimental works have been devoted to the PT from nitroalkanes to anions of various bases.⁴¹⁵ Usually these reactions are studied by spectrophotometry because the anions formed in the reaction exhibit strong absorption bands in the visible region. The PT from 1-nitro-1-(4-nitrophenyl)ethane to the hydroxyl ion has been studied. Aqueous acetonitrile was used as the solvent. The reaction was found to occur in two steps, the PT process taking place in the second step, which follows a unimolecular mechanism (irreversible decomposition of the ‘kinetically important’ intermediate). The PT kinetics has been studied in detail in the temperature range from 289 to 319 K . The rate constant for the PT (289 K) is 11.5 s^{-1} and the primary isotope effect is 26. As the temperature increases to 319 K , the isotope effect decreases to 16.9. The difference between the activation energies and the ratio of the pre-exponential factors for proton

and deuteron transfer have been estimated.⁴¹⁵ The researchers believe that the obtained data point unambiguously to the tunnelling mechanism of the PT reaction.

e. Coupled electron and proton transfer

Coupled electron and proton transfer can occur for the electronically excited states of organic molecules containing two functional groups (for example, 6-hydroxyquinolinone) in aqueous solutions of acids or bases;⁴¹⁶ in donor–acceptor pairs such as Ru(bipyridine)₃²⁺–3,5-dinitrobenzene;⁴¹⁷ in ruthenium complexes on a polycrystalline gold electrode;⁴¹⁸ in triads consisting of carotenoid–porphyrin–quinone molecules;⁴¹⁹ in proteins;⁴²⁰ in photoactive centres of bacteria.⁴²¹

The reaction in question takes place in a complex system which includes an electron and proton acceptor (Ac), several H-bonds and heteroatoms with a free electron pair and a proton donor (H-Dp). Its mechanism includes several successive steps:⁴²² (i) electron transfer on Ac to give a radical anion having a high proton affinity; (ii) the formation of a covalent bond between the radical anion Ac^{•−} and the proton; (iii) rearrangement of the system of hydrogen bonds resulting in elimination of the proton from the H-Dp donor to give the Dp^{•−} anion; (iv) recovery of Dp^{•−} to Dp; (v) the reverse rearrangement of hydrogen bonds resulting in the formation of the initial Ac and H-Dp.

The central point of this scheme is a sharp enhancement of the proton-acceptor properties of the molecule (functional group Ac) and the proton-donor properties of the molecule (functional group H-Dp) upon their oxidation. The rate-determining step of the reaction is electron transfer;⁴¹⁷ nevertheless, the rate constant changes when the bridging H atoms are replaced by D in the Ru(bipyridine)₃²⁺–3,5-dinitrobenzene donor–acceptor pairs.⁴¹⁷ Experimental value for the H/D-isotope effect in the electron transfer varies from 1.34 to 1.7.⁴¹⁷

The theory of these reactions is considered in Section III.3.d; the key references to theoretical studies are also given.

f. Proton and hydrogen atom transfer in biologically active compounds

Proton, hydrogen atom, and hydride ion transfer underlie a large number of processes which take place in biologically active compounds.

First, proton transfer plays a key role in bioenergetics,⁴²³ which is concerned with the mechanisms of energy conversion in redox processes in living organisms. The modern views in this field are based on the ‘chemiosmotic theory,’ which implies the presence of an electrochemical potential difference (‘proton gradient’) in protein complexes^{424,425} and in cytochrome *c*-oxidase.^{426,427} Proton transfer through membranes takes place against the proton gradient, the thickness of biological membranes being about 40–60 Å.⁴²⁵

Second, proton and hydride ion transfer are key steps in one of the most versatile biological oxidation reactions, namely, dehydrogenation of an alcohol to give a ketone or an aldehyde.^{428,429} The process is catalysed by dehydrogenase enzymes. These are dimers or tetramers composed of subunits with a molecular mass of 20 000–40 000. The removed hydrogen atoms (or hydride ions, or protons) migrate to hydrogen-transporting coenzymes, for example, nicotinamide adenine nucleotide, *etc.* The mechanism of this process is not entirely clear.⁴³⁰

Third, a large number of studies have been devoted to the role of strong (short) hydrogen bonds in enzyme-catalysed reactions.¹³ These hydrogen bonds are assumed to stabilise intermediates and/or transition states in the reactions under interest.¹⁴ On the PES of these H-bonds, two wells are separated by a very low barrier (~ 2 kcal mol^{−1}).¹⁵

For the first two of the above-mentioned types of process, detailed description of the thermodynamics and kinetics of PT and hydride ion transfer is missing. Therefore, of considerable interest are kinetic studies of HAT in enzymes.⁴³¹ Enzyme-catalysed C–H bond cleavage has been studied in detail.^{432–433} A specific

feature of this reaction is a very high kinetic H/D-isotope effect, which varies from 17 (see Ref. 434) to 56 (see Ref. 432). Hydrogen atom transfer in these systems is a rate-determining step of the complex process of C–H bond oxidation,⁴³⁴ the rate constant for HAT ranging from several to several hundred reciprocal seconds. Study of the temperature dependence of the rate constants for H and D made it possible to estimate the activation energy, which can reach 24.5 kcal mol^{−1} (see Ref. 433) and the pre-exponential factor. These experimental data suggest that HAT follows a tunnelling mechanism.

Extensive literature is devoted to the theoretical study of PT and HAT reactions in enzymic systems. In order to give a general idea of the methods and approaches used in this, rather specific field, we will mention the results of some most recent studies. Widely used are hybrid approaches^{435–437} which combine quantum-chemical calculations of the PES in the models of reaction centres with calculation of the medium effects using MD or molecular mechanics methods. Oxidation of the enzyme cytochrome P450eryF has been studied;⁴³⁵ proton tunnelling is described as a one-dimensional process (see Section III.1.a). The rate constants for HAT for three model enzymic reactions were calculated in terms of the variational transition state theory;⁴³⁶ the calculated kinetic H/D-isotope effect is in satisfactory agreement with the experiment. The energy profiles of the PT involved in the hydrolysis of peptide bonds by a model enzyme have been obtained.⁴³⁷ Phenomenological models have been used to describe the PT through biological membranes.⁴³⁸

3. Solids

The tunnelling mechanism of PT and HAT reactions in solids has been proved experimentally for a relatively small number of systems. These processes include both intermolecular and intramolecular reactions taking place in molecular crystals and in glasses. The results obtained are analysed in several reviews.^{99,157,439–442} The conclusion concerning the tunnelling mechanism of the reactions is based on three facts:

- the temperature dependence of the reaction rate constant *k* found experimentally deviates from the Arrhenius dependence over a broad temperature range, the Arrhenius dependence (*i.e.*, a linear dependence of log *k* on the reciprocal temperature) being observed at relatively high temperatures;
- a large H/D-isotope effect for the PT and HAT rate constants is found;
- the rate constants reach a plateau at relatively low temperatures.

a. Proton transfer reactions

The intramolecular PT in the molecular crystals of 9-hydroxyphenalenone derivatives has been studied by IR spectroscopy.^{443,444} At 5 K, the IR spectra of 5-bromo- and 5-iodo-9-hydroxyphenalenone exhibit intense bands at 83 and 68 cm^{−1}, respectively. These bands disappear when the bridging proton is replaced by deuterium. It was suggested^{443,444} that these bands correspond to tunnel splitting of the ground vibrational state in non-deuterated molecules.

The proton transfer in carboxylic acid dimers in the solid state often differs sharply from similar processes in the gas phase or in solutions. The reason is the crystal field effect, resulting in asymmetry of the FES along the PT coordinate for the O–H $\cdots$ O fragment, as opposed to the symmetric FES for the gas phase.^{73,74} In the case of a molecular crystal of the benzoic acid dimer, the asymmetry was 35 cm^{−1} (non-deuterated compound) and 108 cm^{−1} (deuterated compound).²³⁶ By passing to crystals doped with dye molecules, the crystal field effects can be minimised.⁴⁴⁵ The double proton transfer in the crystals of benzoic acid dimer was studied by optical spectroscopy,⁴⁴⁶ NMR^{73,74} and quasi-elastic neutron scattering^{446,447} over a broad temperature range. A sharp increase in the rate of proton transfer upon excitation of definite low-frequency vibrations has been established experimentally.⁷³ It was shown that the exper-

imental data (the NMR longitudinal relaxation time) can be adequately interpreted only using at least two-dimensional FES.⁷⁴

Some data on PT dynamics have been obtained by non-elastic neutron scattering for various crystals with intra- and intermolecular hydrogen bonds.^{448–454} Alternative models for the $N\cdots H\cdots O$ hydrogen bond, ionic^{448,449} and neutral ones,^{451,452,454} have been proposed for PT in *N*-methylacetamide crystals (this process is a prototype of PT in peptides). The reasons for choosing these models are not analysed and remain obscure.

b. Hydrogen atom transfer

Apparently, a tunnelling mechanism of the HAT reaction in a solid was observed experimentally for the first time by Wang and Williams,⁴⁵⁵ who studied the kinetics of hydrogen atom capture by methyl radicals in crystalline methyl isocyanate using EPR in the temperature range from 77 to 125 K. The Arrhenius plot for the corresponding rate constant is non-linear. The observed activation energy for the HAT reaction was 1.4 kcal mol^{−1} at 77 K and increased to 4.5 kcal mol^{−1} at 120 K. The isotope effect at 110 K exceeded 1000. It was impossible to obtain a more precise value, as the rate of abstraction of a deuterium atom was too low in the given temperature range to be measured by EPR. Later, a low-temperature limit of the HAT reaction rate has been found experimentally.⁴⁵⁶ Detachment of a hydrogen atom from a methanol molecule (in glasses) by a methyl radical was studied by EPR in the temperature range from 15 to 89 K. At 40 K, a low-temperature plateau was reached. Analogous results have been obtained in a study of hydrogen atom elimination by a methyl radical from acetonitrile,⁴⁵⁷ methanol⁴⁵⁸ and other molecules.^{399,400,459}

A large body of experimental data on the rate constant and H/D isotope effect in the temperature range from 1.4 to 300 K and for pressures from 1 to 30 atm has been obtained for HAT in the fluorene molecular crystals doped with acridine molecules.¹⁵³ In the lower triplet electronically excited state of the acridine admixture, the hydrogen atom is detached from the nearest fluorene molecule and passes to the acridine nitrogen atom. A typical feature of this reaction is the presence of several low-frequency (intra- and intermolecular) modes whose excitation accelerates HAT. This conclusion is based on investigation of the Raman spectra of these crystals at different temperatures.¹⁵⁴ For this reaction, calculations of the PES,⁴⁶⁰ in particular those with explicit allowance for the crystal environment²¹⁶ were published. (The interpretation of the temperature dependence of the rate constant¹⁵² is discussed in Section II.4.c.)

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V. Supplement I. Generalised Langevin equation

For a stochastic variable x corresponding to an oscillator with the mass m_x , the frequency ω_x and the force constant $\mu_x = m_x\omega_x^2$, the generalised Langevin equation (GLE) is written in the form^{55,56,132,461}

$$m_x\ddot{x} + \int_0^t \beta(t-\tau)\dot{x}(\tau)d\tau + \mu_x x = \text{GRF}, \quad (\text{I.1})$$

where GRF is the Gaussian random force (time-dependent). Due to the presence of the dissipative integral term, the dynamics of the coordinate $x(t)$ at time t is dictated by its preceding evolution during the time period $(0, t)$. Such equations are called equations with memory or non-Markov equations. The function $\beta(\tau)$ is called the memory kernel. The regular force $\mu_x x$ is linearised; as a result, Eqn (I.1) describes a harmonic oscillator in a medium. The force linearisation is not obligatory; if the corresponding potential $U(x)$ is not quadratic, the force $(-\partial U/\partial x)$ is used. The generalised

Langevin equation with a double-well potential corresponds to the Kramers equation (13) and reduces to the latter if $\beta(t-\tau) = \gamma\delta(t-\tau)$. This particular case is called the local or Markovian limit. Equation (I.1) can be written in an alternative form

$$m_x\ddot{x} + \int_0^t \phi(t-\tau)x(\tau)d\tau + \bar{\mu}_x x = \text{GRF}, \quad (\text{I.2})$$

with a renormalised force constant

$$\bar{\mu}_x = \mu_x + \beta(\tau=0).$$

The dissipative force in Eqn I.2 depends on the coordinate rather than on the rate. The memory kernels $\beta(\tau)$ and $\phi(\tau)$ are related as follows:

$$\beta(\tau) = \int_\tau^\infty \phi(\tau')d\tau'. \quad (\text{I.3})$$

Important in the GLE theory is the Fourier–Laplace transform^{462,463}

$$\phi(\omega) = \int_0^\infty \exp(i\omega t)\phi(t)dt = \phi_1(\omega) + i\phi_2(\omega), \quad (\text{I.4})$$

where $\phi(\omega)$ is a complex function, its real $[\phi_1(\omega)]$ and imaginary $[\phi_2(\omega)]$ components being even and odd functions of frequency, respectively.

In the steady-state regime, the average $\bar{x} = \langle x \rangle_T$ value is constant. Here $\langle \dots \rangle_T$ means averaging over an equilibrated ensemble with temperature T . The correlation function of the coordinate x is the fluctuation thermal average

$$C(t) = \langle [x(0) - \bar{x}][x(t) - \bar{x}] \rangle_T. \quad (\text{I.5})$$

When $t = 0$, this gives a statistical distribution of the stochastic variable x with the variance $D[x] = C(t=0)$. The Fourier transform of the function $C(t)$

$$C(\omega) = \int_{-\infty}^\infty \exp(i\omega t)C(t)dt \quad (\text{I.6})$$

is related to the imaginary part of the Fourier image of the memory kernel by the relation

$$C(\omega) = \hbar\phi_2(\omega)\text{cth}\frac{\hbar\omega}{2k_B T}. \quad (\text{I.7})$$

This relation is called fluctuation-dissipation theorem (FDT).^{132,461–463} Relation (I.7) holds for quantum systems, its range of applicability being wider than that for the classical GLE (I.2). At the classical limit ($\hbar\omega/k_B T \ll 1$), equation (I.7) assumes the form

$$C(\omega) = \frac{2k_B T}{\omega}\phi_2(\omega). \quad (\text{I.8})$$

Since the function $C(t)$ can be calculated by molecular dynamics methods, relations (I.7) and (I.8) open up the way to microscopic calculation of the key GLE parameters. According to the KGH theory, in the case of GLE with a double-well potential $U(x)$ having a barrier with the height $U^\ddagger$, the following approximate expression for the reaction rate constant is valid:^{55,60,464–469}

$$k_{\text{KGH}} = \frac{\Omega}{2\pi} \sqrt{\frac{\mu_x}{\mu^\ddagger}} \exp\left[-\frac{U^\ddagger}{k_B T}\right]. \quad (\text{I.9})$$

Here, Ω is the decay frequency, which is determined by the characteristic equation

$$\begin{aligned}
-m_x \Omega^2 + \phi(\Omega) + [\mu^\neq - \phi(\omega = 0)] &= 0, \\
\mu^\neq &= m_x (\omega^\neq)^2, \\
\mu_x &= m_x \omega_x^2.
\end{aligned} \tag{I.10}$$

The function $\phi(\omega)$ is defined in Eqn (I.4); it is real for $\omega = 0$. The values μ_x and $\mu^\neq$ are force constants at the bottom of the reactant well and on the top of the barrier. On the barrier, the force constant is negative and the value $\mu^\neq$ is found as its absolute value. In a special case where the memory kernel $\beta(\tau)$ is proportional to the delta-function (Markovian limit), expressions (I.9), (I.10) lead to Eqns (11) and (14) for the rate constant. There exists a multimode generalisation of the KGH theory.^{55, 60, 464–469} Its use is mentioned in Section III.3.a.

VI. Supplement II. Spectral density

In the linear approximation, the collective coordinate of the medium which interacts with the coordinate of the reaction subsystem is the linear combination

$$Q = \sum_v C_v Q_v, \tag{II.1}$$

where Q_v are modes of the medium corresponding to masses m_v and frequencies ω_v . The spectral density^{96, 131}

$$J(\omega) = \frac{\pi}{2} \sum_v \frac{C_v^2}{m_v \omega_v} \delta(\omega - \omega_v). \tag{II.2}$$

is associated with the coordinate Q .

This formula can be used to calculate the sums over the modes of the medium containing the C_v^2 coefficients. It is equivalent to the sum rule:

$$\frac{2}{\pi} \int J(\omega) F(\omega) d\omega = \sum_v \frac{C_v^2}{m_v \omega_v} F(\omega_v), \tag{II.3}$$

where $F(\omega)$ is an arbitrary (rather smooth) function. The combination appearing in the right-hand part is often found in applications [see relation (69)]. By using the sum rule, one can pass from the discrete (simpler and more obvious) to a continuum (more convenient for calculations and transformations) description of the medium coordinates.

A different formulation is also useful. Let us consider a ‘chemical’ variable x which interacts with modes of the medium according to a bilinear law. The interaction potential is

$$h_{x\Omega} = \text{const } xQ = x \sum_v \bar{C}_v Q_v. \tag{II.4}$$

Here, const has the dimensionality of a force constant:

$$\bar{C}_v = \text{const } C_v.$$

In this case, the spectral density $\bar{J}(\omega)$

$$\bar{J}(\omega) = \frac{\pi}{2} \sum_v \frac{\bar{C}_v^2}{m_v \omega_v} \delta(\omega - \omega_v) = \text{const}^2 J(\omega), \tag{II.5}$$

is determined;^{96, 131} here, the sum rule is derived from (II.3) by replacing C_v by $\bar{C}_v$ and J by $\bar{J}$.

The function $J(\omega)$ is often specified parametrically. It should disappear ($J = 0$) when $\omega = 0$ and should rapidly decay at frequencies exceeding some critical value, ω_∞ . The typical representation for non-polar media is

$$J(\omega) = J_0 \left(\frac{\omega}{\omega_\infty} \right)^n \exp \left(- \frac{\omega}{\omega_\infty} \right). \tag{II.6}$$

The power n is usually 1 for processes in disordered media (liquids). In three-dimensional molecular crystals, relation (II.6)

corresponds to the Debye type phonon spectrum, $n = 2$. The frequency ω_∞ cutting the spectrum in the crystal corresponds to the Debye frequency.⁴⁶² In a similar representation for $\bar{J}(\omega)$, the constant factor J_0 is modified.

The spectral density is closely related to the classical generalised Langevin equation, which describes, in the case of interaction (II.4), the relaxation kinetics for the collective variable x . For the GLE in form (I.2), the key result is that

$$\bar{J}(\omega) = -\phi_2(\omega), \tag{II.7}$$

where $\phi_2(\omega)$ is the imaginary component of the memory kernel [see Eqn (I.4)]. It allows one to calculate the spectral density for microscopic models of the medium by MD methods because, according to FDT (I.7), (I.8), the function $\phi_2(\omega)$ can be determined from the correlation function $C(t)$ (I.5) available from an MD computation.

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^d — *Dokl. Chem. (Engl. Transl.)*

^e — *Russ. J. Electrochem. (Engl. Transl.)*

^f — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*

^g — *Russ. J. Org. Chem. (Engl. Transl.)*

Crystal structures of inorganic compounds with atomic defects

O V Frank-Kamenetskaya

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Abstract. Main types of crystal structures with different atomic defects (point, volume, planar and linear) are considered using inorganic compounds as an example. The review presents the results of composite analysis of such real structures. Their symmetry, ordering, ways of description, nomenclature and the possibility of the diagnostics from diffraction patterns are discussed. The results of studies provide evidence that polymorphism is typical of real crystal structures. The bibliography includes 101 references.

I. Introduction

Crystalline compounds are generally chemically inhomogeneous because they contain impurities (atoms, ions, vacancies), which disrupt the three-dimensional periodicity of the host crystal structure. Numerous atomic defects are often distributed over the crystal rather uniformly. In these cases, systems are quasi-homogeneous and can be characterised by a single atomic structure, which is established by diffraction methods. The present review surveys such real crystal structures and the related views on isomorphism, polysomatism, solid solutions, mixed crystals and compounds with non-stoichiometric or variable compositions.

Extensive investigations of the real structures of chemically inhomogeneous crystals are currently underway both in Russia and abroad. In the last decades, new experimental analytical methods (synchrotron radiation, EXAFS spectroscopy, high-resolution electron microscopy, *etc.*) and powerful computer facilities have been developed and designed. Besides, a number of lines of theoretical research dealing with diffraction in quasi-homogeneous systems and their symmetry have been further elaborated. All these advances have provided a higher level of detailed information on real crystal structures. The amount of available information obtained by these methods has increased dramatically and fine details of the local structures of real crystals have been revealed. As a consequence, there is a common impression that each crystal has a unique structure and that it is

impossible to characterise real crystal structures using precise mathematical laws. In addition, a number of complex structures with non-stoichiometric compositions, which could not be described by three-dimensionally periodic models, were studied by diffraction methods and it was reported that these structures can be used for the construction of new composite crystalline materials possessing useful properties.

The aim of the present review is to analyse the available data on real crystal structures of inorganic compounds with atomic defects. Initially, types of distortion of the long-range order in chemically inhomogeneous structures and their basic classification are considered. Then the characteristic features of the main structural types (symmetry, composite character, ordering, *etc.*), the accepted nomenclature and characteristic diffraction features are discussed using inorganic compounds as an example.

The need for such generalisations became apparent long ago. Researchers from different scientific schools often use different nomenclatures for the description of analogously organised real crystal structures, which hinders mutual understanding and does not allow one to obtain the general structural picture. In the present review, relationships between numerous real crystal structures with atomic defects are revealed on the basis of precise mathematical (symmetry) laws and ways of simplifying and generalising their nomenclature are proposed.

II. Main types of quasi-homogeneous structures

Let us consider types of distortions in the ideal three-dimensional long-range order caused by impurity atomic complexes of different sizes (Fig. 1): point (zero-dimensional), linear (one-dimensional), plane (two-dimensional) and volume (three-dimensional) defects.¹

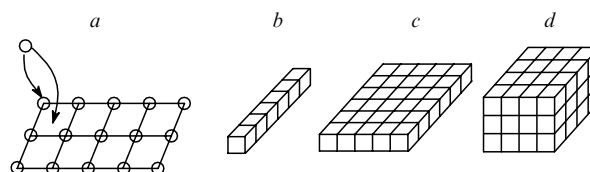


Figure 1. Types of atomic defects formed as a result of normal (a) and anomalous (b–d) isomorphous replacements; (a) point (atom or complex), (b) linear (chain), (c) planar (layer), (d) volume (block) defects.

O V Frank-Kamenetskaya Department of Geology, St. Petersburg State University, Universitetskaya nab. 7/9, 199034 St. Petersburg, Russian Federation. Fax (7-812) 328 44 18. Tel. (7-812) 328 96 47. E-mail: olga@OF3102.spb.edu

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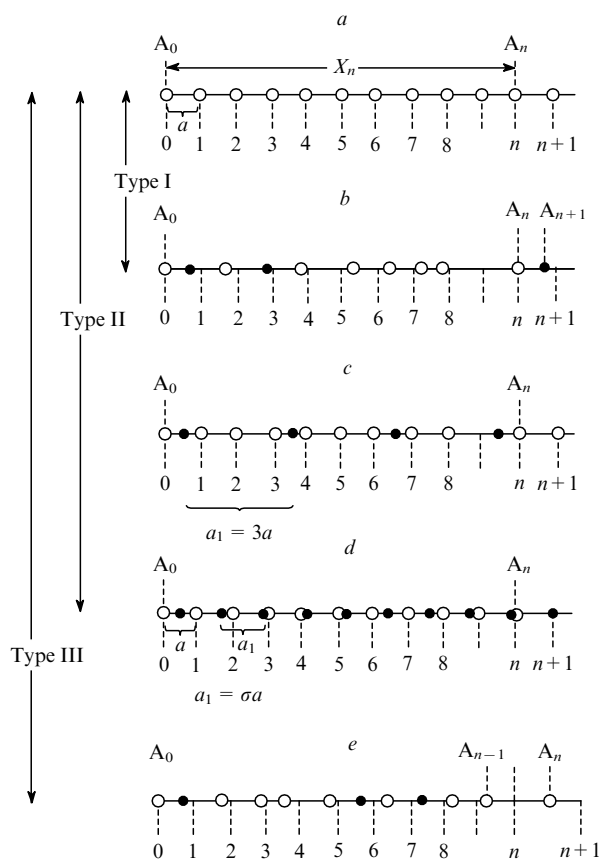


Figure 2. Types of atomic rows in crystal structures with atomic defects (main and impurity atoms are represented by empty and solid circles, respectively);²

(a) structures without impurity atoms; main atoms follow translational symmetry with the parameter a ; (b) main and impurity atoms obey statistical translational symmetry with the parameter a ; (c) main and impurity atoms follow different translational symmetries with the parameters a and a_1 , respectively ($a_1 = na$, where n is an integer); (d) main and impurity atoms obey different translational symmetries with the parameters a and a_1 , respectively ($a_1 = \sigma a$, where σ is an irrational number); (e) a non-periodic atomic distribution.

The insertion of impurity atoms, ions or vacancies into the ideal lattice of the host crystal gives rise to atomic point defects. Such structures contain rows of main and impurity atoms in addition to regular atomic rows along which an ideal translational symmetry with the lattice parameter a of the host crystal is retained (Fig. 2a).² The atom distribution along such rows does not violate the statistical translational parameter, which is equal to the host crystal constant a (in real structures, close to a) (Fig. 2b). This means that the distance X_n between the first (A_0) and n th (A_n) atoms in the row of n atoms approaches na when $n \rightarrow \infty$, whereas the distances between the adjacent atoms may substantially vary. Guinier³ called this type of distortions in the long-range order the ‘replacement disorder’ and considered it as a manifestation of disorder of the first kind. This type of disorder is also associated with thermal vibrations of atoms due to which ideal atomic rows are wholly absent in real crystal structures.

Atomic volume defects appear in crystal structures if the distribution of atomic impurities obeys a three-dimensional translational symmetry, which differs from the symmetry of the host crystal. In this case, the structure necessarily has at least one direction along which the major and impurity structural units are distributed with different periodicities (Fig. 2c,d). As a consequence, the crystal has the superperiods na . If the co-existing three-dimensional sublattices are essentially incommensurate

(Fig. 2d), the parameters of the common crystal lattice can reach several hundred angstroms.

The disorder of another type, *viz.*, disorder of the second kind,³ occurs in the host crystal structure, when the distribution of atomic impurities obeys a translational symmetry in less than three directions, *i.e.*, when structural units in real crystal structures are distributed non-periodically along particular directions and only local regularities take place (Fig. 2e). The difference between X_n and na increases with increasing n . However, the fluctuations of the distances between the adjacent atoms may be of the same order as those observed in the structures with the above-described types of disorder. Disorder of the second kind is typical of structures with atomic planar or linear defects. In the former case, the periodicity of the host crystal structure is distorted only in one direction. In the latter case, the periodicity is violated in two directions.

Hence, only three types of disorder can occur in chemically inhomogeneous structures under consideration. Correspondingly, three types of real crystal structures can be distinguished based on the translational symmetry retained in the crystal (see Fig. 2).^{2,4}

In structures of type I (with atomic point defects), the three-dimensional lattice of the host crystal is statistically retained.

In structures of type II (with atomic volume defects), the disorder is associated with the fact that the major and impurity atoms obey different translational symmetries (Fig. 2c, d). These structures are characterised by two or more three-dimensional sublattices (commensurate or incommensurate) or by a single three-dimensional lattice with superperiods, which are multiples of the lattice parameters of the host crystal.

Structures of type III (with atomic planar or linear defects) are periodic in less than three (in two or one) directions. These structures are characterised by two or more two-dimensional or one-dimensional sublattices (commensurate or incommensurate), which generally contain point defects.

III. Structures with atomic point defects (type I)

1. General views

Point defects, which do not disturb the three-dimensional statistical lattice, are present in virtually all crystals of both natural and synthetic origin. These defects occur due to continuous replacements of structural elements in the host crystal (atoms, ions, vacancies and their associates) as well as through other order–disorder processes. These crystal-chemical effects correspond to the modern views on isomorphism (see, for example, Ref. 5). Order–disorder transformations can be considered as a special case of isomorphism, *viz.*, autoisomorphism, which is characterised by the redistribution of atoms and vacancies in the crystal structure. If the isomorphous replacement is accompanied by a change in the structural type of the crystal, this phenomenon is called isodimorphism.

The isomorphism and related problems were the subject of numerous reviews, including classical monographs by Russian scientists.^{6–10} The morphological aspect of isomorphism, which was described by Mitscherlich¹¹ as a manifestation of the similarity in habits of crystals with different chemical compositions, is already a history. The crystal-chemical interpretation of this phenomenon, which assumes the similarity in the sizes of particles replacing each other as well as the similarity in some of their properties (Goldschmidt’s rule), has also been essentially refined as the notion of the real crystal structures became deeper and more general. The history of evolution of these notions has been described in detail (see, for example, Ref. 12). It is common practice to consider quasi-homogeneous structures, which appear due to isomorphous replacements of different types, as solid solutions (replacement, insertion, subtractions, *etc.*). Besides, such systems are called mixed crystals, isomorphous mixtures, crystals, phases and compounds with variable compositions (see, for example, Refs 6, 10 and 13). The last-mentioned three terms

are less general because they do not take into account autoisomorphism.

2. Composite analysis. Way of description

Idealised structures of solid solutions consist of statistically alternating modules as 'unit cells', which correspond to the real or hypothetical end members of isomorphous (or isodimorphous) series (Fig. 3).² Consequently, crystal structures with atomic point defects are composed of at least two statistically alternating substructures, which are generally isostructural and differ only in composition. Hence, such real structures can be considered as composite structures. If vacancies serve as atomic point defects (Fig. 3b), the corresponding real structures represent one of the possible forms of non-stoichiometry.¹⁴ Due to local displacements induced by impurity atoms, the co-existing 'unit cells' undergo substantial local deformations (Fig. 4).¹⁵

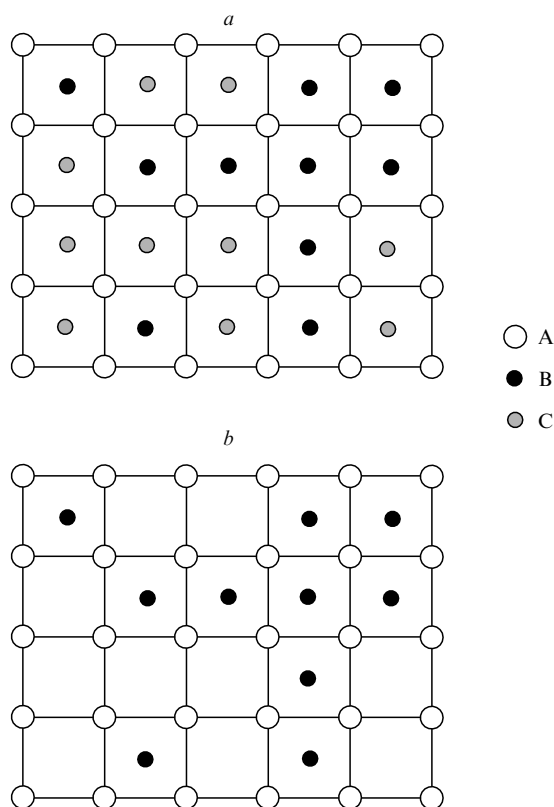


Figure 3. Schematic representation of the structures of the solid solutions $A(B_{0.5}C_{0.5})$ (a) and $A(B_{0.5}\square_{0.5})$ (b); empty cells represent vacancies in the positions of the atoms C.²

The relationship between the parameters of two 'unit cells' of solid solution (a_1, b_1, c_1 and a_2, b_2, c_2) can be described by the following matrix equation

$$A_2 = \sigma A_1, \quad (1)$$

$$\text{where } A_i = \begin{bmatrix} a_i \\ b_i \\ c_i \end{bmatrix}, i = 1, 2; \quad \sigma = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \sigma_{13} \\ \sigma_{21} & \sigma_{22} & \sigma_{23} \\ \sigma_{31} & \sigma_{32} & \sigma_{33} \end{bmatrix}.$$

In the general case, the components of the matrix σ are irrational due to local deformations. Since a system statistically retains the three-dimensional long-range order, the average relational matrix $\bar{\sigma}$ is always a unit matrix and the structure of a solid solution can be described by an averaged unit cell with a mixed occupancy of at least one crystallographic site. This means that the site is occupied in a particular ratio by at least two elements,

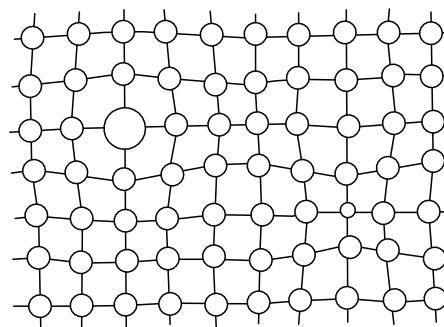


Figure 4. Local deformation of unit cells of a host crystal induced by impurity atoms.¹⁵

such as atoms, ions or vacancies. Partially vacant crystallographic sites are the necessary element in the crystal structures with non-stoichiometric compositions.

3. Symmetry

The symmetry of an average structure is statistically overestimated and is characterised by one of the space groups, viz., G_3^3 . The parameters of a statistical three-dimensional periodic lattice are similar to those of the host crystal. It should be noted that the symmetry of the solid solution can be either higher or lower than the symmetry of the host crystal depending on the ordering of the distribution of impurity elements over regular point systems. If a solid solution is in the middle of an isomorphous (isodimorphous) series or it is formed through order–disorder processes, the notion of the host crystal loses its meaning. The symmetry of a solid solution can change both on crystal growth and in the course of its post-crystallisation transformations. Structural transformations can proceed either stepwise or continuously, both with changes (type I or II isodimorphism) and retention (type I or II polymorphism) of the overall composition of the crystal.^{5, 16}

4. Chemical deformations of average structures

Changes in the composition of a solid solution as a result of isomorphous replacements lead to chemical deformations of the average crystal structure^{9, 12} characterised by changes in the lattice constants, interatomic distances and bond angles. The mutual dependence between these changes enables one to study selected structural features of solid solutions on the basis of the crystal lattice parameters and interplanar distances (see, for example, the studies^{17–20}).

Deformations of coordination polyhedra caused by changes in the chemical composition, temperature or pressure often show traits of similarity (primarily, in crystals with essentially ionic bonds).^{9, 21, 22} Chemical deformations can be quantitatively characterised by the coefficient γ_a (%⁻¹)

$$\gamma_a = \frac{1}{a} \frac{da}{dx},$$

which characterises the relative increment of a particular structural parameter a as the impurity concentration (x) is increased by 1%, by analogy with the thermal expansion coefficients.^{9, 21}

Deformations of different nature can be quantitatively compared by calculating their mutual equivalents. For example, it is convenient to use the ratio γ_a/α [(°C (at.%)⁻¹)]⁻¹, where γ_a is the coefficient of chemical deformations and α is the thermal expansion coefficient, as the thermal equivalent of the chemical deformation of the structure (on the basis of the parameter a for a particular isomorphous replacement).⁹

Local displacements of atoms from ideal sites lead to deviations of both the lattice parameters and average interatomic distances in the solid solution from Vegard's rule, i.e., from the strictly additive behaviour,²³ which lies at the basis of the virtual

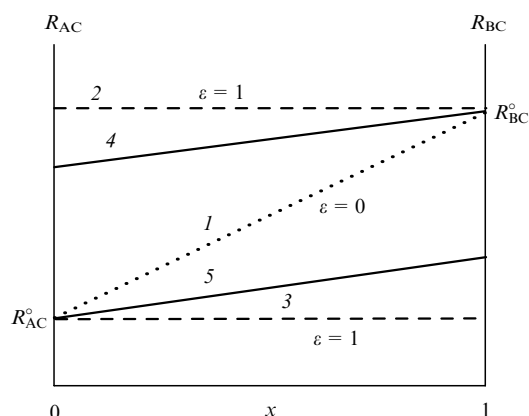


Figure 5. Changes in the B—C and A—C interatomic distances depending on the composition of the solid solution $(A_{1-x}B_x)C$ determined within the virtual crystal model (1) and bond length alternation model (2, 3) and on the basis of experimental data (4, 5) (after V S Urusov²³); (2 and 4) R_{BC} ; (3 and 5) R_{AC} .

crystal model (Fig. 5). These characteristics also do not obey the bond length alternation model according to which the bond lengths in a solid solution are equal to those in pure compounds (end members of the isomorphous series). These models are the hypothetical limiting cases. The actual parameters and interatomic distances in a solid solution are intermediate between the above-mentioned limiting values and the determination of these parameters is the subject of a special experimental study. The degree of structure relaxation of a solid solution can be characterised by the following parameter

$$\varepsilon = \frac{R_{BC} - R_{AC}^0}{R_{BC}^0 - R_{AC}^0},$$

where R_{BC} are the bond lengths in the structure of the solid solution $(A_{1-x}B_x)C$, R_{BC}^0 and R_{AC}^0 are the bond lengths in the structures of the corresponding pure components.²³ Relaxation of the virtual crystal AC with a very small impurity BC approaches zero, whereas relaxation of the crystal with the bond-length alternation is maximum (equal to unity). In real structures of solid solutions, relaxation is incomplete ($0 < \varepsilon < 1$).

5. Short-range order

In crystals of compounds with ionic bonds, the electroneutrality condition requires that atomic defects be generated in pairs (Fig. 6), *viz.*, a vacancy and the corresponding interstitial ion (Frenkel defect), two vacancies of opposite charges (Schottky

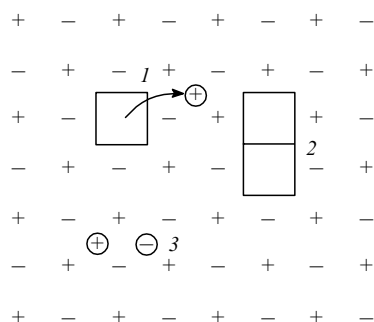


Figure 6. Point defects in the NaCl-type crystals.¹⁵

(1) Frenkel defects, (2) Schottky defects, (3) antipode of the Schottky defect; vacancies and interstitial ions are indicated by squares and circles, respectively.

defect) or two interstitial ions of opposite charges (antipode of the Schottky defect). The formation of defects is accompanied by migrations of the surrounding atoms. Atoms about the vacancies are shifted primarily toward the vacant lattice point, whereas interstitial ions, by contrast, push aside the adjacent atoms. Hence, the fulfilment of the electroneutrality condition for a solid solution primarily through a local charge compensation gives rise to a short-range order (appearance of block isomorphism¹⁵). In non-stoichiometric solid solutions, statistically distributed associates of atoms and vacancies (simple and complex clusters) whose compositions and structures differ from those of the host crystal can occur. Due to the presence of such defect complexes, impurity atoms in the host crystal structure can create coordination conditions typical of the structures of real or hypothetical end members of isomorphous (isodimorphous) series.² If several structural modifications of the compound can occur, the impurity atoms tend to give rise to the coordination typical of the modification that is the nearest to the phase of the host crystal in the phase diagram.²⁴ The possibility of the presence of statistically distributed cluster groups in the structure of a solid solution is often evidenced by unreasonably shortened interatomic distances.

6. Diffraction patterns

Diffraction patterns of quasi-homogeneous structures with atomic point defects represent three-dimensional reciprocal lattices and differ from the patterns of ideal three-dimensionally periodic crystals only by generally insignificant effects of diffusion scattering associated with manifestations of a short-range order.

7. Ordering

The insertions of atomic point defects into an ideal three-dimensional lattice leads to lowering of the internal order of the system. If all symmetry elements, except for translations, are ignored, the crystal structure with these defects can be described as a combination of intersecting translationally equivalent atomic sublattices, into some of which impurity atoms are inserted. The larger is the portion of such statistical atomic sublattices, the lesser is the degree of internal order. It should be noted that crystal structures with atomic point defects are the most ordered form of the naturally occurring condensed state.

IV. Structures with atomic volume defects (type II)

1. General notions

Crystal structures with atomic volume defects (multilattice structures) were found among minerals and can be prepared under laboratory conditions by performing the synthesis in multicomponent systems. These structures show considerable promise in searching for new materials with useful properties. These structures are poorly studied primarily because of the fact that classical X-ray diffraction methods on the basis of three-dimensional space symmetry groups are not sufficiently efficient to solve superstructures (particularly, with large periods). Due to the design of special computer programs involving N -dimensional descriptions of superspace symmetry groups, considerable progress has been made in the determination of multilattice crystal structures in the last decade.

The structures under consideration can appear due to isomorphism, if atomic point defects are inserted into the host lattice in an ordered fashion. This is a way in which superstructures of ordered solid solutions are formed (Fig. 7). In such crystals, the co-existing sublattices are commensurate. Quasi-homogeneous systems with essentially incommensurate three-dimensional sublattices can occur, if the host crystal structure contains periodically distributed fragments (layers or columns) with other structures (Fig. 8). Frank-Kamenetskii^{1,10} related the formation of such structures to anomalous (lamellar) isomorphism (see Fig. 1). According to the modern notions, this is a manifestation of polysomatism.

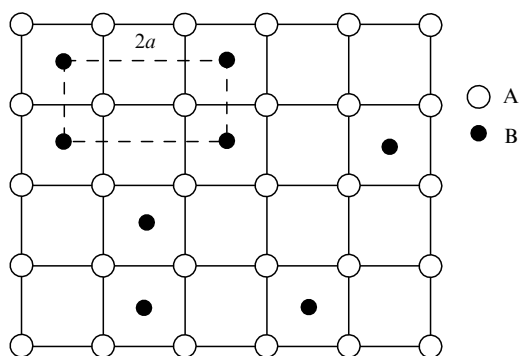


Figure 7. Schematic representation of the formation of a supercell (shown by dashed lines) of an ordered solid solution.²

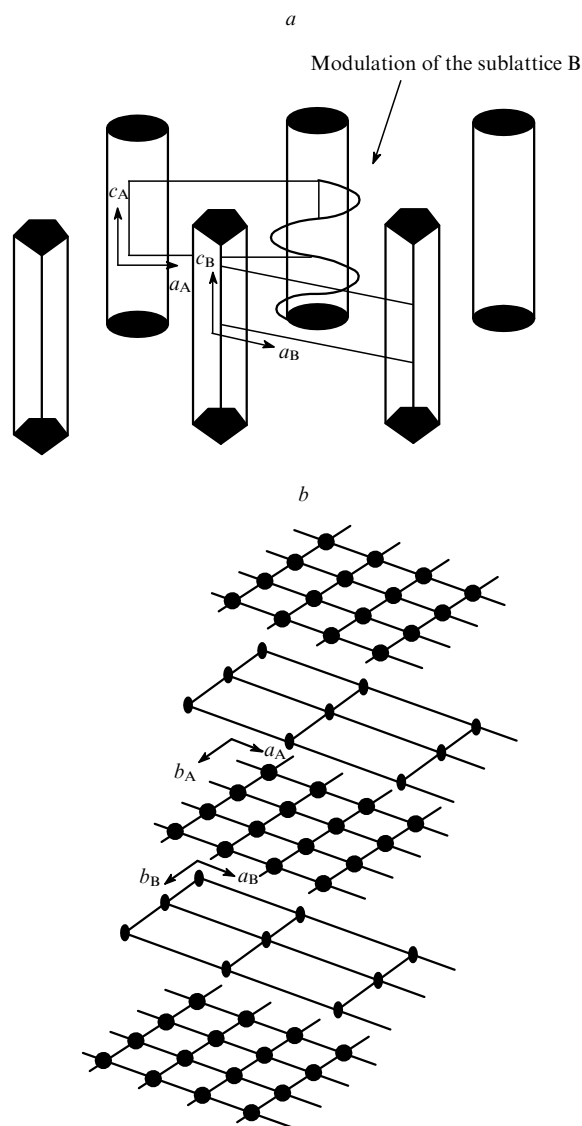


Figure 8. Schematic illustration of the packing of the two sublattices (A, B) in composite structures: column (a) and layer (b) (after P Coppens²⁵). The appearance of a modulation of the sublattice B with the period of the sublattice A is exemplified by columnar structures.

The term ‘polysomatism’ was proposed by Thompson²⁶ for the description of the formation of complex mineral structures from fragments (modules) of different simpler (really occurring in nature) compounds. The commonly accepted extended concept of

polysomatism (see, for example, Refs 27–30) is applied to various series of crystal structures consisting of modules of at least two types. Generally, modules (layers, columns or blocks) differ both in the structure and composition, but they can differ only in one of these parameters. Polysomatism is very widespread in nature and is often, along with isomorphism, responsible for non-stoichiometry of compounds. Apparently, the mechanisms of formation of members of polysomatic series (polysomes) can be described with the use of models developed for polytypes.³⁰ Polysomatic structural series are often described as homologous series.^{31,32}

Crystal structures with incommensurate sublattices are typical of minerals and synthetic (both inorganic and organic) compounds. In nature, such structures most often occur in small amounts and in mixtures with other minerals. These structures are variously referred to as hybrids,³³ intergrowth structures,³⁴ misfit layered structures,^{35–37} incommensurate ladder structures,^{38–41} intercalates,⁴² etc. Due to the structural similarity of multilattice compounds, they are assigned to one group and considered as composite structures.^{25,43,44}

Composite structures were surveyed in the monograph⁴⁵ and reviews.^{25,34–37,44} Unfortunately, data on the structures of this type containing more than two components are very scarce.

The minerals koeninite $[(\text{Mg},\text{Al})(\text{OH})_2]_x[(\text{Na},\text{Ca},\text{Mg})\text{Cl}_2]$ ($x \approx 1.78$)⁴⁶ and valleriite $[(\text{Mg},\text{Al},\text{Fe})(\text{OH})_2]_x[(\text{Fe},\text{Cu})_2\text{S}_2]$ ($x = 1.37–1.56$)^{33,47} are examples of layered composite structures. In the crystal structures of these minerals, the brucite-like octahedral layers alternate with the NaCl-like layers or tetrahedral sulfide layers, respectively. Figure 9 shows the fragment of the composite layered structure of valleriite represented as polyhedra. The minerals cylindrite $[(\text{Pb},\text{Ag},\text{Sn},\text{Sb},\text{Fe})\text{S}]_x \cdot [(\text{Sn},\text{Sb},\text{Fe})\text{S}_2]$ ($x \approx 1.38$),⁴⁸ cannizzarite $[(\text{Pb},\text{Bi})\text{S}]_x[(\text{Pb},\text{Bi})_2\text{S}_3]$ ($x \approx 1.70–1.71$)⁴⁹ and their synthetic analogues provide examples of layered composite structures characterised by superperiods of length > 100 Å. Layered composite structures are known also for graphite intercalates exhibiting high conductivity,⁴² for example, for FeCl_3 -graphite.⁵⁰ Layered structures of superconducting bismuth cuprates $\text{Bi}_2\text{Sr}_2\text{CuO}_{6+x}$ and $\text{Bi}_2(\text{Sr},\text{Ca})_3\text{Cu}_2\text{O}_{8+x}$ can also be described as composite structures $[\text{Bi}_2\text{Sr}_2\text{CuO}_4][\text{O}]_y$ and $[\text{Bi}_2(\text{Sr},\text{Ca})_3\text{Cu}_2\text{O}_6][\text{O}]_y$ ($y \approx 2.2$), respectively.⁵¹

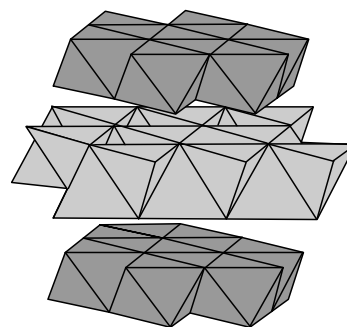


Figure 9. Fragment of the layer composite structure of valleriite.³⁵

The known columnar composite structures are much less in number. For example, these structures are typical of the compounds $\text{Ba}_p(\text{Fe}_2\text{S}_4)_q$.⁵² In the structures of these compounds, the chains of the edge-sharing Fe–S tetrahedra alternate with columns of barium ions. Composite structures containing zigzag chains as two-leg ladders occupy a special place. For example, the structures of $[\text{M}_2\text{Cu}_2\text{O}_3]_{0.714}[\text{CuO}_2]$ ($\text{M} = \text{Bi}, \text{Sr}, \text{Ca}, \text{Y}$ or lanthanides)^{39–41,53} (Fig. 10) contain the Cu_2O_3 layers composed of two-leg ladders, which alternate along the [010] direction with the layers consisting of the CuO_2 chains. If interactions between the ladders are ignored, these structures can be considered as columnar structures, which consist of two types of chains parallel to the [001] direction. One of these phases with composition $\text{Sr}_{0.4}\text{Ca}_{1.6}$.

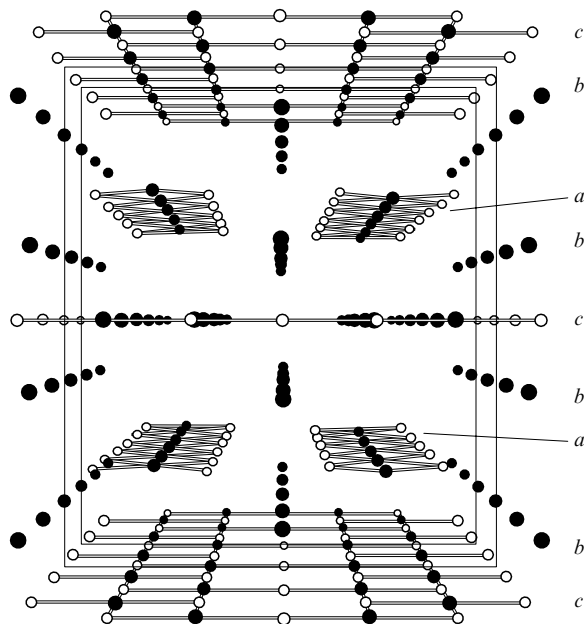


Figure 10. The composite structure of $[M_2Cu_2O_3]_{0.714}[CuO_2]$ ($M = Bi, Sr, Ca$);⁴¹
(a) layers of the CuO_2 chains, (b) layers of the cations M , (c) Cu_2O_3 layers built from two-leg ladders.

$Cu_{24}O_{41+x}$ is transformed into the superconducting state at 9–12 K and 4.5 GPa.⁵⁴ Two-leg ladders are present also in numerous composite structures of intermetallics,³⁸ for example, in $[V]_{17}[Ge]_{31}$, $[Mo]_9[Ge]_{16}$, $[Re]_{17}[Ge]_{22}$, $[Te]_{17}[Si]_7$, etc. In these chimney-ladder structures (often with superperiods of length > 100 Å), chains of Group III and IV metals (ladders) are inserted into the channels of the frameworks of transition metals.

Frank-Kamenetskii¹ considered real crystal structures containing extended chemical defects as solid solutions. These views have been further developed in the study.²⁷ The authors of the cited study proposed that series of structures consisting of analogous modules be considered as fragmentary solid solutions composed not of individual atoms or ions but of structural fragments arranged with different degrees of order. In usual solid solutions, which are formed as a result of isomorphous replacements, the structures are changed due to variations in the chemical composition. By contrast, structural changes are responsible for the formation of fragmentary solid solutions, whereas variations in the composition are manifested only in relation to these structural changes. In the light of these concepts, crystal structures with atomic volume defects can be considered as ordered fragmentary solid solutions.

2. Composite analysis. Ways of description

Crystal structures with atomic volume defects (regardless of the commensurability of the co-existing sublattices) can always be described as superstructures (the lengths of the superperiods can reach hundreds of angstroms) or as composite structures consisting of two or more mutually penetrating three-dimensionally periodic substructures. Ionic-covalent bonds between atoms within substructures are often much stronger than those between atoms belonging to different substructures.²⁵ In many cases, the requirement of electroneutrality is ensured by variable-valence elements. The stronger are interactions between the substructures, the more substantial are mutual periodic distortions (modulations). Modulations of the sublattice B occur with the period of the co-existing sublattice A (see Fig. 8a) and *vice versa*. Hence, composite structures of this type represent the most general case of modulated structures. If the co-existing sublattices are essen-

tially incommensurate and the ratios between the volumes of the subcells deviate from integer values, the structures characterise one of the possible forms of manifestation of non-stoichiometry.^{14, 25, 43}

The co-existence of different substructures in one crystal imposes certain conditions on the components of the matrix σ in Eqn (1). In the case under consideration, Eqn (1) describes the relations between the sublattice parameters.^{25, 43}

If the composite structure consists of columns of two types parallel to the axis c (see Fig. 8a), it is necessary to avoid their overlapping. Columns must fit together into an infinite array in the plane perpendicular to the column axis. For this purpose, the axes a_2 and b_2 are chosen in the planes a_1c_1 and b_1c_1 , respectively. Hence, the minimum requirements for the commensurability of the parameters of the co-existing sublattices are determined by the following matrix

$$\sigma = \begin{vmatrix} n_1 & 0 & \sigma_{13} \\ 0 & n_2 & \sigma_{23} \\ 0 & 0 & \sigma_{33} \end{vmatrix}, \quad (2)$$

where n are integers or rational fractions and σ are irrational values. Consequently, five basis vectors are required for the description of columnar composite structures.

In the case of layered composite structures (see Fig. 8b), the parallel planes cannot overlap, and the minimum requirements for the space fitting of the co-existing sublattices are determined by the following matrix

$$\sigma = \begin{vmatrix} \sigma_{11} & \sigma_{12} & 0 \\ \sigma_{21} & \sigma_{22} & 0 \\ \sigma_{31} & \sigma_{32} & n \end{vmatrix}. \quad (3)$$

Six basis vectors are required for the description of such structures. If the axes a and b of two sublattices can be chosen parallel to each other ($a_1 \parallel a_2$, $b_1 \parallel b_2$), the matrix (3) takes the form

$$\sigma = \begin{vmatrix} \sigma_{11} & 0 & 0 \\ 0 & \sigma_{22} & 0 \\ \sigma_{31} & \sigma_{32} & n \end{vmatrix}. \quad (4)$$

In this case, four basis vectors are sufficient for the description of a layered composite structure.

Composite structures cannot be unambiguously classified according to the type of the matrix relating the co-existing sublattices. If the matrix σ is reduced to a diagonal form, the structure cannot be assigned to rod or layered structures (without considering the characteristic features of chemical interactions). For example, the structures of $[M_2Cu_2O_3]_{0.714}[CuO_2]$ ($M = Bi, Sr, Ca, Y$ or lanthanides)^{39–41, 53} (see Fig. 10) whose sublattices are related by a diagonal matrix can be considered as structures composed of either alternating layers perpendicular to the axis b or alternating columns (rods) parallel to the axis c . Besides, the structure identified according to the corresponding relational matrix as a rod structure can, in fact, contain a framework formed by one of the components through strong hydrogen or covalent bonds. In this case, the second component is located as a guest in the channels of the framework. For example, such guest–host structures are typical of urea-based complexes.²⁵

3. Symmetry

Average structures of all substructures co-existing in the same crystal (without considering possible modulations) and the superstructure as a whole are characterised by the space groups G_3^3 . The space group of the superstructure is determined by the intersection of the symmetry groups of the substructures at their given orientations. If sublattices co-existing in the same crystal are substantially incommensurate, the lengths of the superperiods can reach hundreds of angstroms. In this case, it is reasonable to consider the system as periodic in more than three directions (Fig. 11).²⁵ Then, taking into account mutual modulations whose periodicity is determined by the parameters of the co-existing sublattices (see Fig. 8a), the symmetry of each of the substructure

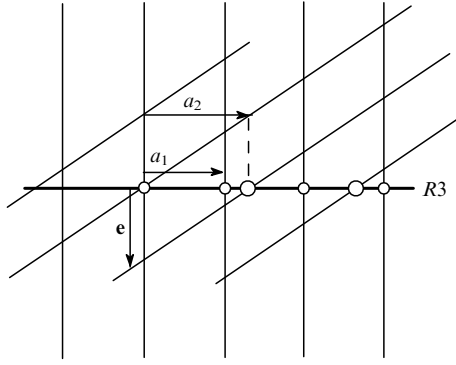


Figure 11. Schematic representation of a two-component composite crystal in the four-dimensional space.²⁵

$R3$ is the three-dimensional space with two different periodicities a_1 and a_2 , e is the unit vector. Lines in the fourth dimension are strings representing the atoms of two substructures without taking into account the modulations.

tures and the system as a whole can be characterised by the superspace groups G_{3+d}^{3+d} (Refs 25, 44). Composite structures with commensurate sublattices can also be described with the use of superspace symmetry groups (see Ref. 44 and other publications).

The theory of superspace groups, which has been extensively developed in the last decades, was considered in the studies^{55–62} and the expressions for structure factors corresponding to these concepts were published in the studies.^{44, 63}

4. Diffraction patterns

In the general case, the diffraction pattern of a composite crystal^{25, 44} is very complicated due to overlapping of the diffraction patterns of all co-existing substructures. In such a pattern, there are the so-called main reflections among which are mixed reflections serving simultaneously as main reflections for one of substructures and as satellite reflections for another substructure. In addition, weak satellite reflections should be present, which are unambiguously indicative of the occurrence of modulations caused by interactions between the substructures. However, satellite reflections are often impossible to reveal by X-ray diffraction methods and mixed reflections are the only source of information on modulations of sublattices. Depending on the incommensurability of sublattices co-existing in the crystal, the diffraction pattern can be virtually indistinguishable from that of either an oriented intergrowth or an ideal three-dimensionally periodic crystal.

In the general case, $3 + d$ basis vectors are required for indexing diffraction patterns of a composite crystal (Fig. 12). The relationship between the parameters of two reciprocal sublattices a_1^* , b_1^* , c_1^* and a_2^* , b_2^* , c_2^* can be described by the following matrix equation:²⁵

$$A_2^* = (\sigma^{-1})^T A_1^* = \sigma^* A_1^*, \quad (5)$$

where $A_i^* = \begin{bmatrix} a_i^* \\ b_i^* \\ c_i^* \end{bmatrix}$, $i = 1, 2$; σ is the matrix from Eqn (1);

T is a transpose operation.

In the case of columnar composite structures for which the relationship between the sublattices is determined by the matrix (2), the matrix σ^* takes the form

$$\sigma^* = \begin{bmatrix} 1/n_1 & 0 & 0 \\ 0 & 1/n_2 & 0 \\ -\sigma_{13}(n_1\sigma_{33}) & -\sigma_{23}(n_2\sigma_{33}) & 1/\sigma_{33} \end{bmatrix}. \quad (6)$$

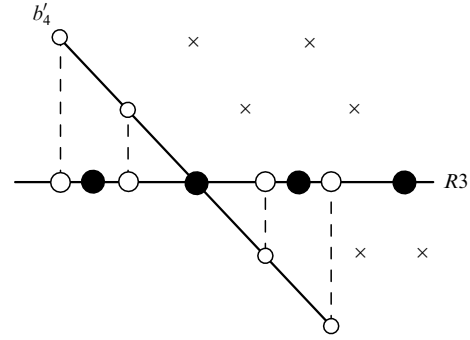


Figure 12. Schematic representation of the four-dimensional reciprocal space of a two-component composite crystal.²⁵

$R3$ is the three-dimensional space with two sets of reflections with different periodicities, b_4^* is an additional coordinate axis. Main reflections of two sublattices are shown by circles. Satellite reflections are indicated by asterisks.

Hence, the axes a_1^* and b_1^* are parallel to the axes a_2^* and b_2^* , respectively (in the reciprocal space, the $hk0$ plane is common to both substructures), and the diffraction pattern can be described by four basis vectors ($d = 1$).

In the case of layered composite structures for which the relationship between the sublattices is determined by the matrix (4), the matrix σ^* takes the form

$$\sigma^* = \begin{bmatrix} 1/\sigma_{11} & 0 & -\sigma_{31}(n\sigma_{11}) \\ 0 & 1/\sigma_{22} & -\sigma_{32}(n\sigma_{22}) \\ 0 & 0 & 1/n \end{bmatrix}. \quad (7)$$

Here, only the axis c^* is common to both substructures, and the diffraction pattern is described by five basis vectors ($d = 2$).

5. Ordering

The appearance of superperiods decreases the homogeneity of the crystal structure. In different structures, the degree of ordering varies substantially and decreases with increasing incommensurability of the co-existing sublattices (with increasing volume of the unit cell characterising the superstructure). It should be remembered that structures with atomic volume defects virtually always contain atomic point defects as well. Therefore, structures of type II are characterised by lower degrees of internal ordering compared to those observed in the above-described structures of type I (usual solid solutions).

V. Structures with atomic planar and linear defects (type III)

1. General views. Probability-statistical models

Chemically inhomogeneous structures, which consist of modules (layers or columns) with different compositions alternating in a disordered fashion, are also rather widespread among natural and synthetic compounds. According to the results of high-resolution electron microscopy (see, for example, Refs 64 and 65), structures with two-dimensional defects represent one of the most widespread types of crystal inhomogeneity. Irregularly alternating modules can have either different or identical atomic structures. Structures of the first type are characteristic of members of polysomatic series, whereas structures of the second type are typical of intermediate compositions of isomorphous series. The weaker are interactions between atoms belonging to different modules, the more substantial is the deviation of the real crystal structure from a homogeneous three-dimensionally periodic structure. If the scale of structural inhomogeneity, *i.e.*, the maximum possible thickness of the packet of impurity modules, is smaller than the average size of the coherent scattering domains (CSDs) and if numerous defects are rather uniformly distributed over the crystal, interactions between alternating modules are

rather strong and the irregular structure is quasi-homogeneous. Such structures can be described within the framework of a single probability-statistical model whose parameters characterise the ratios between the co-existing one- or two-dimensional fragments and their distribution along directions that lose periodicity.

Probability-statistical models have been developed only for one-dimensionally disordered structures. The first of these models allowed one to describe only completely disordered layer packings without considering possible interactions between the layers.^{66–68} Later on, it has been proposed that interlayer interactions be characterised by the factor of the short-range order R , which is equal to the number of layers responsible for the probability of the occurrence of a particular layer in the crystal.^{69–72} More recently, the probability parameters were suggested for the description of the character of alternation of the layers at $R = 0$ or 1.^{73–75} Probability-statistical models of irregular layered structures and the diffraction theory based on these models were generalised and developed in the studies.^{76–78} Unfortunately, irregular mixed-layer structures studied with the use of probability-statistical models are few in number. Most of these structures were surveyed in the monograph⁷⁷ and reviews.^{78–80} Examples of the application of these models to the description of irregular mixed-layer structures of chemically inhomogeneous crystals are given in Table 1.

Quasi-homogeneous structures with two- and one-dimensional defects can arise in the course of both crystal growth (in particular, in the course of formation of a composite zoning) and post-crystallisation changes, for example, upon decomposition of solid solutions or metasomatic replacements. Irregular mixed-layer structures are often generated in the course of transformations of layered silicates at high p and T .⁸¹

Disordered mixed-layer structures are typical of various natural and synthetic compounds, *viz.*, silicates, sulfides, carbonates, graphite intercalates, perovskite-like cuprates and other oxides and hydroxides. Mixed-layer layered silicates (see Refs 66, 67, 77, 78 and other publications) were studied in most detail. Since the latter minerals are widespread in nature and very sensitive to changes in the thermodynamic conditions, they are successfully used as indicators of the geochemical conditions of formation. Their crystal structures are built from layers of different clay minerals, which are present in variable amounts (Fig. 13).³⁰ The interlayer space can be filled either with com-

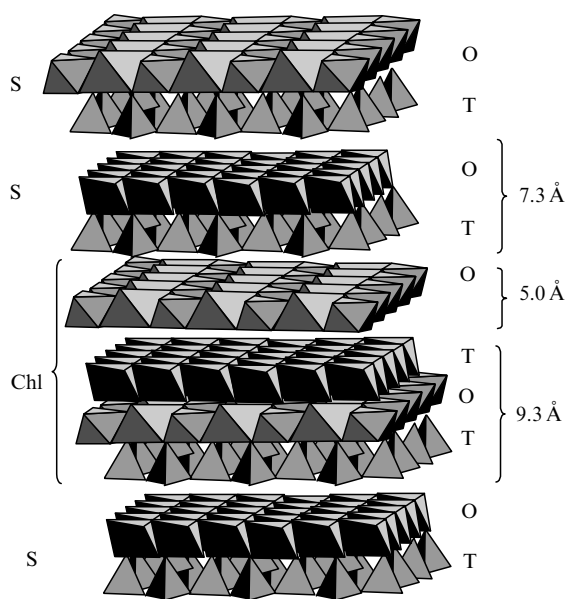


Figure 13. Diagrammatic structure of the chlorite/serpentine interlayering (S is serpentine, Chl is chlorite).³⁰ Layers of tetrahedra (T) and octahedra (O) are shown.

plexes of cations with water molecules or with potassium and sodium cations. Quasi-homogeneous structures with the maximum possible degree of short-range order are widespread among mixed-layer layered silicates. The structures with a very low degree of order were found among illite- and kaolinite-montmorillonites.⁸² Probability-statistical models of irregular mixed-layer structures were applied also to the investigation of the chemical imperfection in the structures of non-stoichiometric perovskite-like cuprates $\text{Bi}_2\text{Sr}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+4}$ ($n = 1-3$)^{80, 83, 84} (Fig. 14)

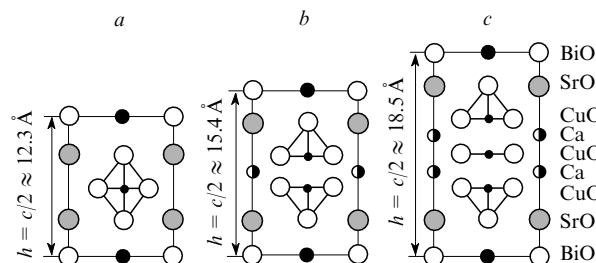


Figure 14. Crystal structures of members of the polysomatic series $\text{Bi}_2\text{Sr}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+4}$.⁸⁰ (a) Bi-2201, $n = 1$, $T_c \approx 20\text{K}$; (b) Bi-2202, $n = 2$, $T_c \approx 90\text{K}$; (c) Bi-2203, $n = 3$, $T_c \approx 110\text{K}$ (T_c is the superconducting transition temperature, h is the height of the layer).

and $\text{YBa}_2\text{Cu}_3\text{O}_x$ ($x = 6, 7$)⁸⁵ (Fig. 15). This approach made it possible to estimate the concentration and characteristic features of the distribution of impurity layers, which belong to phases with other n or differ from matrix layers due to the in-layer distribution of cations and vacancies (see Table 1). The relationships between the probability characteristics of the real structure, synthesis conditions and post-growth treatment of the crystals were revealed and their correlations with the average temperature and the width of the temperature range of the transformation into the superconducting state were found.^{86, 87} Besides, probability-statistical models were successfully used in studies of the fine oscillatory zoning in crystals of garnets of the grossular-andradite series $\text{Ca}_3(\text{Al}, \text{Fe})_2(\text{SiO}_4)_3$ (see Ref. 88) and the decomposition structure of the solid solution $(\text{K}, \text{Na})(\text{Ca}, \text{Na})_2(\text{Mg}, \text{Fe})_5(\text{Si}, \text{Al})_8\text{O}_{22}(\text{OH}, \text{F})_2$, *viz.*, the calcium amphibole edenite.⁸⁹ Investigations of irregular structures formed as a result of layer isomorphism^{79, 80} demonstrated that the common feature of these structures is a high degree of segregation of layers with the same

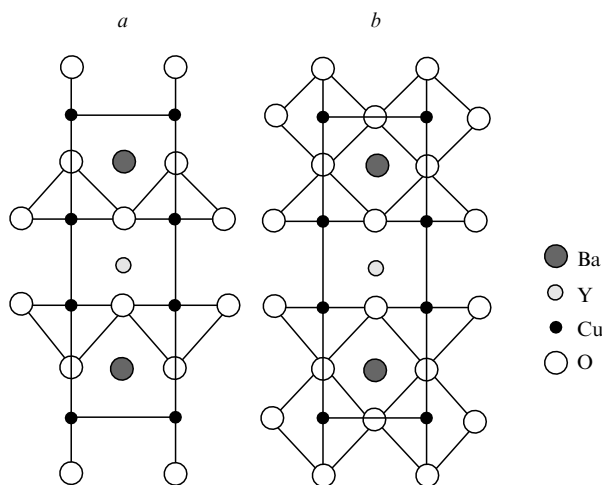


Figure 15. Crystal structures of the non-stoichiometric phases $\text{YBa}_2\text{Cu}_3\text{O}_x$. $x = 6$ (a), 7 (b).

Table 1. Examples of the use of binary probability-statistical models ($R = 1$) for the description of irregular mixed-layer crystal structures of selected inorganic compounds.⁸⁰

Compound	$h_i / \text{\AA}$	Limits of variations in composition of layers	Probability-statistical parameters					
			M	W_i	P_{ii}	K_s	$L / \text{\AA}$	$l / \text{\AA}$
$\text{Bi}_2\text{Sr}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+4}$ ($n = 1-3$)	15.45	$(\text{Bi}_{1.9-2.0}\text{Cu}_{0.1-0.0})(\text{Sr}_{1.7-2.0}\text{Bi}_{0.3-0.0})\text{Ca}_{1.0}\text{Cu}_{2.0}$	10	0.95	0.95	—	154	12
	12.15	$\text{Bi}_{2.0}(\text{Sr}_{1.5-2.0}\text{Bi}_{0.3-0.0}\text{Ca}_{0.2})\text{Cu}_{1.0}$		0.05	0.00			
$(\text{Bi,Cu})_2(\text{Sr,Bi})_2\text{CaCu}_2\text{O}_8$	15.38–15.57	$(\text{Bi}_{1.9-2.0}\text{Cu}_{0.1-0.0})(\text{Sr}_{1.6-1.9}\text{Bi}_{0.4-0.1})\text{Ca}_{1.0}\text{Cu}_{2.0}$	11–13	0.60–0.70	0.95–0.90	0.67–0.81	170–200	43–63
	15.55–15.25	$(\text{Bi}_{2.0-1.8}\text{Cu}_{0.0-0.2})(\text{Sr}_{1.9-1.3}\text{Bi}_{0.1-0.7})\text{Ca}_{1.0}\text{Cu}_{2.0}$		0.40–0.30	0.93–0.77			
$\text{YBa}_2\text{Cu}_3\text{O}_x$ ($x = 6, 7$)	11.67–11.71	$x = 6.70-7.00$	100–140	0.60–0.90	1.00	1.00	1170–1640	140–470
	11.72–11.69	$x = 6.85-6.70$		0.40–0.10	1.00			
$\text{Ca}_2(\text{Al,Fe})_2(\text{SiO}_4)_3$ (garnets)	4.21	$\text{Ca}_3(\text{Al}_{0.70-0.65}\text{Fe}_{0.30-0.35})_2$	320–380	0.65–1.00	0.98–1.00	0.97–1.00	1350–1600	240–460
	4.23	$\text{Ca}_3(\text{Al}_{0.50-0.45}\text{Fe}_{0.50-0.55})_2$		0.35–0.00	0.99–1.00			
$(\text{K,Na})(\text{Ca,Na})_2(\text{Mg,Fe})_5$	9.03	$(\text{K}_{0.3}\text{Na}_{0.7})(\text{Ca}_{1.65}\text{Na}_{0.35})(\text{Mg}_{4.25}\text{Fe}_{0.75})$	60	0.85	0.98	0.88	540	70
$[(\text{Si,Al})_8\text{O}_{22}(\text{OH,F})_2]$ (amphibole)	9.10	$(\text{K}_{0.7}\text{Na}_{0.3})\text{Ca}_{2.0}(\text{Mg}_{3.0}\text{Fe}_{2.0})$		0.15	0.90			

Note. h_i is the height of the layer of type i ($i = 1, 2$); M is the total number of layers in the coherent scattering domain (CSD); W_i is the portion of the layers of type i in CSD; P_{ii} is the conditional probability of the layers of type i following the layer of type i ; K_s is the segregation coefficient; L is the average size of CSD along the normal to the layers; l is the maximum possible thickness of the packets of impurity layers.

symmetry groups of layers G_2^3 or rods G_1^3 , respectively. The determination and analysis of these groups were reported, for example, in the monograph.⁹³

Two-component mixed-layer structures can be divided into two groups according to the symmetry of alternating layers.^{45, 78} The first group includes structures consisting of alternating layers with hexagonal and trigonal symmetry. The second group involves structures built from alternating layers with hexagonal and tetragonal symmetry. Examples of the first group are provided by disordered varieties of valleriite and koenenite. The second group involves, for example, cylindrite and cannizzarite.

4. Diffraction patterns

The weaker are the interactions between the co-existing two- or one-dimensionally periodic substructures, the more similar is the diffraction pattern of the real crystal to a two- or one-dimensional reciprocal lattice, respectively. However, perturbations in the periodicity are most often insignificant and are manifested in the broadening, asymmetric shape, non-integer indices and weaker intensities of particular groups of diffraction reflections. The detection of these characteristic features presents a serious experimental problem, which becomes more complicated at lower concentrations of impurity modules disturbing the long-range order.

Diffraction patterns of irregular mixed-layer structures were discussed in the monographs^{76, 77, 90} and reviews.^{78–80} Analysis of basal reflections made it possible to distinguish three families of real structures characterised by different ratios between the heights of alternating layers.^{78, 80}

1. The heights of layers with different structures differ substantially from each other (by several angstroms). Diffraction patterns of such structures are characterised primarily by non-integer values of basal reflections. If this effect is not observed at low concentrations of impurity layers, the asymmetry of the profiles of different reflections of a series, which is manifested to a variable extent and on different sides of reflections (and is often accompanied by broadening of some reflections), serves as a diagnostic indicator. These diffraction features are characteristic of members of different polysomatic series. Non-integer indices are often observed in diffraction patterns of mixed-layer silicates.

2. The heights of layers with different structures are multiple of each other. In this case, the positions of basal reflections generally correspond to integer indices, but their intensities can be changed in parallel with l . Such diffraction patterns are often difficult to distinguish from those of the corresponding structures with regular superperiods. For example, these patterns are typical of hypothetical mixed-layer structures (see Fig. 13) with the irregular alternation of 7 and 14 Å thick layers.

3. The heights of layers, which differ only in occupancies of crystallographic sites, are nearly identical (differ by only hundredths or tenths of angstroms). In this family, the asymmetry of reflection profiles (in the case of integer basal reflections), which is manifested on the same side and increases in parallel with the diffraction angle, serves as the major criterion for the occurrence of perturbation in the periodicity. These diffraction patterns are typical of intermediate members of isomorphous series and are also obtained for some layered silicates consisting of layers, which differ in the distribution of cations occupying octahedral positions.

5. Ordering

Real structures periodic in less than three directions are less homogeneous compared to all the structures described above. One-dimensionally periodic structures consisting of irregularly alternating columns are not only less ordered than irregular mixed-layer structures but also represent the least homogeneous real form of the crystalline state.

In addition, it should be remembered that the disordered alternation of two- or one-dimensionally periodic modules generally differs from the statistical distribution and tends to be either

ordered or segregated. Hence, the degree of order within each of two subgroups, *viz.*, the structures with planar and linear defects, varies substantially. The degree of order in the real structures under consideration is additionally reduced due to the insertions of atomic point defects and also due to the non-identity of the co-existing sublattices giving rise to mutual modulations.

VI. Conclusion

The present review surveys real crystal structures, which remain rather homogeneous (quasi-homogeneous) in spite of the presence of numerous atomic impurities (atoms, ions or vacancies). In the structural classification of condensed states (see, for example, Ref. 94), such systems occupy an intermediate place between ideal crystals and one-dimensional periodic structures (polymers and liquid crystals) according to the degree of order. In spaces of dimension m ($m \geq 3$), the main types of real structures, which are categorised according to the characteristic features of disorder induced by atomic impurities, are characterised by the symmetry groups G_n^m periodic in n dimensions ($m \geq n$, $n \geq 1$). Real structures of different types differ in the degree of internal order and, in most cases, are reliably identified from diffraction patterns. These real structures represent all possible structural forms of non-stoichiometry of compounds. In each of three structural types, the degree of order varies substantially and the boundaries between these types overlap.

Atomic impurities present in the structures of host crystals are nucleations of other (real or hypothetical) compounds.¹³ Hence, the characteristic feature of the real crystals under considerations is their composite nature. Structures of types I and II consist of two or more three-dimensionally periodic substructures, which are distributed statistically or in an ordered fashion, respectively. Structures of type III are composed of two- or one-dimensionally periodic substructures alternating with different degrees of order. Consequently, real structures of the first type can be described by an average unit cell with mixed occupancies of certain crystallographic sites. Real structures of the second type (without considering mutual modulations) can be represented by two or more types of unit cells, which differ in the structure and/or composition. Real structures of the third type can be described within the framework of probability-statistical models.

Due to the composite properties, quasi-homogeneous structures with atomic defects of different types can be considered as solid solutions (in essence, always fragmentary), because these compounds are characterised, first, by a rather uniform distribution of components over the bulk of the compound and, second, by the theoretical possibility to vary their ratio (in most cases, this possibility is realised). In principle, these chemically inhomogeneous crystals can be called mixed, if this rather uncertain and seemingly archaic notion is assigned a real structural meaning. It should be remembered that the boundary between composite quasi-homogeneous structures and crystal overgrowths, including epitaxial and syntaxial overgrowths, is substantially blurred.

Crystal structures with atomic defects surveyed in the present review are widespread among minerals and synthetic inorganic compounds (including new promising materials). The above-considered basic classification enables one to substantially simplify their nomenclature.

Taking into account the diversity and specificity of defects found in real crystal structures in exact agreement with their morphogenesis (see, for example, Ref. 80), Zorkii raised the question as to whether it is adequate to discuss the polymorphism of real crystalline substance.⁹⁵ The basic classification of crystal structures with atomic defects on the basis of symmetry (primarily, translational symmetry)^{2, 4} allows one to state that such a phenomenon as polymorphism actually occurs. Analysis of thermodynamic and energy characteristics of the above-considered types of real crystal structures is beyond the scope of the present review. One can become acquainted with the energy theory of classical solid replacement solutions by reading the monographs

by Urusov^{8,96} and publications of his colleagues (see, for example, Refs 97 and 98). The possibilities of the use of superspaces for calculations of the energies of incommensurate composite structures were discussed in the review.²⁵

The polymorphism of amorphous compounds was studied.^{99,100} The data published in the literature provide evidence that this phenomenon is typical of all structural forms of the condensed state.

Early in the 20th century, when discussing the real crystal structures, E S Fedorov wrote: 'When we dealt with perfect crystals, we operated with one of the most precise sciences of the mathematical field, the so-called theoretical crystallography. When our attention is directed to imperfections in the crystal formation, we go beyond the scope of this science and enter in the field of empirical sciences. There is no doubt that new areas of the science will be developed, which will allow one to study such phenomena using precise mathematical laws'.¹⁰¹

The data surveyed in the present review provide evidence that the accumulated knowledge enables one to make steps forward in this direction. The above-described basic classification on the symmetry basis can be considered as the starting point for developing the notion of the polymorphism of real crystals.

I am grateful to Professors F F Grekov, B B Zvyagin, P M Zorkii, Yu O Punin and S K Filatov for helpful discussion and valuable advice.

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Skeletal rearrangements of monoterpenoids of the carane series

V A Chuiko, O G Vyglazov

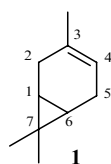
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Abstract. Data on rearrangements of monoterpenoids with the bicyclo[4.1.0]heptane skeleton occurring by ionic, radical and concerted mechanisms are generalised and analysed. The bibliography includes 135 references.

I. Introduction

One of the most widespread monoterpene hydrocarbons is 3-carene, or 3,7,7-trimethylbicyclo[4.1.0]hept-3-ene (**1**), which is a constituent of many essential oils and turpentine.^{1,2}



The interest in 3-carene stems from the presence in its molecule of a *gem*-dimethylcyclopropane ring, a unique fragment, which is an important structural unit of many biologically active compounds. These include, for example, natural and synthetic pyrethroids, stercularic acid and its esters, aminocyclopropanecarboxylic acid derivatives, *etc.* In addition, 3-carene and related compounds, like other bicyclic terpenoids, can undergo various skeletal rearrangements. As a result, they are very promising models for studies in fundamental organic chemistry and are useful starting compounds for the synthesis of valuable products: sesquiterpenoids,³ pheromones,⁴ juvenoids,⁵ pyrethroids^{6,7} and fragrance compounds.^{7–9}

The currently known skeletal rearrangements of compounds of the carane series result in several types of structure, namely, with bicyclo[3.1.0]hexane, bicyclo[3.2.0]heptane, *p*- and *m*-menthane and 1,1,4-trimethylcycloheptane skeletons. According to their mechanisms, these rearrangements are classified as ionic, radical and concerted.

The available reviews on carane-type monoterpenoids were mainly written more than 25 years ago. They do not reflect the diversity of skeletal rearrangements studied over the past decades. A detailed review by Arbuzov and Isaeva¹⁰ dealt with rearrangements that occur by the ionic mechanism. Yet another review¹¹ mainly describes rearrangements of carane monoterpenoids in which the cyclopropane ring opening affects the 'external' bonds to give compounds of the *p*- and *m*-menthane series.

The extensive monograph 'Chemistry of Monoterpenes' by Erman¹² provides an excellent and systematic description of data on reactions of monoterpenes and on the mechanisms of these reactions; however, the experimental data on the transformations of terpenoids belonging to the carane series only includes literature data published before 1976. Since then, new results have been obtained, and new concepts on the mechanisms of certain reactions discussed in the monograph cited have appeared. The reviews that are published from time to time^{13,14} just state the facts rather than analyse them, therefore they generally do not consider or discuss the mechanisms of the transformations described. The most recent reviews dealing with the rearrangements of terpenoids^{3,15,16} give almost no consideration of the transformations of compounds with the carane skeleton.

The purpose of the present review is to generalise data on the skeletal rearrangements of terpenoids belonging to the carane series accumulated over the time period since the publication of reviews by Arbuzov and Isaeva¹⁰ and by Erman.¹² Earlier publications are only considered if the history of the problem is of interest or if a new understanding of the known facts has appeared. The rearrangements are discussed according to their mechanisms. The most thorough attention is given to concerted rearrangements, because these data have not been generalised or discussed so far.

II. Rearrangements of carane monoterpenoids occurring by the ionic mechanism

The realisation of the ionic mechanism in molecular rearrangements of carane monoterpenoids is due to the interaction of the cyclopropane ring with the electron-deficient carbenium centre at the α - or β -position with respect to the ring. Rearrangements of this type are of interest because they can provide intermediates with a delocalised charge. According to the classification suggested in the review by Arbuzov and Isaeva,¹⁰ ionic rearrangements of carane structures are divided into homoallylic rearrangements, rearrangements with the transannular involvement of the cyclopropane ring (CPR) and the Wagner–Meerwein rearrangements with contraction of the six-membered ring. However, this classification does not reflect the diversity of ionic

V A Chuiko Institute of Physical Organic Chemistry,
National Academy of Sciences of Belarus, ul. Surganova 13, 220072
Minsk, Belarus. Fax (37-517) 284 16 79. Tel. (37-517) 284 20 45.
E-mail: loc@ifoch.bas-net.by

O G Vyglazov Tereza-Inter Ltd, Olimpiiskii prosp. 22, 129110 Moscow,
Russian Federation. Fax (7-095) 281 51 31. Tel. (37-517) 216 17 06.
E-mail: ilb_vyglazov@mail.ru

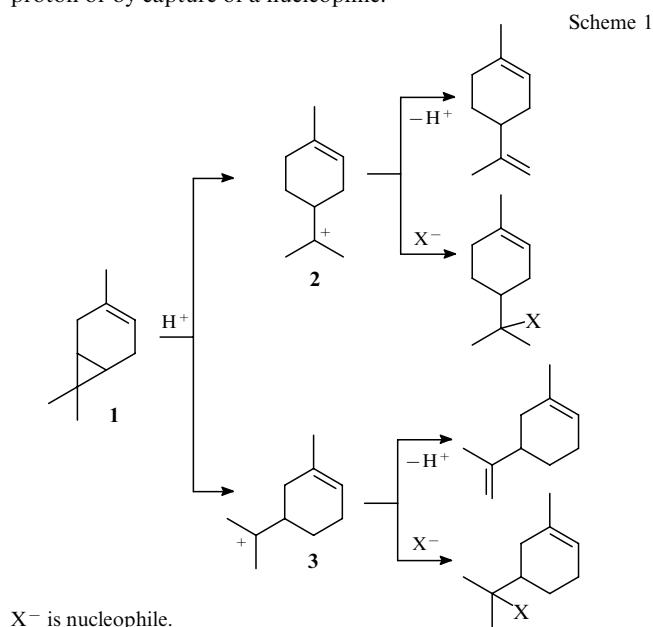
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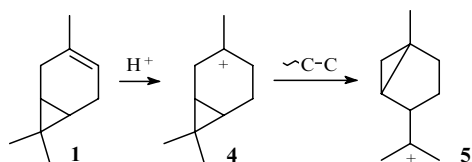
rearrangements of carane structures and is arbitrary. The homoallylic rearrangement is not the only one of the possible skeletal transformations *via* a carbocation with a delocalised charge: carane structures containing double bonds can also contain a pentadienyl-type cation; the latter may be formed in different ways from different compounds. In addition, we believe that it is more correct to consider rearrangements with transannular involvement of the CPR and the Wagner–Meerwein rearrangements together with concerted reactions because they involve alkyl shifts in charged systems.

1. Carbenium-ion rearrangements

A molecule of 3-carene contains two reactive fragments: a double bond and a cyclopropane ring. Both of these fragments have enhanced electron density, which makes the molecule reactive with respect to electrophilic agents. The rearrangement of 3-carene which occurs under the action of acids to give compounds of the *p*- and *m*-menthane series is well known.¹² It is likely that in this case the cyclopropane ring acts as an isolated reaction centre to form carbenium ions **2** or **3** (Scheme 1). The double bond is remote and does not interact with the carbon atom which carries a positive charge. The ions are stabilised by elimination of a proton or by capture of a nucleophile.



This transformation occurs in those cases where the CPR is initially protonated. Obviously, the addition of a proton to the double bond of the hydrocarbon **1** should give a tertiary ion **4**.



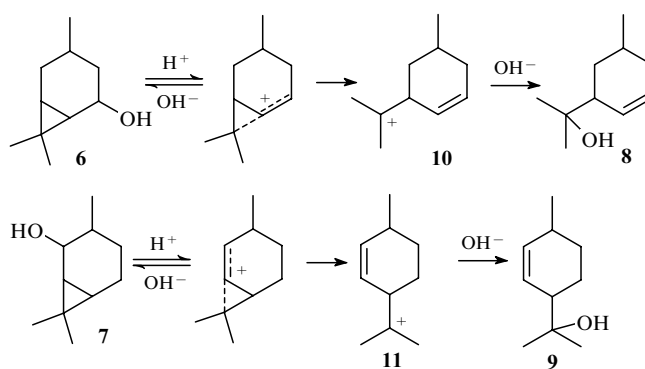
Ions of this type can undergo a rearrangement due to the so-called 'transannular cyclopropyl participation'¹⁰ (see Section IV.4), but this would result in an ion **5** and other products.

The fact that it is the CPR rather than the double bond that is protonated in the case of 3-carene can be rationalised in terms of the HSAB (Hard–Soft Acid–Base) principle. Cyclopropane is a harder base than the double bond (the ionisation potentials are 10.9 and 9.3 eV, respectively). In a molecule of 3-carene, the difference between the energies of the highest occupied molecular orbitals (HOMO) of the corresponding fragments is somewhat

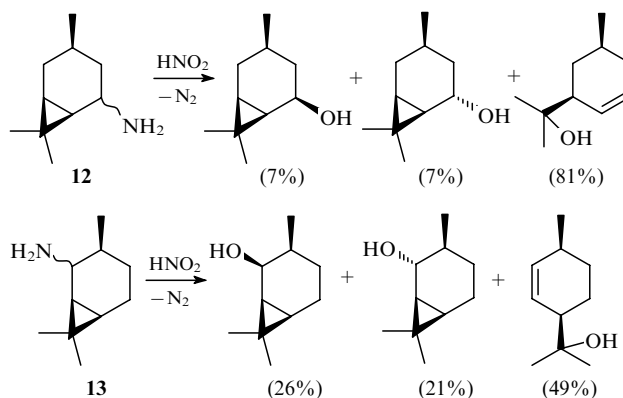
smaller but still rather high (9.16 and 8.61 eV).¹⁷ A hard acid, *viz.*, a proton, is first added to the hard base, *viz.*, the CPR. In fact, the reaction between equimolar amounts of 3-carene and hydrogen chloride gives derivatives with *p*- and *m*-menthane skeletons.¹⁸ The similarity of the electronic structures of the double bond and the CPR¹⁹ predetermines the similarity of their reactivities.²⁰ The existence of a cationoid site at the α -position with respect to the cyclopropane ring results in their conjugation and formation of a homoallylic ion. The direction of the reaction of this ion with a nucleophile depends on spatial factors, on the nature of the leaving group and on the degree of solvation of the molecule (in solvolysis reactions), *etc.*

If the subject of the attack in the homoallylic ion is the CPR, the latter is opened; in carane derivatives, a skeletal rearrangement occurs.

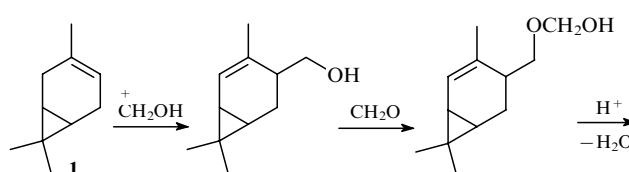
For example, under conditions of acid catalysis, caran-5-ol (**6**) and caran-2-ol (**7**) are isomerised to *m*- (**8**) and *p*-menthen-8-ols (**9**), respectively, as a result of a hydroxide attack on the C(8) atom in homoallylic ions **10** and **11**.^{21,22} These reactions can be considered as regiospecific.

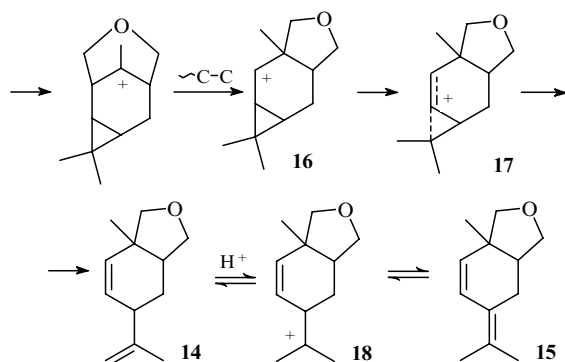


Deamination of 5- (**12**)- and 2-aminocaranes (**13**) occurs in a similar way; however, the presence of bicyclic alcohols among the products shows that the reaction was not completed in this case.²³



Homoallylic rearrangements can occur along with other ionic rearrangements. For example, the Prins condensation of 3-carene with formaldehyde gives, among other reaction products, two cyclic ethers **14** and **15**. Their formation is explained by the occurrence of the Wagner–Meerwein rearrangement followed by a homoallylic rearrangement.^{24,25}

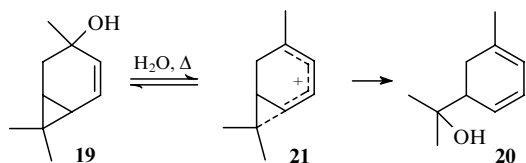




In this case, the Wagner–Meerwein rearrangement, which occurs as an alkyl shift, does not change the carane structure. However, the alkyl shift is only possible because the charge delocalisation in the secondary ion **16** with involvement of the cyclopropane ring results in ring opening to give the homoallyl ion **17** which has a lower energy. The ion **17** is stabilised by elimination of a proton from one of the geminal methyl groups giving the ether **14**. In an acidic medium, this ether isomerises to the ether **15** via the classical cation **18**.

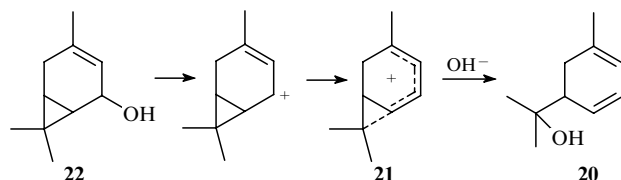
2. Rearrangements that occur via ions with a high degree of charge delocalisation

Obviously, the system CPR–charged carbon atom can comprise one or more double bonds. The resulting homopentadienyl ion has a higher degree of charge delocalisation, and hence a lower energy, than the homoallyl ion. Therefore, reactions involving homopentadienyl ions occur more readily than those involving homoallyl ions. The isomerisation of 4-carene-3-ol (**19**) to hydroxydiene **20** occurs upon boiling in water, even in the absence of acid catalysts:²⁶

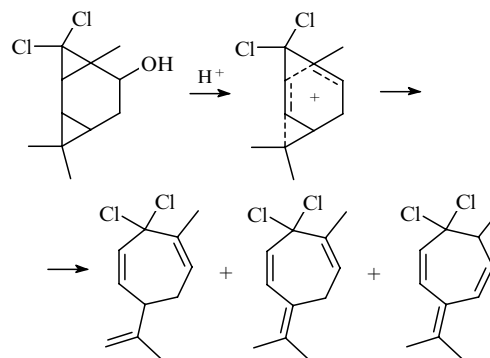


As in the isomerisation of compounds **6** and **7**, the irreversibility of the attack on the cyclopropane fragment of the ion **21** makes the reaction regiospecific.

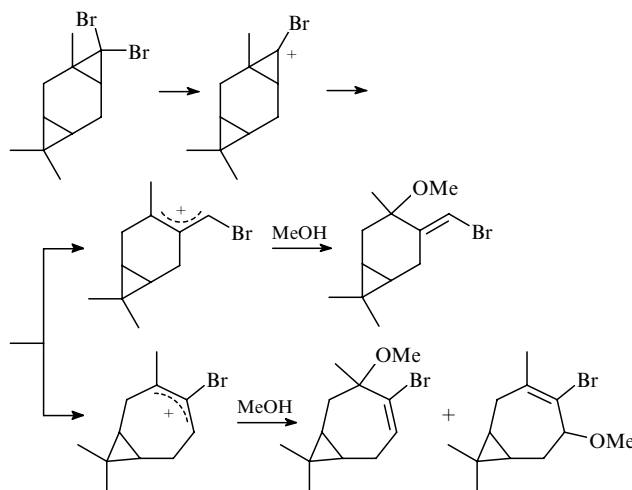
It should be noted that the neighbourhood (and, possibly, conjugation) of the double bond and CPR in a neutral molecule is not prerequisite for the formation of a homopentadienyl ion and hence, for a skeletal rearrangement. From the viewpoint of the reaction mechanism, the selective isomerisation of car-3-en-5-ol (**22**) to *m*-mentha-1,3-dien-8-ol (**20**) is of interest: the double bond and the CPR are united in a conjugated system by a carbocationic centre that is formed between them.²⁷



The conjugated system cationoid centre–CPR can involve not only the adjacent double bond but also the second three-membered carbocycle. The involvement of such an intermediate in the reaction results in the rearrangement of the tricyclooctane skeleton into a substituted cycloheptadiene.²⁸ This rearrangement is interesting because in this case it is the internal bond of the *gem*-dichlorocyclopropane ring that cleaved, whereas it is the external bond that cleaved in the *gem*-dimethylcyclopropane ring.

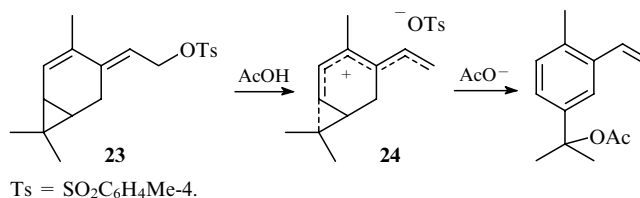


It is evident from the examples of ionic rearrangements presented above that the cleavage of the ‘external’ bond is a rule, which has almost no exceptions, for the *gem*-dimethylcyclopropane ring. On the contrary, the three-membered ring with two halogen atoms behaves in different ways. In the methanolysis of the adduct of 3-carene with dibromocarbene, the CPR opens in two ways, giving rise to both products with the retention of the carane structure and to rearrangement products.²⁹



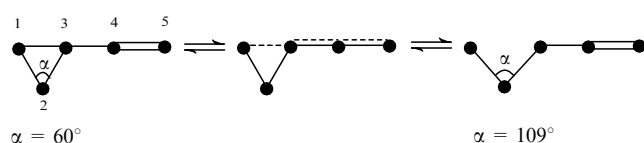
The fact that different bonds of the three-membered rings are cleaved in ionic reactions may be due to the nature of geminal substituents. The *gem*-dimethyl group shortens (and strengthens) the opposite cyclopropane bond,³⁰ whereas two geminal chlorine atoms lengthen and weaken this bond. The effect of geminal bromine atoms has the same direction but is weaker.³¹

Acetolysis of toluene-*p*-sulfonate **23** occurs extremely readily;³² in this case, the degree of charge delocalisation in the intermediate (homoheptatrienyl ion **24**) is even higher than that in the homopentadienyl ion.

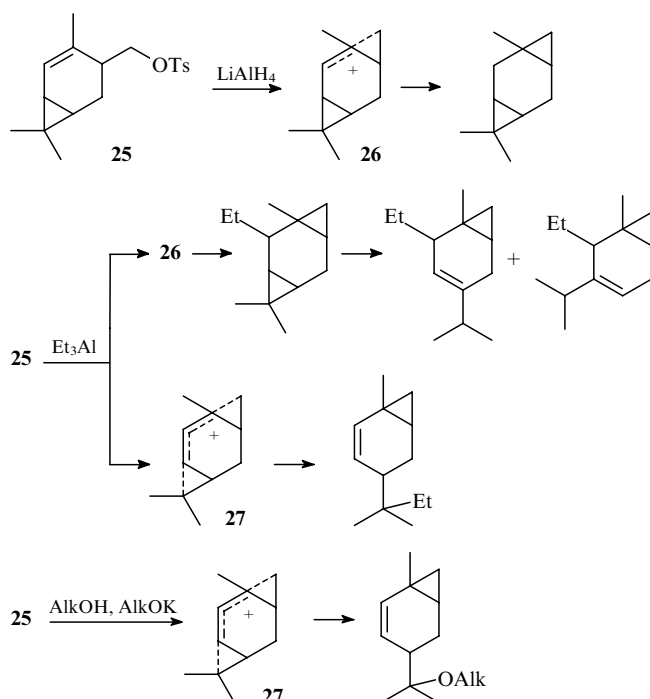


It was mentioned above that homoallylic and homopentadienyl rearrangements are irreversible; however, this statement is not quite correct. In fact, such transformations of carane derivatives can be carried out with a 100% degree of conversion. This is due to the geometry of the ion and the resulting molecule. The C(2) atom of the CPR, which is not involved in the conjugation chain, changes its hybridisation from sp^2 to sp^3 in the process of stabilisation of the homoallyl ion. As a result, the C(1)–C(2)–C(3) angle, which equals 60° in the cyclopropane molecule, increases to 109° in the molecule formed; in turn, this increases the distance between C(1) and C(3). However, if these

atoms are brought closer in some way, the formation of a homoallyl ion becomes possible again.

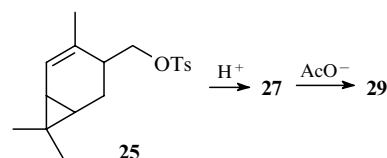
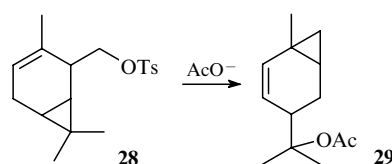


In practice, compounds with the menthane skeleton are never transformed into carane-type compounds. However, it was in the carane structures (owing to their specific features) that it was possible to observe the retro-homoallylic rearrangement, in which a homoallyl ion is formed from a linear fragment of the molecule and the three-membered ring is closed. Such an effect was observed in the reaction of toluene-*p*-sulfonate **25** with lithium aluminium hydride³³ or triethylaluminium,³⁴ as well as upon its solvolysis.³⁵

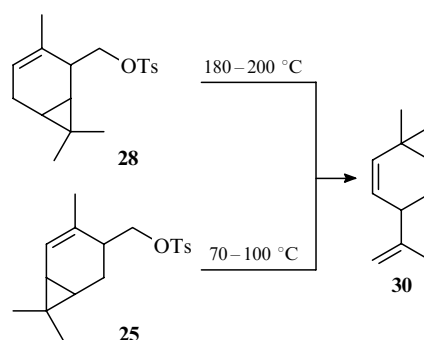


Obviously, in an ideal case, this reaction should occur according to the S_N1 mechanism. However, it is likely that the reaction involves contact ion pairs: very strong polarisation of the substrate occurs, with an almost complete charge separation; however, the resulting cation is stabilised by the counter-ion. Elimination of the toluene-*p*-sulfonate group from compound **25** gives a cation with a charge on the primary carbon atom; it is much less stable than the tertiary ions formed upon protonation of the CPR. The ion can be stabilised due to conjugation of the charged atom with the double bond; in this case, the *p*-orbitals overlap through space rather than through the σ -bond. The tight solvate environment favours the approach of these fragments, because the process is likely to be fast. This pathway gives the homoallyl ion **26** and/or the dihomopentadienyl ion **27**. If the reaction occurs *via* the intermediate ion **27**, quite an unusual rearrangement occurs: in fact, one molecule undergoes two rearrangements in different directions simultaneously, *viz.*, a homoallylic rearrangement, which results in the cyclopropane ring opening, and a retro-homoallylic rearrangement where a new three-membered carbocycle is closed.

It is appropriate here to note a very interesting fact: both 2-tosyloxymethyl-3-carene (**28**) and 4-tosyloxymethyl-2-carene (**25**) give the same ether **29** upon acetolysis.³⁶



The mechanism of the formation of the acetate **29** remains obscure so far. It is also of note that no products are formed which might be expected based on the data on the transformations of the ester **25**. The authors of the present review have observed yet another, rather unusual transformation of the toluene-*p*-sulfonate **28**: its pyrolysis results in the same hydrocarbon as that formed from the toluene-*p*-sulfonate **25**, *viz.*, 1-methyl-4-isopropenyl-bicyclo[4.1.0]hept-2-ene (**30**).³⁶



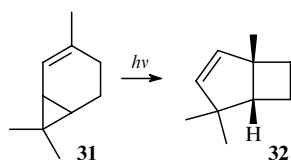
The pyrolysis mechanism of the ester **25**³⁷ will be discussed below, along with the possible mechanism of the pyrolysis of the toluene-*p*-sulfonate **28**.

Certainly, the mechanisms of ionic rearrangements involving ions with charge delocalised along the conjugation chain are hypothetical and are based on the structures of the final products. It is still unclear whether conjugation in such systems is really possible. As shown below when discussing hydrogenation of 2-carene (**31**), the neighbourhood of a double bond and the CPR by no means ensures their conjugation, at least for a neutral molecule in the ground state.^{17,38} It would be highly important to use modern quantum-chemical calculation methods in order to check whether charge delocalisation is possible in a conjugation system, which involves a CPR as an element, in rearrangements of compounds belonging to the carane series.

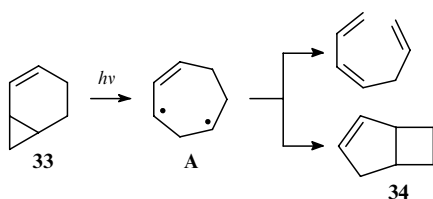
III. Rearrangements occurring by the radical mechanism

Generally, radical rearrangements of monoterpenoids belonging to the carane series occur in photochemical reactions. The photochemical transformations of such compounds have been reviewed in detail.¹² Here we consider only those which involve radicals, with emphasis on non-trivial skeletal rearrangements.

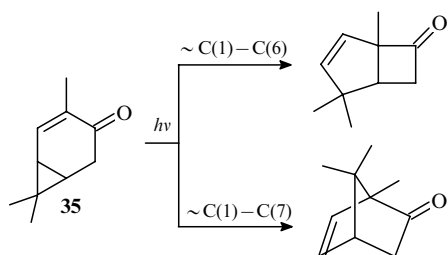
For 3-carene, no rearrangements under irradiation have been observed. Only its photochemical oxidation to give three hydroperoxides has been reported.³⁹ Upon irradiation in the presence of a sensitizer, the isomeric 2-carene is rearranged into 1,4,4-trimethylbicyclo[3.2.0]hept-2-ene (**32**), which has been employed in the synthesis of grandisole.⁴



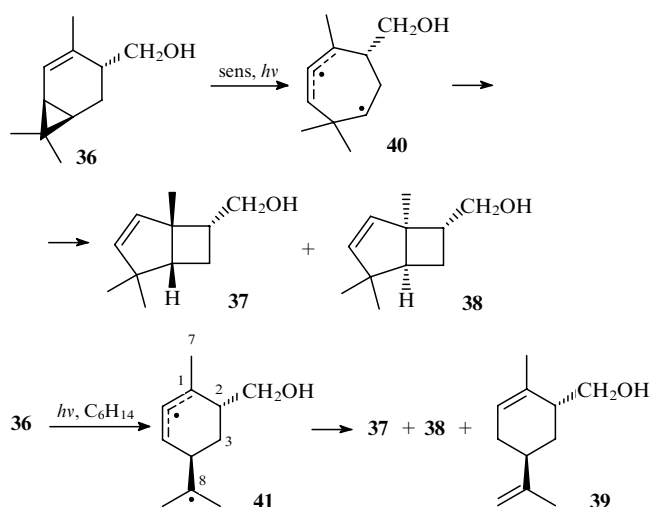
The rearrangement mechanism was not studied in this case; however, the mechanism for a related compound, *viz.*, 2-norcaradiene (**33**), has been reported.⁴⁰ Irradiation of compound **33** resulted in *cis*-hepta-1,3,6-triene as the main product, *i.e.*, the $[2\pi + 2\omega + 2\sigma]$ -process predominated. The formation of a small amount of bicyclo[3.2.0]hept-2-ene (**34**) allowed the authors to assume a common biradical intermediate **A** with a seven-membered ring:



There is a viewpoint^{12,41} that the formation of compounds with the bicyclo[3.2.0]heptane skeleton from certain carane terpenoids upon irradiation can occur as a photo-induced sigmatropic rearrangement. This assumption is supported by the fact that a bornene structure is formed in parallel from ketone **35**.



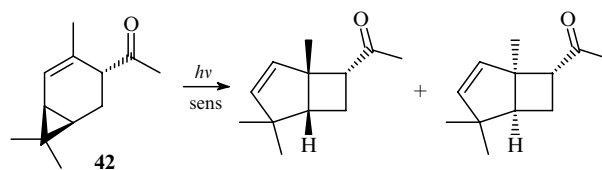
The concerted mechanism of rearrangement of ketone **35** is indirectly supported by the results of irradiation of 4-hydroxymethyl-2-caradiene (**36**) with a high-pressure mercury lamp:⁴² if a sensitizer is present, only stereoisomeric bicyclic alcohols **37** and **38** are formed, whereas direct irradiation in hexane gives rise to a monocyclic alcohol, *viz.*, compound **39**, in addition.



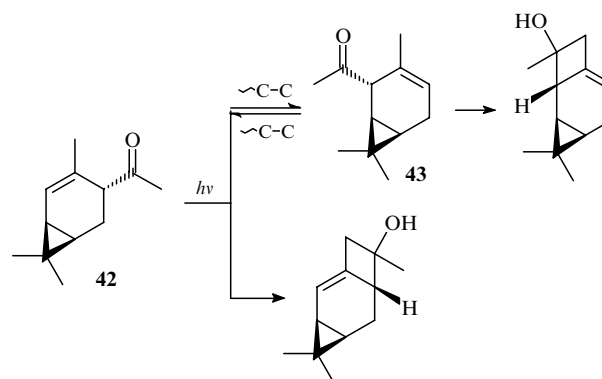
Kropp, who studied this reaction,⁴² drew an analogy with a 1,3-conjugated system and postulated the formation of allyl radicals. In this case, the CPR can undergo homolytic opening

with cleavage of an internal and of one of the external bonds. Probably, if a sensitizer is present, the molecule is transformed to biradical **40** from the triplet state: in this case, the weakest bond in the CPR is cleaved. In the singlet excited state, the molecule has higher energy, resulting in the cleavage of both possible bonds in the CPR. In this case, cleavage of the C(1)–C(7) bond occurs rather than its shift. Obviously, recombination and formation of a new bond between the C(1) and C(8) atoms in radical **41** (which would result in a bornane skeleton) are impossible because the distance between these atoms is larger than that between the atoms with unpaired electrons in biradical **40**.

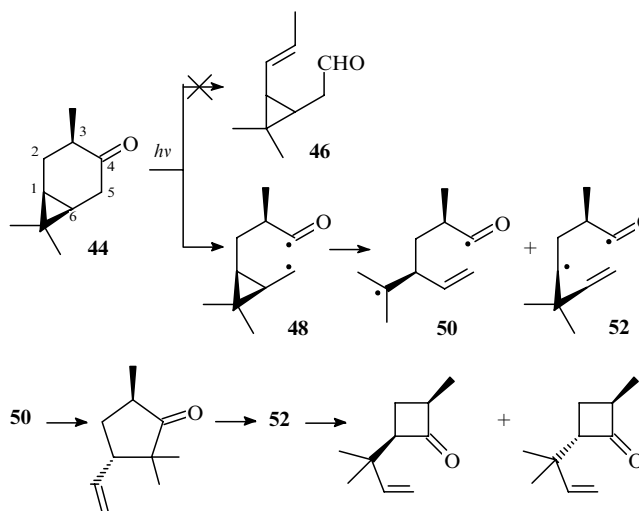
Irradiation of 4-acetyl-2-caradiene (**42**) in the presence of a sensitizer gives products with the bicyclo[3.2.0]heptane structure,⁴³ *i.e.*, replacement of a hydroxymethyl group by an acyl group does not alter the mechanism.

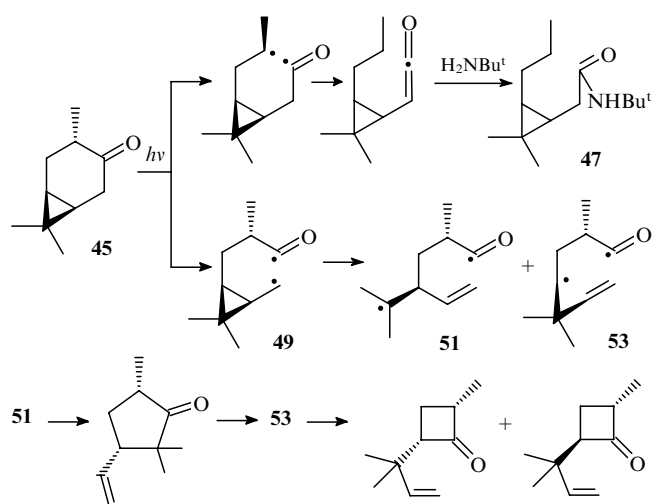


However, irradiation of the ketone **42** in the absence of sensitizers results in a fundamentally different rearrangement leading to the product of a 1,3-acyl shift [2-acetyl-3-caradiene (**43**)] and to tricyclic alcohols, *i.e.*, the Norrish type II cyclisation products of both ketones present in the reaction medium.⁴³



A somewhat unusual behaviour of *cis*- (**44**) and *trans*-4-caradiene (**45**) is observed in their irradiation. Although the structures of these molecules enable the Norrish type II cleavage of two bonds, *viz.*, C(3)–C(4) and C(4)–C(5), the phototransformation products of *cis*-caradiene (**44**) only contained compounds formed as a result of the C(4)–C(5) bond cleavage.⁴⁴





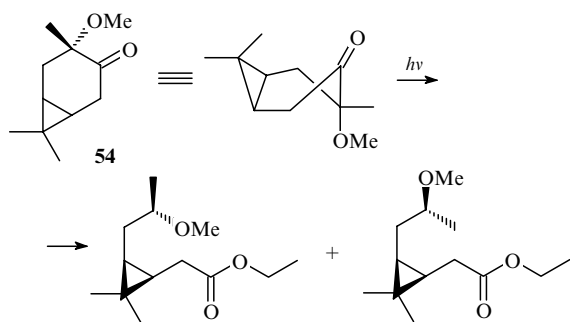
Contrary to expectations, no formation of aldehyde **46** or epimerisation of the ketone **45** was observed. However, upon irradiation of the latter in the presence of *tert*-butylamine, the reaction products contained a small amount ($> 1\%$) of amide **47**, which indicated that homolytic cleavage of the C(3)–C(4) bond does occur but quite insignificantly.

Formally, the photochemical behaviour of ketones **44** and **45** is very similar to the allylic rearrangements of β,γ -unsaturated ketones.⁴⁵ Kropp *et al.*⁴⁴ believed that the photochemical rearrangement of caranones **44** and **45** is the first example of the cyclopropyl analogue of the photochemical allylic rearrangement. However, the reaction is reversible for β,γ -unsaturated ketones and irreversible for ketones **44** and **45**.

By analogy with β,γ -unsaturated ketones, the direction of α -cleavage of carbon–carbon bonds is presumably determined by the ‘allylic’ effect of the CPR, which weakens the C(4)–C(5) bond owing to either the conjugation or inductive effect. In the radicals **48** and **49** formed, the C(1)–C(6) or C(1)–C(7) bonds should be cleaved. The ratio of cyclopentanones and cyclobutanones in the reaction products (3 : 1) reflects the preferential cleavage of the more substituted C(6)–C(7) bond and the comparative stability of the tertiary (**50**, **51**) and secondary (**52**, **53**) radicals.

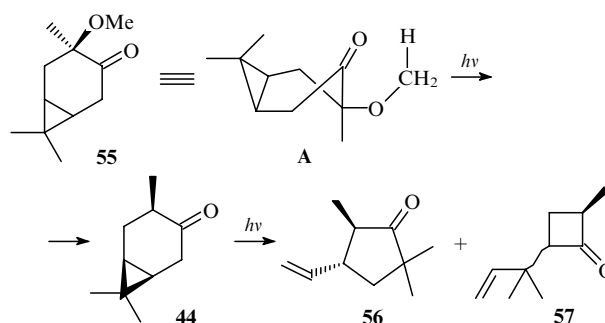
There is yet another difference between allylic photochemical rearrangements of β,γ -unsaturated ketones and similar rearrangements of cyclopropyl ketones. The allylic rearrangement is believed to be a concerted process.⁴⁵ However, Heckert and Kropp⁴⁴ consider that the transformations of caranones **44** and **45** cannot be a concerted reaction, at least as judged by the formation of epimeric cyclobutanones.

The direction of the skeletal photochemical rearrangement of terpenoids belonging to the carane series depends on the orientation of substituents: direct irradiation of *trans*-3-methoxy-4-caranone (**54**) in ethanol occurs with opening of the six-membered ring with cleavage of the C(3)–C(4) bond (which is non-typical of β,γ -cyclopropyl ketones) and addition of ethanol.³⁹



In the case of *cis*-3-methoxy-4-caranone (**55**) with an equatorial methoxy group, the only reaction observed is the Norrish type II elimination, resulting in the caranone **44**; the required planar

six-membered transition state (TS) **A** is formed readily, and the formation of the ketone **44** competes successfully with the cleavage of the C(3)–C(4) bond.³⁹



When exposed to light, the ketone **44** undergoes homolytic cleavage of the C(4)–C(5) bond and homoallylic rearrangement, which is typical of β,γ -cyclopropyl ketones.^{44, 46} This reaction gives cyclopentanone **56** and cyclobutanone **57**.

Thus, the photochemical rearrangements of carane monoterpenoids may be divided in two groups, *viz.*, those where the cyclopropane part of the carbon skeleton and the double bond serve as the chromophores, and those where this role is played by a functional substituent. In the presence of sensitizers, rearrangements of the former type occur, giving rise to bicyclo[3.2.0]heptane derivatives. Irradiation in the absence of sensitizers generally results in rearrangements of the latter type; in this case, the following reactions are possible: opening of the large or small ring, contraction of the large ring or formation of a tricyclic structure. In each specific case, the direction of the reaction depends on the nature and position of the substituent which acts as the chromophore.

IV. Concerted reactions

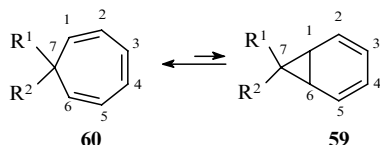
Ionic reactions of carane compounds are dealt with in numerous publications and these works have repeatedly been systematised, whereas concerted transformations have been studied to a much lesser extent, and the results have not been generalised so far. To be fair, it should be noted that not all reactions attributed to the concerted type actually correspond to this type. For example, in the case of 2,4-caradiene (**58**), the 1,5-thermal shift is formally a concerted sigmatropic reaction. However, first, this occurs *via* a biradical intermediate rather than *via* a cyclic TS (with simultaneous cleavage and formation of C–C bonds); second, it is not a sigmatropic process in essence. In certain cases, the concerted mechanism involves a strongly polarised TS or is coupled with the ionic mechanism. However, the reaction classification would be overcomplicated if these features were taken into account; therefore, in this section we shall discuss the transformations which are traditionally attributed to concerted reactions.

We believe that a survey of such reactions of carane monoterpenoids is especially interesting because it is these that sometimes result in unique transformations that are characteristic only of these compounds (for example, the Berson–Willcott rearrangement⁴⁷). Studies of concerted reactions expand substantially our knowledge about the mechanisms of chemical reactions in general.

1. Norcaradiene–cycloheptatriene interconversion

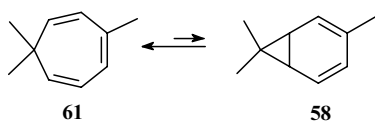
One of the most interesting skeletal transformations of carane structures, *viz.*, rearrangements which relate terpenoids of the carane and 1,1,4-trimethylcycloheptane series, attracted the attention of researchers; this resulted in the discovery of such a remarkable phenomenon in organic chemistry as the norcaradiene–cycloheptatriene ‘rapid’ equilibrium. Many studies on this subject have been carried out in the last third of the twentieth century.^{47–55} The fast equilibrium of the valence tautomers of norcara-2,4-diene (**59**) and cyclohepta-1,3,5-triene (**60**) is caused

by a typical concerted reaction, *viz.*, disrotatory opening and closure of the three-membered carbocycle; this process obeys the conservation of orbital symmetry rules formulated by Woodward and Hoffmann.⁵⁶



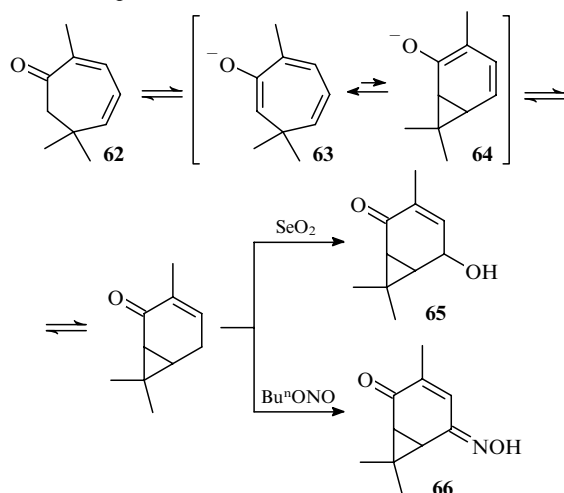
For the unsubstituted hydrocarbon ($R^1 = R^2 = H$), this equilibrium is so much shifted to the monocyclic tautomer **60** that norcaradiene could not be detected by any physical method. Its existence was postulated on the basis of the behaviour of substituted analogues ($R^1 = CN$, $R^2 = CF_3$; $R^1 = CO_2Me$, $R^2 = Ph$; $R^1 = CO_2Me$, $R^2 = C_6H_4OMe-4$), which were found as equilibrium mixtures with the corresponding cycloheptatrienes in low-temperature NMR studies of the latter.⁵⁵ It was only in 1981, a quarter of a century after the hypothesis about the valence tautomerism of cycloheptatriene appeared, that unsubstituted norcaradiene was detected during the low-temperature (77 K) photolysis of tricyclo[3.2.2.0^{2,4}]non-6-ene-8,9-dione.⁵⁷

It was found experimentally that the bicyclic structure can be stabilised by π -accepting substituents at position 7.⁵⁵ An elegant explanation of the nature of this stabilisation was given by R Hoffmann within the framework of the frontier MO method.⁵³ Obviously, methyl substituents cannot serve as stabilisers; therefore, the equilibrium for the system 2,4-caradiene (**58**)–3,7,7-trimethylcyclohepta-1,3,5-triene (**61**) is always shifted towards the monocyclic partner. However, these valence tautomers are different compounds that really exist. They possess different reactivities, which should be reflected (and is actually reflected, as will be shown below) in chemical reactions.

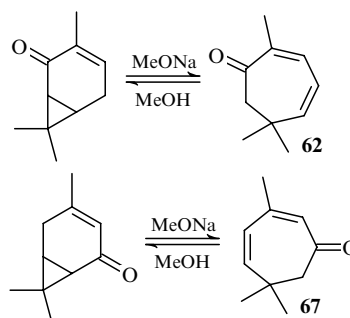


Rearrangements caused by valence tautomerism described above will be discussed in more detail than ionic rearrangements, because the tautomerism of norcaradiene has almost not been considered in Russian scientific literature. Unfortunately, even researchers who work in the field of terpenoid chemistry employ insufficiently substantiated hypotheses to explain the expansion of the carane skeleton to the cycloheptane one.^{12, 58}

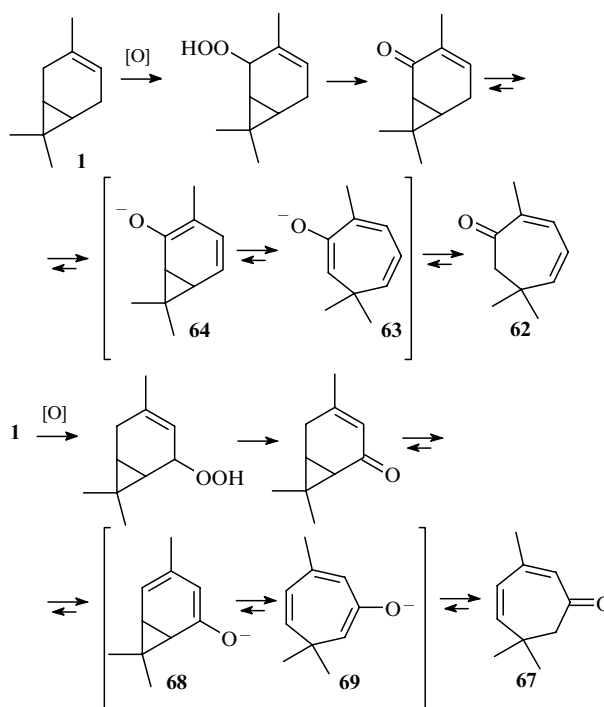
The cycloheptatriene–norcharadiene rearrangement has been discovered in a study of the chemical transformations of eucarvone [2,6,6-trimethylcyclohepta-2,4-dienone (**62**)], a terpenoid first synthesised by Baeyer⁵⁹ and then discovered in the essential oils of various plants.⁶⁰



The hypothesis about the valence tautomerism of mono- and bicyclic enols **63** and **64** as a possible explanation of the skeletal rearrangement of the ketone **62** during the formation of 3,7,7-trimethyl-5-hydroxy-3-carene-2-one (**65**) and 3,7,7-trimethyl-5-oxyimino-3-carene-2-one (**66**) was put forward in 1956.^{61, 62} It was then found that rearrangements of carane derivatives into trimethylcycloheptane ones are much more common, because the equilibrium in the dynamic interconversion of the two tautomers is strongly shifted toward the monocyclic partner.⁶³



2,5,5-Trimethylcyclohepta-2,4-dienone (**67**), like the ketone **62**, has been found in the turpentine obtained from *Pinus silvestris* L.⁶⁴ Probably, the presence of these ketones in turpentine oil is explained by the formation, during plant growth, of carane-type unsaturated ketones from 3-carene (one of the major turpentine components); these are then transformed into monocyclic dienones in a concerted electrocyclic reaction. This is supported by the results of liquid-phase oxidation of 3-carene: the percentage of ketones **62** and **67** in the reaction products was 20% and 28%, respectively.⁶⁵

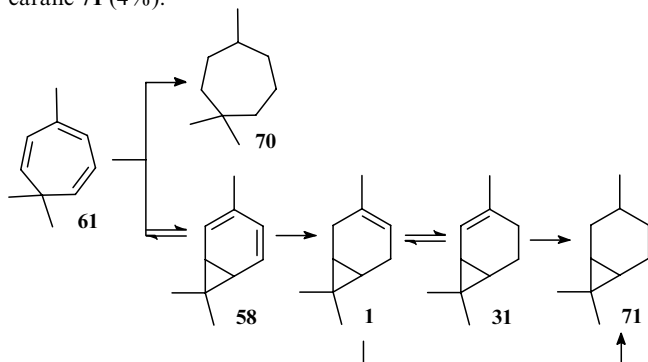


It should be noted that the $64 \rightarrow 63$ and $68 \rightarrow 69$ rearrangements represent the only currently feasible explanation of the presence of seven-membered ketones in essential oils. The general scheme of the biogenesis of terpenes^{66, 67} does not envisage any formation of such compounds at all. However, the widespread occurrence of 3-carene and its derivatives in nature and also the fact that trimethylcycloheptanes are only present in those essential oils which contain carane-type terpenoids, may be considered as indirect evidence in favour of the assumption about the formation of terpenoids with a seven-membered ring. We believe that the assumption that eucarvone (**62**) can be formed during biosyn-

thesis¹² in the same way as Baeyer⁵⁹ had synthesised it, *viz.*, by hydrobromination of carvone followed by dehydrobromination of the resulting 8-bromo-1-menthen-6-one, is much less likely.

Finally, a serious argument in favour of the **58** → **61** rearrangement as the reason for the formation of cycloheptane terpenoids both *in vitro* and *in vivo* is the detection of triene **61** in pine turpentine oil and in oleo-resin from certain pine (*Pinus silvestris*) trees.⁶⁸ Since this triene coexists with cara-2,4-diene, which is present in turpentine and in oleo-resin, it may be concluded that 2-carene, which is also present in turpentine, can undergo catalytic (enzymic) dehydrogenation.

The dual nature of triene **61** is very evident in its hydrogenation: reaction products of incomplete hydrogenation contain not only trimethylcycloheptadienes and trimethylcycloheptenes but also 3-carene (**1**) and 2-carene (**31**). Exhaustive hydrogenation results in a mixture of 1,1,4-trimethylcycloheptane (**70**, 96%) and carane **71** (4%).⁶⁹



Certainly, the ratio of the final hydrogenation products (**70**:**71** = 96:4) does not reflect the content of the tautomers in the original equilibrium mixture. A comparatively large percentage of carane **71** may be due to the fact that the planar diene system of caradiene **58** competes successfully with non-planar diene parts of the triene **61** in the 1,4-addition of hydrogen.

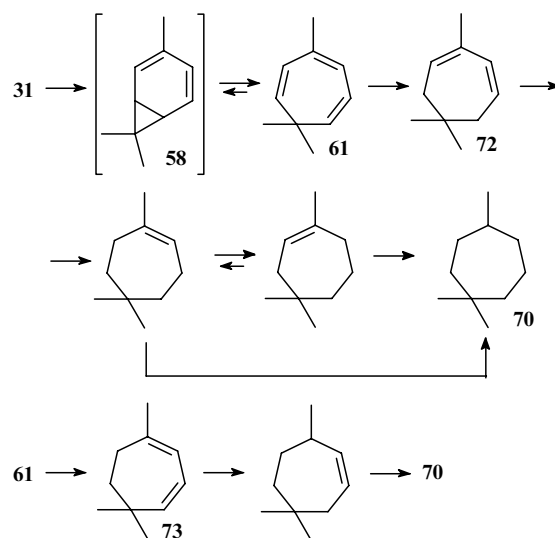
3-Carene is hydrogenated in an unusual way. Cocker *et al.*⁷⁰ discovered in 1966 that hydrogenation of 3-carene over platinum results in a mixture of compounds **71** (98%) and **70** (2%), whereas hydrogenation over palladium gives rise to the hydrocarbon **70** as the major product (74%).⁷⁰ It was found later that hydrogenation of 3-carene on a copper–nickel catalyst results exclusively in 1,1,4-trimethylcycloheptane (**70**).⁵⁸ The authors of both studies believed that this reaction pattern was due to the isomerisation of 3-carene (**1**) to 2-carene (**31**) and 1,4-addition of hydrogen to the vinylcyclopropane system of the latter to give a hydrocarbon with a seven-membered ring.

It was implied that the possibility (or impossibility) of 1,4-addition, which is the key step of the rearrangement, depends on the nature of the catalyst. However, 1,4-addition is only possible if there is conjugation in the diene fragment (or a homodiene fragment in the hydrocarbon **31**). However, the molecule of terpene **31** is in the planar chair-like conformation,³⁸ which casts doubts that such conjugation is possible. The photoelectron spectrum shows that the π -orbital and the HOMO of the dimethylcyclopropane ring in the molecule of compound **31** essentially do not interact.¹⁷ The impossibility of 1,4-addition for the 2-carene molecule (**31**) has been confirmed experimentally.⁷¹ It was shown that the reaction of singlet oxygen, which is an extraordinarily reactive dienophile, with this terpene gives only allylic hydroperoxides, whereas its other reactions, *e.g.*, with α -phellandrene and α -terpinene, give endoperoxides, which are 1,4-addition products.

In their discussion of the reaction mechanism, Cocker *et al.*⁷⁰ did not take their own results into account: if palladium was used as the catalyst, the content of hydrocarbon **70** increased with the increase in the hydrogenation temperature and was 100% at temperatures above 70 °C, *i.e.*, the ratio of the reaction products is primarily affected by temperature. A similar temperature

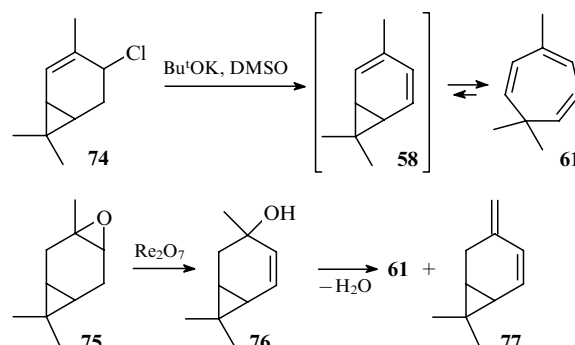
dependence was established later for hydrogenation over platinum: at 20 °C, the percentage of hydrocarbon **70** is 2%–3%, whereas at 70 and 90 °C, it is 37% and 46%, respectively.⁷²

The rationale for the skeletal rearrangement of 3-carene during hydrogenation is that both platinum and palladium catalyse both the direct and reverse reactions and can fulfil dehydrogenation in the presence of free hydrogen.⁷³ Hydrogenation of 3-carene upon addition of hydrogen to the double bond gives rise to carane; dehydrogenation of 2-carene, which always exists in the reaction medium (due to isomerisation of 3-carene, which occurs on the catalyst in the presence of hydrogen), results in the diene **58**, triene **61** and other compounds with modified skeletons.⁷⁴ An increase in temperature favours endothermic dehydrogenation and hence increases the content of rearranged products. It should be noted that hydrogenation on a copper–nickel catalyst carried out at high temperatures (180 °C) gave the hydrocarbon **71** as the only product.⁵⁸



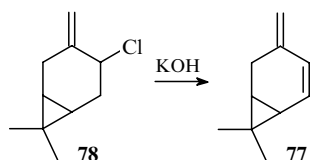
The direct proof that it is this mechanism that is actually realised is that 2- and 3-carenes undergo disproportionation over palladium and platinum in the absence of free hydrogen. In this case, the triene **61** was identified among the products, which confirms the assumption that dehydrogenation of 2-carene (**31**) is a step which is responsible for the formation of rearranged products.⁷⁵ In addition, the reaction mixture contained trimethylcycloheptadienes **72** and **73**. However, none of the known pathways of the isomerisation of terpenes **1** and **31** (including catalytic reactions) results in such ring expansion.

Based on the above considerations, it may be concluded that rearrangement of carane structures into trimethylcycloheptane structures occurs if the formation of the diene **58** (or its derivatives) is possible during the reaction. The simplest way to caradiene **58** is that from 2- and 4-carene derivatives with a functional group in the allylic position. Thus, dehydrochlorination of 4-chloro-2-carene (**74**) results in the triene **61**.⁷⁶ The transformation products of epoxide (**75**) in the presence of

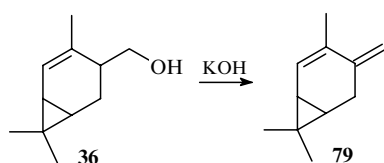


rhodium catalysts contained 4-carene-3-ol (**76**), which also gives the hydrocarbon **61** upon dehydration.⁷⁷

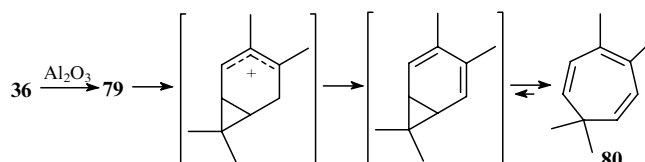
Theoretically, dehydration of the alcohol **76** can also follow another direction, *viz.*, with the formation of a terminal methylidene group. The corresponding hydrocarbon, 3(10),4-caradiene (**77**), was in fact detected among the reaction products formed from the epoxide **75**.⁷⁷ Hydrocarbon **77**, which was originally obtained by dehydrochlorination of 4-chloro-3(10)-carene (**78**),⁷⁸ is the first stable diene with the carane skeleton.



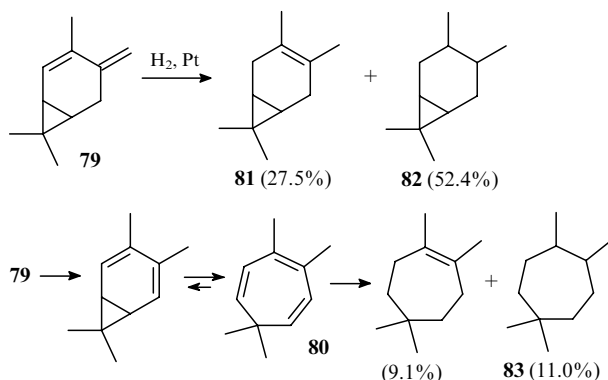
Dehydration of the alcohol **36** in the presence of potassium hydroxide resulted in the second compound of this series, *viz.*, 4-methyl-3(10),4-caradiene (**79**).⁷⁹



Dienes **78** and **79** are stable (*i.e.*, they do not undergo tautomeric transformations), as, unlike compound **58**, they have a transoid diene system, which cannot undergo electrocyclic closure, and hence, concerted rearrangement. However, these compounds are highly reactive: even weak acids, such as salicylic and benzoic acid, isomerise the transoid diene system into a cisoid system; after that, a concerted rearrangement into cycloheptatrienes occurs.⁸⁰ The dehydration products of the alcohol **36** with Al_2O_3 (Lewis acid) were found not to contain even traces of the diene **79** (unlike its alkaline dehydration⁷⁹); however, 3,4,7,7-tetramethylcyclohepta-1,3,5-triene (**80**) was present.⁸¹

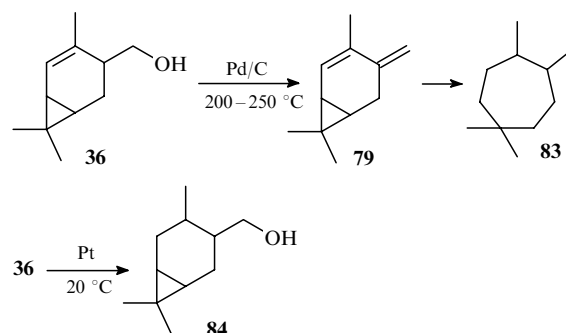


Hydrogenation of the diene **79** over platinum black at 20 °C also occurs with a rearrangement, which obviously results from its isomerisation on the catalyst.⁸⁰ In this case, of note is that the exhaustive hydrogenation products contain a rather high percentage of compounds **81** and **82** with a bicyclo[4.1.0]heptane skeleton. This means that the rate of hydrogen addition to the diene **79** is higher than the rate of its isomerisation, which is a side process (at least, at room temperature).

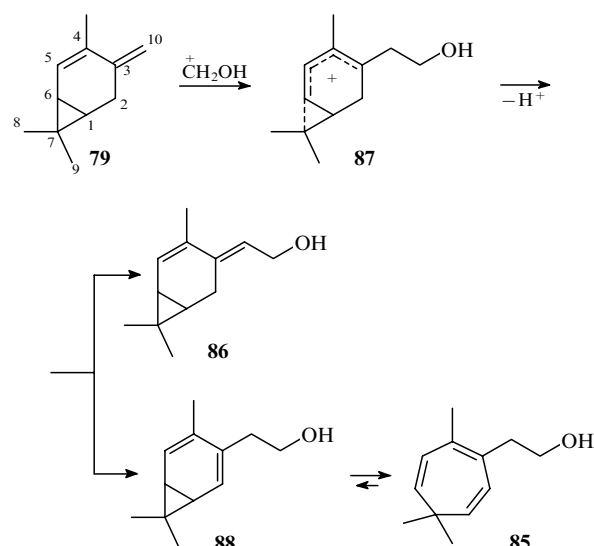


As a result of the three reactions altogether, *i.e.*, dehydration, isomerisation and hydrogenation, the catalytic hydrogenation of the alcohol **36** under drastic conditions yields 1,4,4,5-tetramethyl-

cycloheptane (**83**).⁸² Over platinum at 20 °C, the reaction does not involve isomerisation; it occurs by simple hydrogen addition to the double bond and gives rise to 4-hydroxymethylcarane (**84**).⁸³

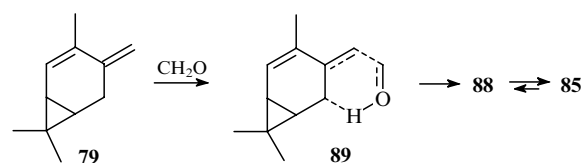


The rearrangement which occurs due to the valence tautomerism makes it possible to obtain functional derivatives of cycloheptatriene. For example, the diene **79** undergoes the Prins reaction to give two hydroxymethylation products, *viz.*, a mono- (**85**) and bicyclic one (**86**).⁸⁴



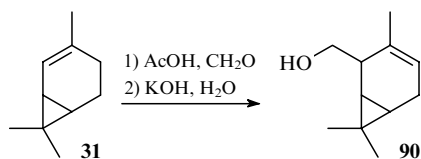
Electrophilic attack on the terminal double bond in compound **79** by a protonated formaldehyde molecule results in homodienyl ion **87**, which is stabilised by deprotonation (i) from C(5) to give the alcohol **88**, or (ii) from C(10) to give the allylic alcohol **86**. The alcohol **86**, when treated with an acid, is isomerised to caradiene alcohol **88**, which then rearranges into the alcohol **85**.

The monocyclic alcohol **85** can also be formed by yet another mechanism. If the initial hydrocarbon adds a formaldehyde molecule, the first reaction step occurs as a concerted process *via* a six-membered polarised TS (**89**)⁸⁵ to give the bicyclic alcohol **88**. Subsequent rearrangement yields the reaction product **85**. Thus, the transformation of the diene **79** into the trienic alcohol **85** can occur as a sequence of two concerted reactions.

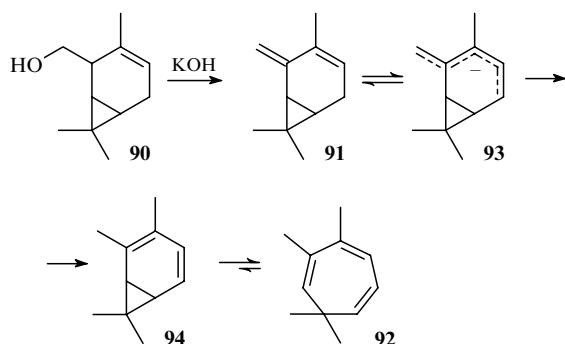


It should be noted that the attack of an electrophilic agent (a charged molecule or a dipole) is directed to the C(10) atom in compound **79**, *i.e.*, to one end of the conjugated homotrienyl system, which is more accessible spatially. However, in the reaction with 2-carene (**31**), the protonated formaldehyde mole-

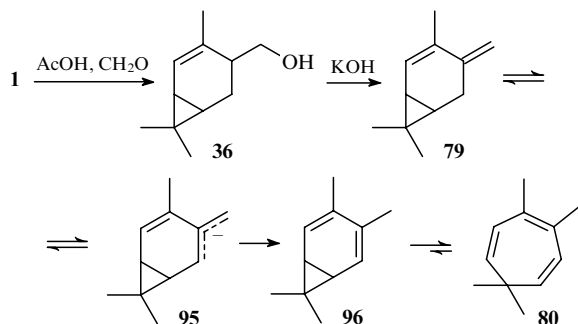
cule adds to the least substituted end of the double bond to give homoallylic alcohol **90**,⁸⁶ which is additional evidence for the absence of conjugation in the 2-carene molecule.



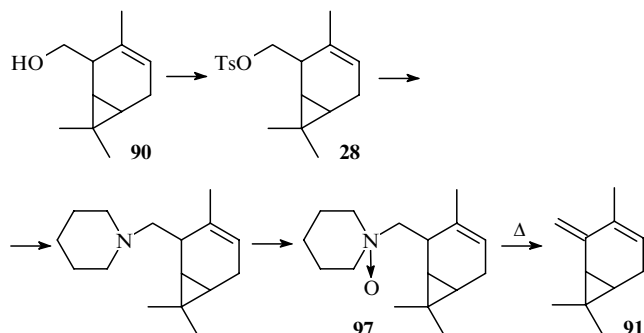
It should be noted that dehydration of 2-hydroxymethyl-3-carene (**90**) with potassium hydroxide does not give a caradiene with an exocyclic double bond (**91**) as the main product; instead, this yields 2,3,7,7-tetramethylcyclohepta-1,3,5-triene (**92**), which is obviously formed *via* intermediates **93** and **94**.⁸⁶



Dehydration of the alcohol **36** gave not only the triene **80** but also the diene **79** as the reaction products.⁸⁴ Charge is delocalised to a greater extent in the pentadienyl anion **93** than in the allylic anion **95**; therefore, the transformation of the diene **91** into the final product **92** occurs more readily than the transformation of the diene **79** into the diene **96** and further into cycloheptatriene **80**.

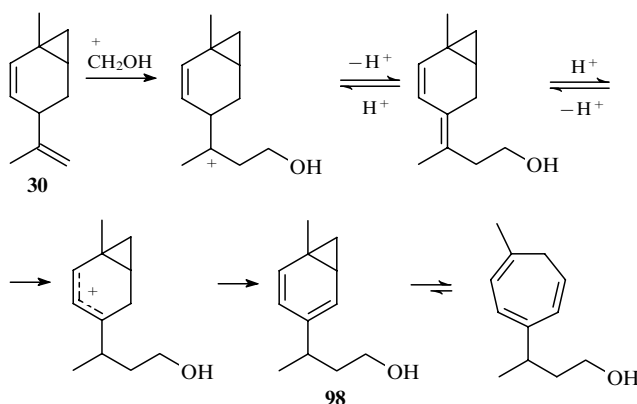


Generally, concerted rearrangements of transoid caradienes occur very readily, therefore special measures are to be taken to avoid this reaction and obtain very labile non-rearranged dienes. For example, thermal decomposition of *N*-oxide **97** was the only approach that allowed hydrocarbon **91** to be prepared from the alcohol **90**.⁸⁶



Turning back to the Prins reaction, it may be noted that when a hydrocarbon molecule that has the bicyclo[4.1.0]hept-2-ene system contains an additional isolated double bond (as in com-

pound **30**), the initial attack of formaldehyde is directed at this bond. However, under conditions of acid catalysis, the bicyclic alcohol formed initially readily isomerises to give a bicyclo[4.1.0]hepta-2,4-diene system (*e.g.*, compound **98**), in which a concerted rearrangement occurs.⁸⁶

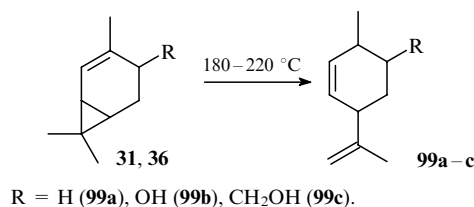


2. Sigmatropic rearrangements

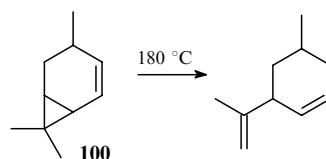
Thermal rearrangement of 2-carene (**31**) and its derivatives was the first example of the transformations which were later called the 1,5-homodienyl shift.⁸⁷

It is well known that vinylcyclopropane is transformed into cyclopentene at temperatures above 330 °C; the reaction occurs as a homolytic bond cleavage followed by isomerisation of the biradical formed and subsequent recombination.⁸⁸ The activation energy of this rearrangement is rather high and equals 208 kJ mol⁻¹ (see Ref. 89).

However, 2-carene and its derivatives, whose molecules contain the vinylcyclopropane moiety, undergo a rearrangement at a temperature as low as 180 °C to give the corresponding derivatives of *trans*-isolimone **99a–c**.^{90,91} 4-Carene (**100**) reacts similarly.⁹²



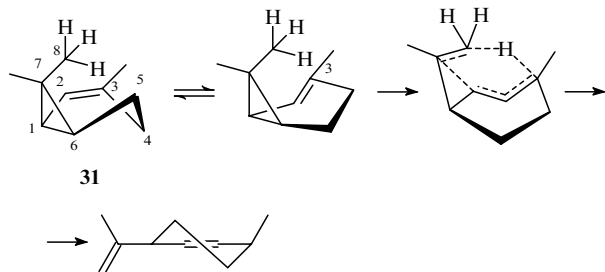
R = H (**99a**), OH (**99b**), CH₂OH (**99c**).



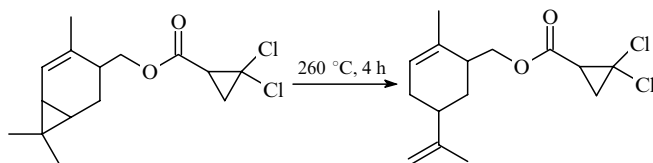
This transformation is determined by specific features of the structure of 2- and 4-carene derivatives: just as the 1,5-dienyl shift of hydrogen is possible in *cis*-1,3-diene systems, a 1,5-homodienyl shift is possible in carene compounds which have a vinylcyclopropane fragment. The reaction occurs *via* a six-electron transition state and obeys the selection rules for thermal hydrogen shifts.⁵⁶ No homolytic cleavage of the carbon–carbon bond occurs, since the activation energy of the 1,5-homodienyl shift is much lower than the energy of the vinylcyclopropane rearrangement; in the case of 2-carene, it equals 118 kJ mol⁻¹ (see Ref. 91).

The prerequisite for the 1,5-shift is the *endo*-orientation of the C–H bond and the vinyl group involved in the formation of the transition state.⁹³ This is the only stereochemical requirement for the thermal rearrangement of *cis*-1-methyl-2-vinylcyclopropane; the positions of the substituents in its molecule do not cause any additional strain. This requirement is also met for the 2-carene (**31**) molecule; however, the double bond is part of the six-membered ring and therefore it deviates from the direction

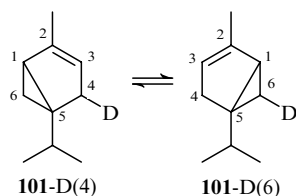
which is optimal for conjugation with the CPR and formation of the TS. The distance between C(3) and the hydrogen atom at C(8) is ~ 3.1 Å in the planar chair-like conformation.³⁸ This means that the molecule of 2-carene (**31**) on heating should first change its conformation [as a result, the C(3)–H(8) distance decreases to 2.3 Å], and only then undergoes the 1,5-homodienyl shift.



The nature of the substituent at position 4 can affect the activation energy of the conformation transition, but even bulky substituents do not prevent the 1,5-shift; however, the thermal rearrangement of such compounds requires higher temperatures.⁹⁴

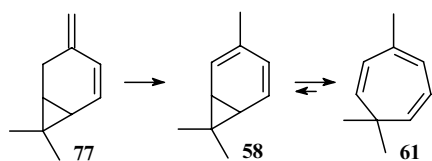


α -Thujene (**101**), whose molecule also contains a vinylcyclopropane fragment, remains unchanged when heated above 300 °C. However, experiments using a deuterium label showed that a degenerate vinylcyclopropane rearrangement actually occurs. In this case, the TS required for the 1,5-homodienyl shift is hard to access: the distance between D(4) and C(5) or C(3) is ~ 2.8 Å.⁹⁵



It should be noted that, owing to the geometry of their molecules, it is the carane structures that turned out to be suitable models for studying the 1,5-homodienyl shift. In the thermal isomerisation of terpenoids with the bicyclo[4.1.0]hept-2-ene skeleton, the 1,5-homodienyl shift occurs regio- and stereospecifically; this makes it possible, *e.g.*, to synthesise new oxygen-containing terpenoids from 2-carene derivatives.⁹⁶

The presence of an *endo*-oriented vinylcyclopropane fragment and an appropriate C–H bond in compounds of the carane series does not necessarily mean that thermal 1,5-hydrogen shift is possible. For example, heating of caradiene **77** at 120 °C gave the triene **61** as the major (or the only one, at relatively low temperatures) transformation product.⁹⁷ At higher temperatures (170–190 °C), small amounts of *p*- and *m*-cymenes (up to 3%) formed as well.



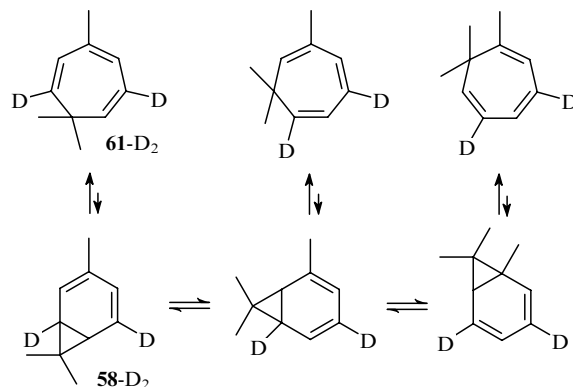
It might seem that the 1,5-homodienyl shift should be the most likely process under these conditions: the vinyl group and one of the C(8)–H bonds have an *endo*-orientation; the C(4)–H(8)

distance is ~ 2.2 Å, *i.e.*, it is easy to attain the ideal TS for the 1,5-shift calculated theoretically.⁹³ However, such a transformation should give *m*-mentha-1(7),4,8-triene, which is not formed in reality. A vinylcyclopropane rearrangement is also impossible at these temperatures, as they are not high enough for a radical reaction. It might be assumed that valence tautomerism is responsible for skeletal rearrangement. Then the thermal isomerisation **77** $\rightarrow$ **61** is actually reduced to the transformation of the transoid diene **77** to the cisoid diene **58**. This is formally a 1,3-sigmatropic shift.

It is generally believed that the non-catalysed hydrogen 1,3-shift does not occur in thermal reactions, since the transition state of the allowed antarafacial shift is hardly accessible because of the high angular strain in the propene fragment.⁹⁸ The suprafacial shift, which is quite possible as regards spatial aspects, is forbidden due to the orbital symmetry conservation rules. However, an *ab initio* calculation of the 1,3-shift in propene showed that the forbidden suprafacial hydrogen transfer requires a lower activation energy than the allowed antarafacial transfer.⁹⁹ This unexpected result was explained using a hypothesis about the subjacent orbital control.¹⁰⁰ This hypothesis underlies the assumption that a 1,3-shift occurs in the molecule of the diene **77**.

The mechanism of the thermal isomerisation of caradiene **77** was also studied by kinetic methods.⁹⁷ The transformation of the hydrocarbon **77** into the triene **61** is a sequence of two concerted reactions; for quite obvious reasons, the first one (the assumed 1,3-shift) is the limiting step. Kinetic studies showed that this step is described by a first-order equation. The activation energy determined from experimental data is 112 kJ mol^{–1}, which is close to the calculated activation energy of the antarafacial 1,3-shift (115 kJ mol^{–1}).⁹⁹ The high negative activation entropy, which equals 96 kJ mol^{–1} deg^{–1} (–23 eu), suggests that a 1,3-shift is possible in this reaction. Comparison of this value with the corresponding parameter for the 1,5-shift (–8 to –16 eu) shows that the transition state of the thermal rearrangement of caradiene **77** is highly ordered and that the participating atoms are bound very strongly. The activation energy of 1,5-shift in 2-carene (**31**) (118 kJ mol^{–1})⁹¹ is somewhat higher than the activation energy of the thermal isomerisation of the diene **78**; this may explain why the 1,5-shift does not occur in this case.

Of special interest is the thermal rearrangement discovered by Berson and Willcott.⁴⁷ Formally, it is migration of the methyl group over all the possible positions of the triene system in the molecule of the hydrocarbon **61**. Nevertheless, this should be considered in the series of carane rearrangements, because, in fact, it is a 1,5-shift of the dimethylmethylene group rather than a 1,3- or 1,5-alkyl shift that occurs in the caradiene tautomer **58**, as shown using deuterium labelling.

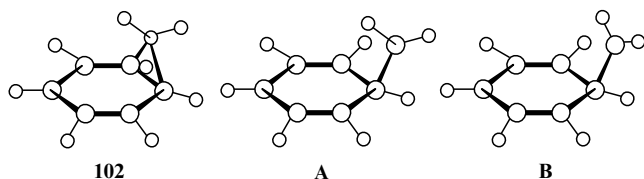


This specific reaction served as the impetus for the development of experimental and theoretical studies, which expanded considerably, and changed somewhat, the classical concepts of sigmatropic reactions. The triene **61** turned out to be an excellent model for these studies, since the rearrangement only occurs if a *gem*-dimethyl group is present: in the absence of geminal sub-

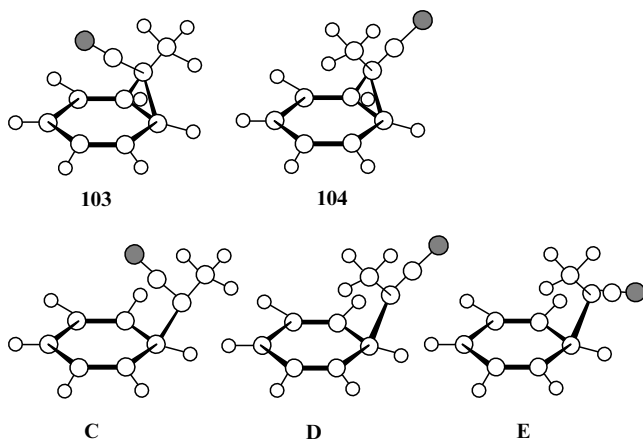
stituents, cycloheptatriene undergoes 1,5-hydrogen shift at temperatures above 100 °C.¹⁰¹ The presence of the third methyl group, which ‘walks’ along the triene system of the seven-membered ring, made it possible to detect this rearrangement (‘walk rearrangement’).

It should be noted that the mechanism of this shift does not allow the rearrangement of the heptatriene **61** to be considered completely concerted, because it occurs *via* a biradical intermediate at temperatures ~ 400 °C. This rearrangement involves a shift of the cyclopropane bond, which is not a σ -bond in the original molecule; this does not allow this rearrangement to be considered sigmatropic. Still, it was considered for a rather long time that the rearrangement of the triene **61** meets completely the selection rules for concerted sigmatropic migrations of alkyl groups, *i.e.*, it occurs as a suprafacial rearrangement with retention of the configuration of the migrating group. Elegant studies by Klärner *et al.*^{102–104} rebutted these concepts completely: they replaced one methyl group by an alkoxy carbonyl, nitrile or alkoxyalkyl group and proved that the rearrangement occurs with retention of the configuration, *i.e.*, by a ‘forbidden’ pathway.

Recently, this phenomenon was explained on the basis of *ab initio* calculations in two theoretical papers issued almost simultaneously.^{105,106} In the case of non-substituted norcaradiene **102**, the methylene group with an unpaired electron is somewhat more remote from the six-membered ring in the biradical TS **A** for the forbidden thermal 1,5-alkyl shift than in the TS **B** of the allowed shift, which decreases the energy of the TS for the forbidden shift by ~ 4 kJ mol^{–1} (see Ref. 105).



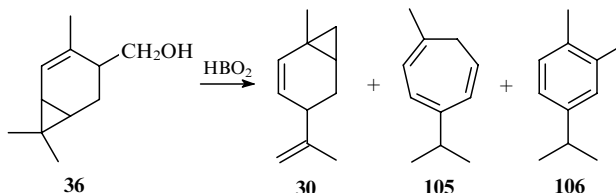
The transition states **C** and **D** for the 1,5-shift in *cis*- (**103**) and *trans*-7-cyano-7-methylnorcaradienes (**104**), which occurs with reversal of the configuration (and is therefore forbidden), is 12 and 13 kJ mol^{–1}, respectively, more favourable than the TSE of a similar shift with retention of the configuration (which is therefore allowed). The distance between the hydrogen atoms of the methyl group and the ring in the forbidden TS **C** and **D** is by 0.12 and 0.37 Å shorter than that in the allowed TS **E**.¹⁰⁶



On these grounds, Houk *et al.*¹⁰⁶ conclude that when sigmatropic rearrangement occurs *via* a biradical intermediate, steric factors can dominate over electronic factors, resulting in a violation of the fundamental orbital symmetry conservation rules. It is appropriate to remind here that the studies which have led to this amazing result started with an investigation of terpenoids, *viz.*, the triene **61** and its valence tautomer, the diene **58**.

3. Thermal elimination

Attempts to dehydrate the alcohol **36** with boric acid gave a mixture of hydrocarbons **30**, **105** and **106**, instead of the expected diene **79**.¹⁰⁷

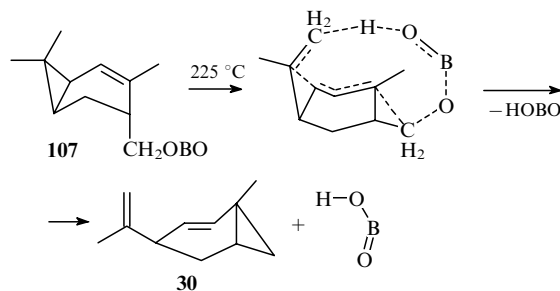


It was later found that these hydrocarbons are also formed upon thermal decomposition of mono-, di- and triesters of boric acid and the alcohol **36** (*i.e.*, intermediates of the dehydration described above), and that bicyclic hydrocarbon **30** is formed initially; other transformation products were identified as well.¹⁰⁸ Toluene-*p*-sulfonate and chloroacetate of the alcohol **36** reacted similarly; the corresponding acetate and aminoacetate underwent the 1,5-homodienyl shift.¹⁰⁹

Thermolysis of esters is a well-studied reaction, which is used as a route to olefins by elimination of an acid residue and a hydrogen atom bound with the β -carbon atom. Elimination occurs *via* a six-electron (aromatic) TS. However, pyrolysis of the alcohol **36** and its derivatives results not in the formation of a double bond but rather in cleavage of one of the bonds in the *gem*-dimethylcyclopropane ring with simultaneous closure of a new three-membered carbocycle. Additional studies were carried out in order to study the mechanism of this unusual rearrangement: the kinetics of the thermal decomposition of the toluene-*p*-sulfonate **25** in pyridine³⁷ and its solvolysis³⁵ were studied.

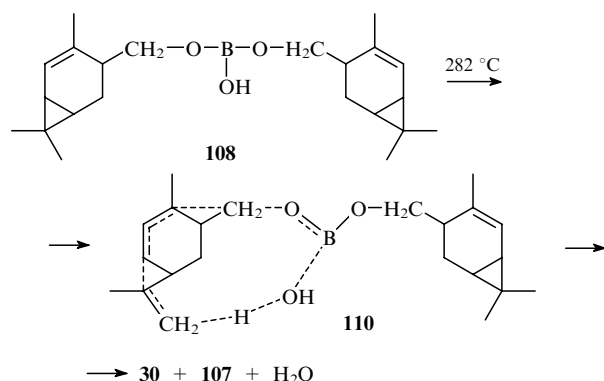
These studies made it possible to propose the mechanism of this rearrangement.³⁷ This occurs as a concerted rearrangement *via* an aromatic ten-electron transition state, unlike the classical six-electron TS. Although the hypothesis about a ten-electron TS has not been used before in organic chemistry, it does not suffer fundamental self-inconsistencies. Recently, a ten-membered TS was calculated for the Cope [5,5]-sigmatropic rearrangement using the B3LYP/6-31G* method.¹¹⁰ A calculation using the density functional shows that a ten-membered TS may be non-planar but maintains aromaticity.¹¹¹

We believe that the spatial factor is responsible for this unusual reaction pathway. The formation of a six-membered TS upon elimination of acid fragments requires that the acid residue in ester **107** have an eclipsed conformation with respect to the H(4) atom. This allows the oxygen atom of the acid residue and a hydrogen atom of the *endo*-methyl group, which is linked with the cyclopropane ring, to approach each other and ensures that the vinylcyclopropane fragment is involved in the transition state. The aromaticity criterion (*i.e.*, fulfillment of the Hückel rule) requires that the p-orbitals of non-neighbouring atoms [C(3), C(11)] overlap. The formation of the cyclopropane ring and simultaneous transformation of the vinylcyclopropane fragment into the 1,4-diene system occur as a result of such through-space overlap.

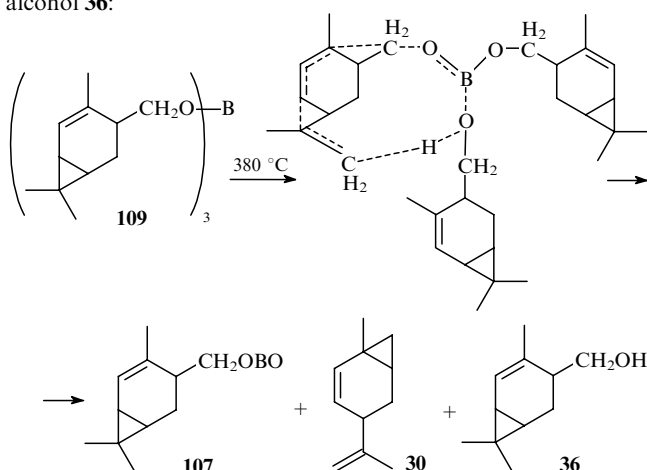


This viewpoint was confirmed experimentally.³⁷ A detailed study of the decomposition of esters **107–109** showed that these

reactions result in various products. For example, the pyrolysis products of the ester **108** also contained water (3%–5%):



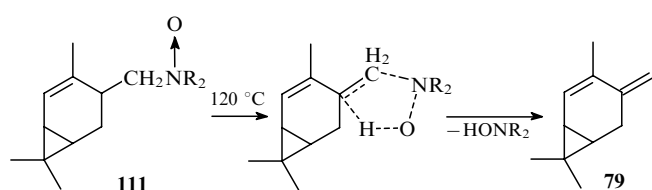
The first pyrolysis step occurs as the fragmentation of the molecule of the diester **108** via a ten-membered TS **110**, which includes a hydroxy group. This results in the bicyclic hydrocarbon **30**, water and ester **107**. Further, the ester **107** decomposes according to the scheme described above to give boric acid and a second molecule of the hydrocarbon **30**. The pyrolysis products of the ester **109** contained (in addition to the hydrocarbon **30** and its transformation products) 2- and 3-carenes, menthadienes and the alcohol **36**:



The first stage gives the hydrocarbon **30** and also the ester **107** (which decomposes according to the scheme described above) and the alcohol **36**. The latter undergoes partial deformation under the reaction conditions (380 °C) to give 3-carene (**1**).⁹¹ As a result of acid isomerisation of this terpene, 2-carene and menthadienes appear among the products.

It should be noted that pyrolysis of *N*-oxide **111**, whose structure is similar to that of esters **107**–**109**, gave quantitatively the hydrocarbon **79** containing an exocyclic double bond.¹¹² This result may be considered as an indirect proof that the spatial factor plays a decisive role in such rearrangements.

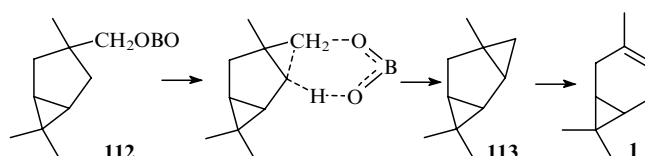
In the oxide **111**, the functional group has one member less than that in esters **107**–**109**; as a result, the formation of a five-membered (but six-electron, *i.e.*, still aromatic) transition state becomes possible; this is smaller in size and its C(4) atom has a *gauche*-conformation.



Undoubtedly, the TS in the thermal decomposition of esters is highly polarised; its structure depends on the nature of its

constituent atoms. Therefore, the acetate, borate and toluene-*p*-sulfonate of the alcohol **36** manifest different reactivities in this reaction. The reactivity even depends on the secondary effects of the heteroatoms: acetate and aminoacetate undergo a 1,5-homodiényl shift; thermolysis of the toluene-*p*-sulfonate occurs at 90 °C, that of chloroacetate at 180 °C, and that of mono-, di- and triborates at 225, 282 and 380 °C, respectively.¹¹³

Pyrolysis of borate **112**, in which 1,2-elimination is impossible *a priori*, gives rise to 3-carene (**1**), formed presumably upon acid isomerisation of the initial pyrolysis product, *i.e.*, tricyclic hydrocarbon **113**. None of the esters of 3,6,6-trimethylbicyclo[3.1.0]hexan-3-ylmethanol tested in this reaction (toluene-*p*-sulfonate, acetate, amino- and chloroacetates) behaved in this way.



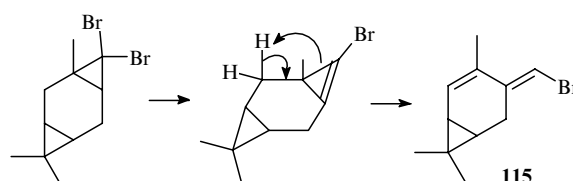
As we noted in Section II.2, the solvolysis of toluene-*p*-sulfonates **25** and **28** results in the same product **29**.³⁶ Pyrolysis of these compounds also affords a single reaction product **30**, although the pyrolysis of the ester **28** requires a higher temperature (180–200 °C) than that of the ester **25** (70–100 °C). We assume that this can be explained by preliminary 1,3-shift of the tosyloxymethyl group, which occurs at high temperature. A similar shift of the acyl group was observed in the photolysis of the ketone **42**⁴³ (see Section III).

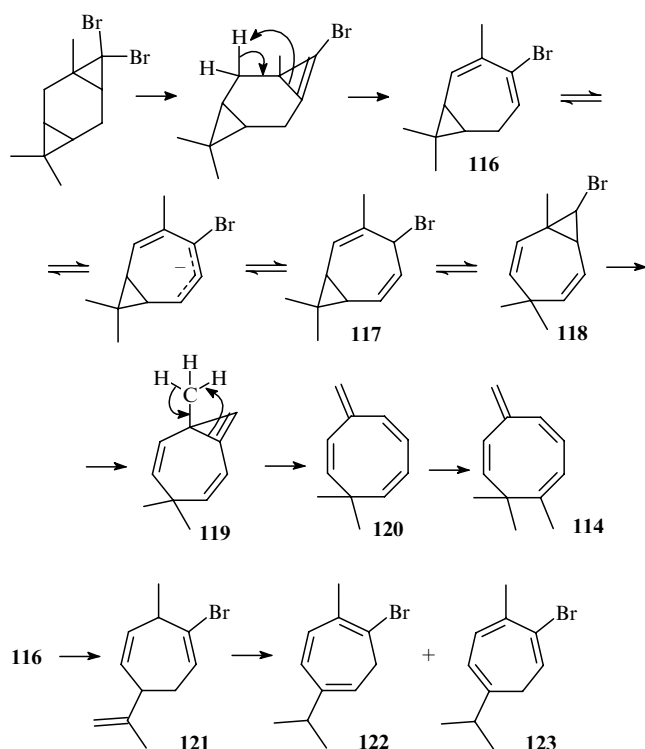
4. Ionic reactions and valence tautomerism

We have already mentioned the ionic transformations of carane monoterpenoids (*e.g.*, compounds **74** and **76**) to give a 2,4-caradiene structure, which underwent electrocyclic opening of the three-membered ring with rearrangement into a trimethylcycloheptatriene structure. In such cases, the skeletal rearrangement occurs due to valence tautomerism. Compounds of the carane series, which have a more complex carbon skeleton, can undergo ionic rearrangements of another type, giving rise to structures that are prone to tautomeric transformations.

For example, the adduct of 3-carene with dibromocarbene undergoes dehydrobromination on treatment with a superbasic system KOR–DMSO ($\text{R} = \text{H}, \text{Bu}^t$) with selective formation of 1,8,8-trimethyl-5-methylenecycloocta-1,3,6-triene (**114**).¹¹⁴ When the concentration of the dehydrobrominating agent was decreased, additional products were isolated from the reaction mixture; this allowed a scheme of the rearrangement to be proposed.¹¹⁵

Elimination of the first molecule of hydrogen bromide is accompanied by the isomerisation of the three-membered ring to give bromides **115** and **116**. Bromide **115** with an intact carane skeleton is formed by opening of the three-membered ring with cleavage of the external bond and does not undergo further transformations on treatment with the KOH–DMSO system. Compound **116** isomerises to give bromide **117**, which contains a *cis*-divinylcyclopropane system. This undergoes the Cope rearrangement¹¹⁶ by concerted opening of the CPR to give a valence tautomer **118**. Dehydrobromination of compound **118** results in cyclopropene **119**, which isomerises to a more stable cyclooctatriene derivative **120**. The latter is methylated by the dimsyl anion under the reaction conditions.





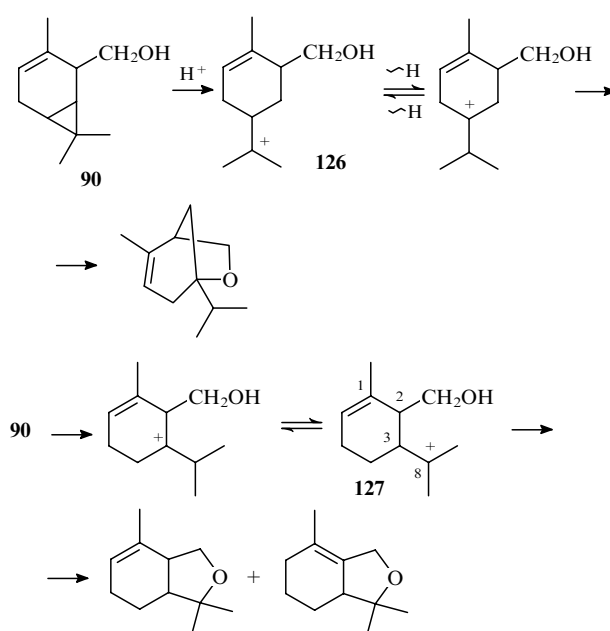
This reaction involves yet another concerted rearrangement. Bromide **121** is formed due to a 1,5-homodienyl shift; subsequent ionic isomerisation of this compound results in bromides **122** and **123**.

5. Sigmatropic shifts in charged systems

The transformations of carane structures on treatment with superacids are of considerable interest. In superacidic media, the life time of carbocations increases, enabling their more profound secondary transformations and involves all the possible reaction centres (CPR, double bonds if any, functional groups) in rearrangements. One of these possibilities comprises the sigmatropic shifts of hydrogen or alkyl groups. This gives new cations, each with its own destiny. Certainly, the diversity of the intermediates involved in these rearrangements predetermines the diversity of the reaction products.

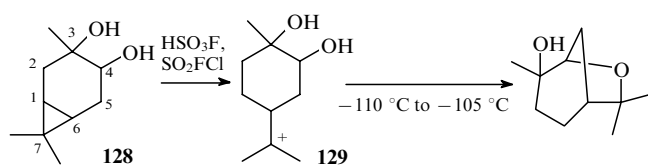
The reaction of the alcohol **36** or its derivatives with the superacid system $\text{HSO}_3\text{F}-\text{SO}_2\text{FCl}$ affords a mixture of products, the formation of which is explained by sigmatropic shifts in the ions **124** and **125** formed initially (Scheme 2).³⁶

The rearrangement of the isomeric alcohol **90** occurs similarly.³⁶



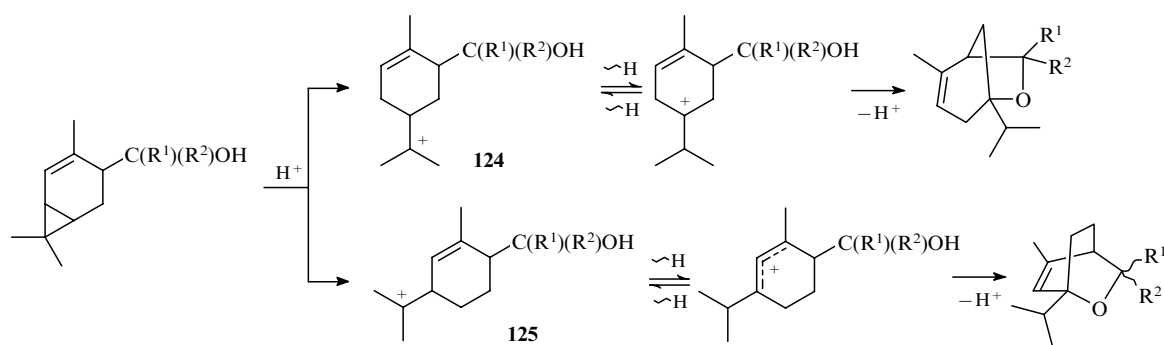
This type of cyclisation requires a 1,2-hydrogen shift in the *p*-menthene ion **126**, since the oxygen atom of the hydroxymethyl group is remote from the C(8) atom where the initial charge appears. In systems where the oxygen atom of the hydroxymethyl group is closer to the C(8) atom, cyclisation occurs *via* the *m*-menthene ion **127** formed initially. Certainly, the 1,2-shift occurs in the ion **127** as well, but the oxygen atom and the C(3) atom (where positive charge is localised after the shift) are too close, therefore cyclisation cannot occur because of the steric strain.

Cyclisation of diol **128** occurs, without initial hydrogen shift, *via* the *p*-menthane ion **129**, in which the oxygen atom is closer to the charged carbon atom than in ion **126**. This reaction involves selective opening of the cyclopropane ring with cleavage of the C(1)–C(7) bond; the reason for such selectivity has not been elucidated yet.³⁶

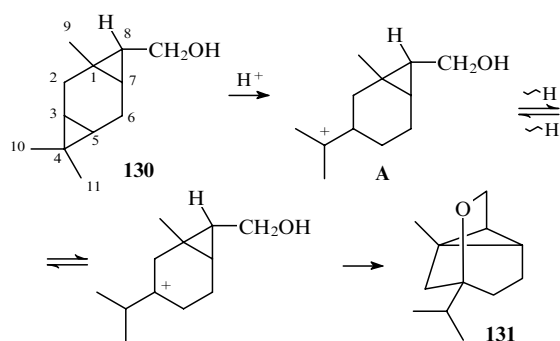


Tricyclic alcohol **130** rearranges in superacidic media with cleavage of the C(4)–C(5) bond, giving rise to compound **131**. The cyclisation occurs due to the 1,2-hydrogen shift in cation **A**.³⁶

Scheme 2

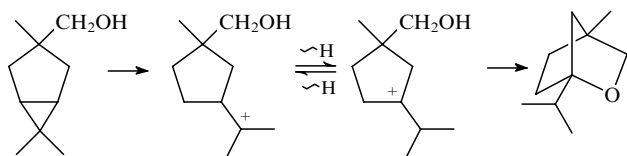


$\text{R}^1 = \text{H, Me; R}^2 = \text{H, Me, CH}_2\text{CH}=\text{CH}_2$.



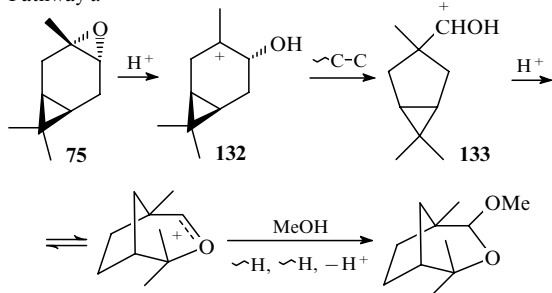
A characteristic feature of the rearrangement of the alcohol **130** is that its molecule has two three-membered rings, but only one of them opens on treatment with a superacid. This may be due to the difference between the HOMO energies of both cyclopropane fragments having different substituents, although the electrostatic effect of the hydroxymethyl group on the process, which is charge-controlled, seems unexpectedly strong.

Rearrangements accompanied by cyclisation occur in superacidic media for secocarane structures as well.³⁶ In this case, the positive charge should approach the oxygen atom in order that a bond can be formed:

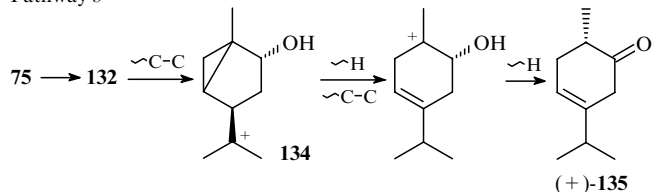


In the rearrangements of α -*trans*-3,4-epoxycarane[†] (**75**) in superacidic media, the intermediate ions undergo not only hydrogen but also alkyl shifts; these shifts are responsible for the transformation of the carane skeleton.¹¹⁷

Pathway a



Pathway b

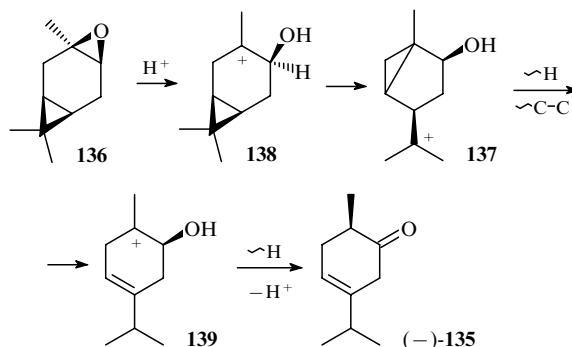


The 4-hydroxycarane-derived ion **132** should undergo a 1,2-alkyl shift with contraction of the six-membered ring to give ion **133**; elimination of a proton and ionisation of the CPR make cyclisation possible (pathway a).

The second pathway of the transformation of ion **132**, which formally occurs as a 1,3-alkyl shift and results in ion **134** (path-

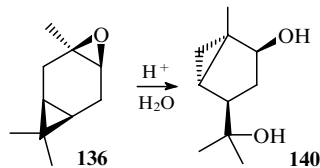
way b), is more interesting. However, 1,3-alkyl shifts cannot occur in charged systems: the C(2) atom lacks an appropriate p-orbital. Thus, a 1,2-alkyl shift actually occurs, but the formation of the TS involves non-adjacent carbon atoms [C(1) and C(3)]. Through-space rather than through- σ -bond overlap occurs; this shift may be called homoenylic. This eventually results in the closure of the three-membered ring and gives ion **134** (β -cyclopropyl rearrangement¹¹⁸), which successively undergoes a hydrogen shift and an alkyl shift to give the final ketone (+)-**135**.¹¹⁷

In order to explain the rearrangements of β -*cis*-3,4-epoxycarane (**136**) in superacidic media, a mechanism was suggested which involves bicyclic ion **137** isomeric to ion **134**.¹¹⁸ This results in the stereospecific formation of the ketone (–)-**135**; the latter is not only a stereoisomer but also an enantiomer of the ketone (+)-**135**, which is formed due to rearrangements of the epoxide **75**.

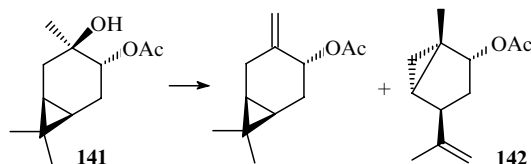


The different reactivities of epoxides **75** and **136** are explained¹¹⁸ by thermodynamic and orbital factors: the orientation of the migrating bond and the vacant orbital in ions **132** and **138** is favourable for ring contraction. For ion **132**, ring contraction is more energetically favourable, whereas β -cyclopropyl rearrangement (via cations **137** and **139**) is favourable for ion **138**, since the orientation of the vacant orbital in this cation is more favourable for the rearrangement than that in **132**.

The above transformation schemes of epoxides **75** and **136** only cover the most probable ways for the formation of the final products. No compounds with the 4-isopropyl-1-methylbicyclo[3.1.0]hexane skeleton, which might have formed from ions **134** and **137**, were found in the transformation products of epoxycaranes in superacidic media. However, diol **140** with the same skeleton was obtained in 1962 by acid-catalysed hydration of *cis*-epoxide **136**,¹¹⁹ and its structure was confirmed in 1972.¹²⁰



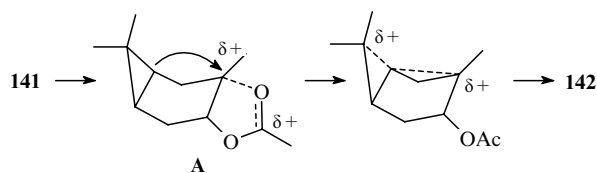
As shown in 1966, dehydration of 3 β ,4 α -caranediol monoacetate **141** gives rise to *trans*-4-isopropenyl-1-methylbicyclo[3.1.0]hexan-2-ol acetate (**142**) as one of the products.¹²¹



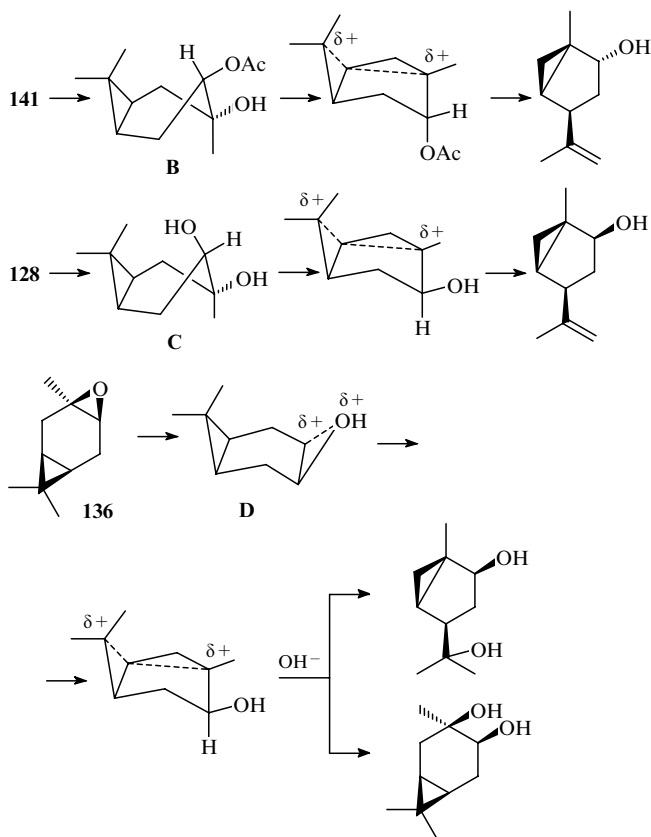
Kropp who studied this reaction¹²¹ regarded it as the first documented example of rearrangement with transannular cyclopropyl participation.¹⁰ He believed that CPR in nucleophilic substitution reactions acts as an internal nucleophile and the role of stereochemical factors is very high in such reactions: it is required that there is a spatial possibility for the dimethylcyclopropane ring to attack the C(3) atom, which carries a β -substituent. Also of importance is the existence of an α -sub-

[†]In the chemistry of terpenoids, the α and β symbols traditionally designate the spatial arrangement of functional groups in carane derivatives: α substituents and the three-membered ring are located on different sides of the cyclohexane ring (*trans*), whereas β substituents are located on the same side as the CPR (*cis*).

stituent at the C(4) atom, required for fixing the six-membered ring in the 'syn-boat' conformation **A**.¹²¹

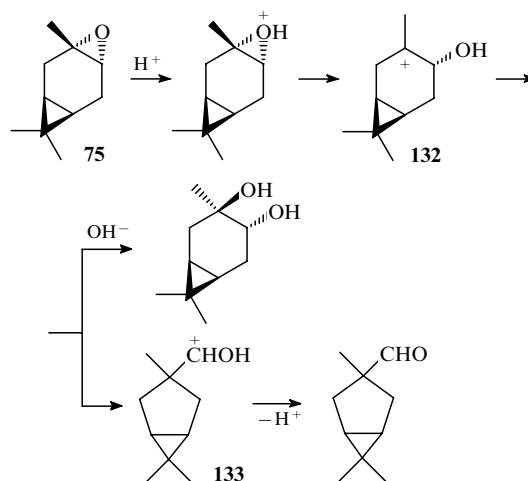


Different opinions existed regarding the stereochemical conditions of 'cyclopropyl participation' stated by Kropp. For some time, his interpretation of the spatial features of such reactions was considered generally accepted and was cited in special literature.¹² However, subsequent studies^{10, 122–128} made it possible to put forward a statement (and confirm it experimentally) that the molecules of the reacting carane compounds have the 'anti-boat' conformation (**B–D**) in the transition state; the orientation of the substituent at C(4) does not matter.^{122, 123, 129}



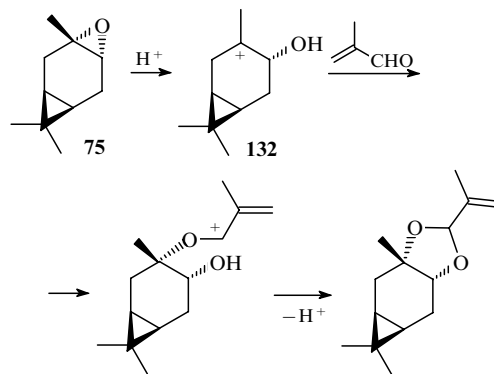
In fact, the 'transannular participation of CPR' is reduced to the 1,2-homoenyl shift, which can occur (and does occur) in charged systems. The absence of 'transannular cyclopropyl participation' products upon rearrangement in superacids is caused by the fact that, owing to the very low nucleophilicity of the medium and low temperatures, ionic processes occur to a greater extent and are highly selective. Therefore, transformations in superacids do not stop in ion **137**, but proceed further to give ion **139**, which leads to the final reaction product.

This approach explains the similarity of transformations of the epoxide **136** under the conditions of usual acid catalysis and in superacids, but new questions arise. The transformation of the epoxide **75** in superacids gives products which imply the intermediate formation of ion **134**, whereas solvolysis of compound **75** does not yield 4-isopropyl-1-methylbicyclo[3.1.0]heptane structures. As a side process, ring contraction occurs due to an alkyl shift in the ion **132** giving the ion **133**, which is stabilised by elimination of a proton; in a superacid, the ion **133** rearranges.^{125, 130}

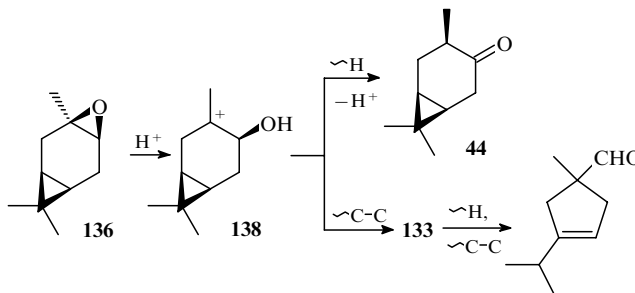


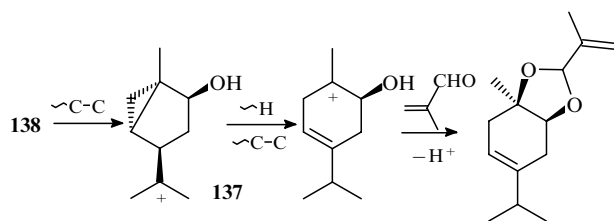
Undoubtedly, epoxides **75** and **136** react differently under usual conditions due to differences in their spatial structures. However, in superacids this difference is insignificant with respect to 'transannular cyclopropyl participation', or at least this does not play an important role. It may be assumed that charges are separated more deeply in superacids, which alters the geometry of the carane skeleton and enables the 1,2-shift. In usual acids, only partial charge is located on the involved atoms,¹²¹ therefore the geometry of the carane skeleton is changed insignificantly. However, it should be noted that the ion **133** is formed under conditions of usual acid catalysis, which at present cannot be explained in terms of the above argumentation.

The reactions of α -epoxycarane with aldehydes over ascanite-bentonite clay (an alumosilicate catalyst) do not give any products which would imply that the ion **134** is involved in the reaction.¹³¹



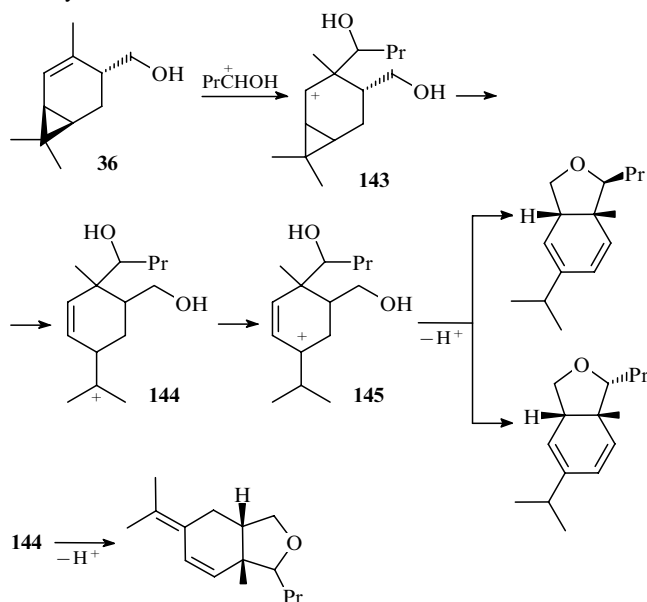
In this case, no profound transformations of ions occur, as the aldehyde traps the ion **132**, and the reaction follows a different pathway. On the other hand, under similar conditions the epoxide **136** gives products which imply that ion **138** undergoes not only a 1,2-homoenyl but also a 1,2-alkyl shift to give the ion **133** (which was not observed in superacids¹¹⁸), which is then rearranged.





As a result of the specific features of catalytic transformations on solid surfaces, the reaction of the epoxide **136** does not give an acetal with a carane skeleton; instead, it yields the ketone **44**, which is absent in the products of the reaction starting from the epoxide **75**.

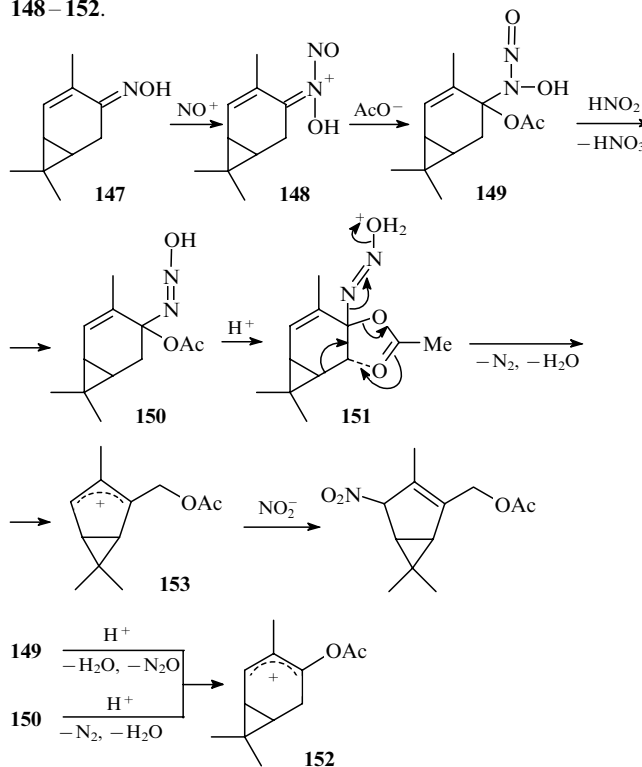
3-Carene does not react with aldehydes on ascanite-bentonite clay,¹³¹ but under these conditions the alcohol **36** yields a series of rearranged products, the structure of which depends on the aldehyde used.¹³²



The suggested reaction mechanism¹³² involves the attack of protonated butyraldehyde on the more substituted end of the double bond to give a secondary cation **143** rather than a more stable tertiary cation. Rearrangement of the former with opening of the CPR gives ions **144**, **145** and then the reaction products. Section II.1 gives a different viewpoint on the formation of products with a similar skeleton.^{24,25} The mechanism proposed by Barkhash *et al.*¹³² is supported by the formation of tricyclic products in the reaction of the alcohol **36** with α -methylacrolein (Scheme 3).

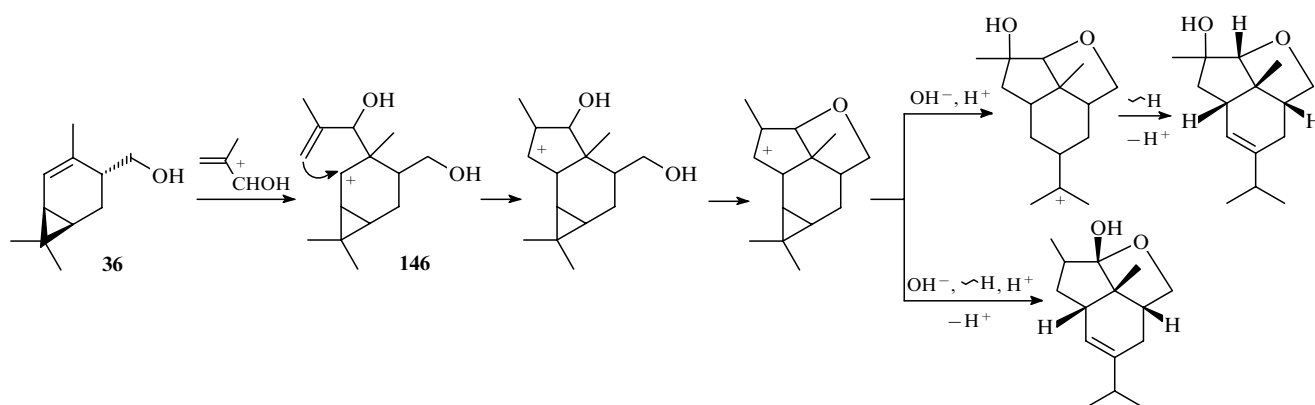
The proximity of the double bond to the cationic centre in ion **146** can result in cyclisation, which is believed to be due to the presence of a methyl group at the α -position of methylacrolein.

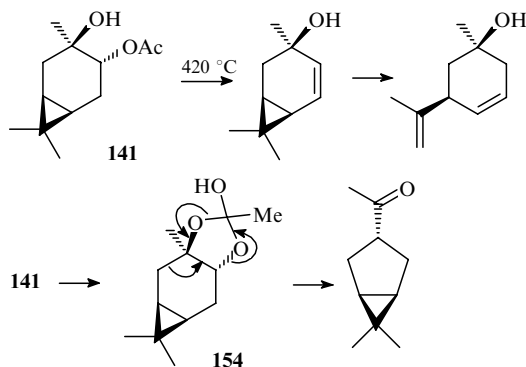
We have already described the rearrangements of the carane skeleton into the bicyclo[3.1.0]hexane one, for epoxycaranes as examples. A formally similar rearrangement of the carane skeleton is observed during the transformation of car-2-en-4-one oxime (**147**) on treatment with nitrous acid.¹³³ Considering the nature of the functional substituent, the most probable pathway for the transformation of oxime **147** involves intermediates **148**–**152**.



Obviously, it is the shift of the alkyl group in the charged system that is responsible for the rearrangement of the carane skeleton. Using quantum-chemical calculations, it was concluded¹³³ that the 1,2-alkyl shift in ion **152** is impossible from the viewpoint of its spatial structure and from thermodynamical considerations. As regards ion **151**, it is assumed that concerted elimination of nitrogen occurs in it, with simultaneous attack of the acetate group and migration of the C(5)–C(6) bond. Cation **153** is stabilised by capturing a NO₂[−] anion. A transition state of the type **151** has been postulated earlier^{130,134} in order to explain the pyrolysis of caranediol monoacetate **141**.

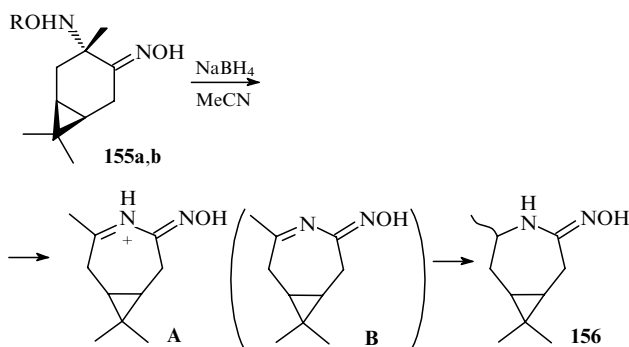
Scheme 3





However, the suggested cyclic intermediate **154** accounts for the rearrangement of bonds but formally and schematically. It is obvious that the thermal shift of the C(2)–C(3) bond can only occur in an ion. Probably, acetic acid that has already been eliminated (by a concerted mechanism) and is present in the reaction mixture favours the formation of intermediate ions.

An even more surprising example of skeletal rearrangements caused by the participation of the oximine group has been reported.¹³⁵ 3 α -Hydroxyaminocaran-4-one oxime (**155a**) and 3 α -(*O*-acetyl)hydroxyaminocaran-4-one oxime (**155b**) react with sodium borohydride in acetonitrile resulting in reaction product **156** with a fused seven-membered ring.



R = H (a), Ac (b).

In this case, acetonitrile is probably not only a solvent but also a reagent, because rearrangement does not occur when it is absent. The authors postulate two possible intermediates of this reaction (**A** or **B**) but note that the mechanism of their formation is not clear yet.

* * *

The vast material considered in this paper indicates that studies of the chemical transformations of carane derivatives goes far beyond the scope of the area of organic chemistry which is customary to regard the chemistry of terpenoids. 3-Carene is a really unique natural compound that offers wide opportunities to scientists. Owing to the accessibility of this compound, a lot of new compounds are being obtained from it; these are interesting both by themselves and as excellent models for studying reaction mechanisms. We believe that only benzene can compare with 3-carene as regards its contribution to theoretical and synthetic chemistry. The authors are far from thinking that nature has deliberately taken care of organic chemists, but it is hard to overestimate the generosity of this natural gift. We do hope that our readers feel the same way.

Although we attempted to consider the mechanisms of the known rearrangements, attentive readers have surely noticed that these mechanisms are often hypothetical and sometimes questionable. There is no doubt that studies in this field will be continued and will not only provide answers for the today's questions but also raise new ones.

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Multicomponent cascade heterocyclisation as a promising route to targeted synthesis of polyfunctional pyridines[†]

V P Litvinov

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Abstract. The review surveys the state-of-the-art in the methodology of multicomponent cascade heterocyclisation and its prospects as applied to the targeted synthesis of polyfunctional pyridines and their hydrogenated and fused analogues. The bibliography includes 405 references.

I. Introduction

A fundamental problem of synthetic organic chemistry is to design new chemo-, regio-, stereo- and enantioselective methods for the synthesis of polyfunctional carbo- and heterocycles possessing practically important properties. Such methods should not only be based on simple and commercially available substrates and reagents and characterised by low cost of the final products but also be ecologically safe.

In this connection, recent years have witnessed a rapidly growing interest in the one-pot synthesis involving two groups of reactions. One group includes successive reactions in the course of which another reagent, substrate or catalyst is added or the reaction temperature is changed without isolation of intermediates. Another group includes cascade reactions proceeding under the same conditions without the addition of any other reagents or catalysts. In these processes, the functional groups that are formed in earlier steps are transformed in each subsequent step. This type of processes is referred to as domino or tandem reactions. It should be noted that there is no strict difference between these terms.

Multicomponent cascade processes are of particular interest, which is reflected in the reviews^{1–11} that have been published. These reactions can serve as the basis for both targeted organic synthesis and combinatorial chemistry, which allows one to synthesise simultaneously several thousand samples for biological screening with the use of automated efficient approaches.^{12–20}

Analysis of named reactions in organic chemistry shows that many of these reactions, particularly, those giving rise to heterocyclic compounds, are based on the methodology of multicomponent cascade heterocyclisation. Examples are the Hantzsch

reaction involving cyclocondensation of β -keto esters or β -diketones with aldehydes and ammonia to form substituted pyridines,^{21,22} the Gattermann–Skita reaction, *viz.*, the synthesis of pyridine derivatives by condensation of sodium malonate with dichloromethylamine (as a version of the Hantzsch reaction),²³ the Guareschi–Thorpe reaction, *viz.*, the preparation of pyridine derivatives by cyclocondensation of ester (amide) of cyanoacetic acid or α -allylacetoacetic ester with ammonia,^{24,25} the Doebner reaction involving condensation of aromatic, heteroaromatic or fused polycyclic amines with aldehydes or pyruvic acid to yield quinolinecarboxylic acids,²⁶ the Ullmann–Fetvadjan reaction, *viz.*, the synthesis of benzacridines by condensation of β -naphthol with aldehydes and aromatic amines²⁷ and many other reactions.

In the last 15 years, the chemistry of functionalised pyridine-chalcogenones has been extensively developed, which is reflected in many reviews^{28–41} and dissertations^{42–54} that have been published. This is associated with both a theoretical interest in this class of organic compounds and a very broad spectrum of the practical uses of pyridine derivatives. For example, more than 10% of the most commonly used modern medicines contain pyridine or the hydrogenated pyridine ring.⁵⁵ A new class of calcium antagonists was constructed on the basis of 1,4-dihydropyridines^{56,57} (in particular, the drug nifedipine used for the treatment of high blood pressure and stenocardia⁵⁵). Among these compounds are highly efficient cardiotonics^{58–107} (including the drugs amrinone and milrinone^{98–107}), tranquilisers^{108–118} and compounds possessing antiinflammatory, hypoglycemic, antiulcer, antispasmodic, antifungal, antibacterial, pesticide and other biological activities.^{112–142} Pyridine derivatives are used as the starting substrates for the construction of new CH-antioxidants,^{143–146} analogues of folic acid,¹⁴⁷ vitamin B₆,¹⁴⁸ other biologically active compounds^{143, 147–151} and models of the redox coenzymes NAD and NADP.¹²⁵ Here, it is worthwhile mentioning that substituted cyclopentaspiperidone is used in the synthesis of the known anxiolytic buspirone which prevents drug adaptation.¹⁵² The only known natural alkaloid containing a nitrile group, *viz.*, 3-cyano-4-methoxy-1-methyl-1*H*-pyridin-2-one,¹⁵³ also belongs to this class of compounds.

In the last decade, the development of the chemistry of functionally substituted pyridines was stimulated mostly by the fact that among compounds of this class are highly active inhibitors of HIV-1 specific reverse transcriptase (potent agents

V P Litvinov N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 135 88 37. E-mail: vpl@ioc.ac.ru

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[†]Dedicated to Professor Salo Gronowitz (Department of Organic Chemistry 1, Lund University, Sweden), in whose laboratory I worked in 1979–1980, on his 75th birthday.

for AIDS treatment),^{154–166} agents for protection of skin during UV radiation (diethone), an antihypertensive and antianginal drug [foridone (riodipine)], a neurotropic and antidiabetic drug (cerebrocrast), a neuroprotective agent (glutapryrone), an agent promoting growth of agricultural animals (diludin) and amphiphilic compounds possessing properties of cell-transfection agents necessary for gene therapy.¹⁶⁷

Besides, compounds of this class can be used as stabilisers for polymers and lacquers,¹⁶⁸ pigments and diazo components in the synthesis of dyes,^{169–176} acid–base indicators in titrimetric analysis,¹⁷⁷ liquid crystals¹⁷⁸ and other compounds of practical importance.

Considerable practical potential of pyridinechalcogenones and their derivatives have given impetus to the development of procedures for their synthesis, which would enable one to overcome inactivity of the pyridine core in functionalisation with the use of electrophilic substitution. It appeared that this purpose could be accomplished by performing the synthesis under conditions of one-pot multicomponent cascade heterocyclisation.

The success of this methodology depends radically on the starting substrates and reagents, which should be readily available and possess polyfunctional properties. The simplest and most convenient procedures for the synthesis of functionalised pyridinechalcogenones are based on the use of cyanoacetamides and their thio and seleno analogues, malononitrile, cyanoacetic ester and other CH-acids as reagents. The presence of several reactive centres in these compounds is responsible for the diversity of their highly regioselective (often stereoselective) chemical transformations, which proceed under mild conditions and with the use of rather simple apparatus. The tremendous synthetic potential of these reagents was considered in the monograph³⁴ and reviews.^{28, 39, 40}

Aliphatic, aromatic and heteroaromatic mono- and dicarbonyl compounds, their enamines, cycloalkanones, *etc.* are used as substrates in multicomponent heterocyclisation.

The direction of the reactions can be easily changed by varying the reaction conditions or the nature of the substituents in the substrates and reagents.

The successful use of the methodology of multicomponent cascade heterocyclisation is exemplified primarily by the development of regio- and stereoselective procedures for the preparation of previously unknown partially hydrogenated pyridinechalcogenones, polyfunctional 1,4- and 3,4-dihydropyridines, 1,2,3,4-tetrahydropyridines, 6-oxo-1,2,3,4-tetrahydropyridine-2-thiolates of non-betaine origin, 4,5-*trans*-6-hydroxy-1,4,5,6-tetrahydropyridine-2-thiolates, tetrahydropyridones, spiro-fused partially hydrogenated pyridines and quinolines and other compounds of the pyridine series, which potentially possess biological activities and are promising substrates for fine organic synthesis. The main procedures for the preparation of partially hydrogenated pyridinechalcogenones involve the same approaches that were successfully used in the synthesis of their aromatic analogues, *viz.*, condensation of α,β -unsaturated carbonyl, 1,3-dicarbonyl compounds and their enamines, α,β -unsaturated nitriles and other substrates with CH-acids (cyanoacetamide, its thio and seleno analogues, malononitrile, derivatives of cyanoacetic acid, *etc.*).^{28, 42–46, 179–194} It was postulated that Michael adducts and partially hydrogenated pyridinechalcogenones are formed as intermediates of cascade heterocyclisation. In many cases, these intermediates were isolated as stable compounds and their structures and reactivities were studied in sufficient detail.

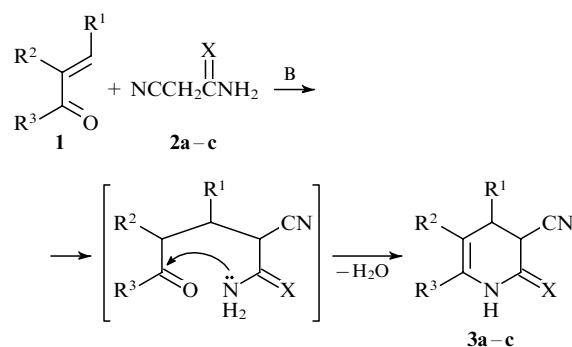
It should be emphasised that the tremendous synthetic potential of this methodology is based on the possibility of varying the nature of the starting substrate with retention of the structure of the reagent, by changing the nature of the reagent with retention of the type of substrate used, by varying simultaneously the nature of both components of the reaction or by changing their ratio and number.

The present review surveys for the first time data on the application of multicomponent cascade heterocyclisation to the

synthesis of pyridine derivatives, which have been published in the last 15 years. The synthesis methods are classified according to the nature of the reagents and substrates used. Emphasis is given to the development of optimum methods for the preparation of partially hydrogenated pyridinechalcogenones and their derivatives, which show the most promise from the practical viewpoint.

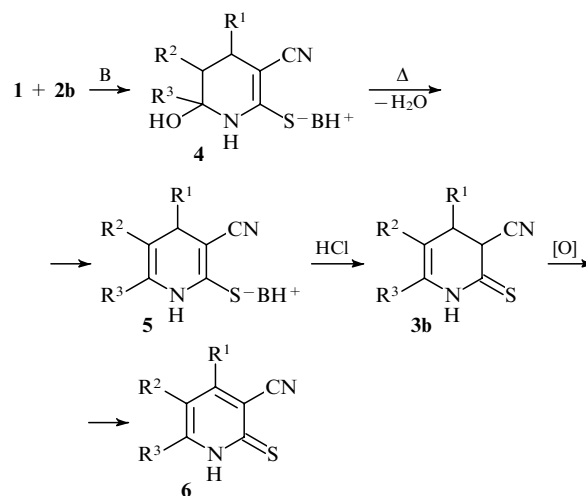
II. Cascade heterocyclisation involving α,β -unsaturated carbonyl compounds

The reactions of α,β -unsaturated carbonyl compounds **1** with CH-acids of type **2** in the presence of organic bases proceed through the cascade heterocyclisation mechanism. The first step affords Michael adducts, whose subsequent cyclocondensation gives rise to 3,4-dihydro-1*H*-pyridine-2-chalcogenones **3**.



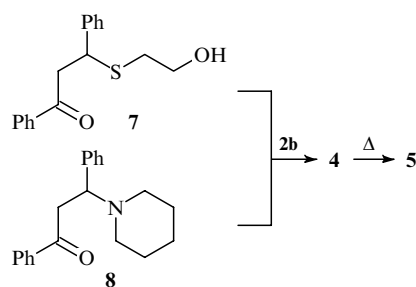
$\text{R}^1, \text{R}^2, \text{R}^3 = \text{Alk, Ar, Het}; \text{X} = \text{O (a), S (b), Se (c)}$
 B is an organic base.

The formation of 3,4-dihydro-1*H*-pyridine-2-chalcogenones **3b** as intermediates in the reactions of arylideneacetone or arylideneacetophenone with cyanothioacetamide (**2b**) was described for the first time in 1980.¹⁹⁵ Later on, it was demonstrated that treatment of compounds **1** with amide **2b** in ethanol in the presence of an equimolar amount of an organic base at 20 °C afforded hydrogenated 3-cyano-1*H*-pyridine-2-thiones **3b**, which were isolated and characterised as stable salts **4** and **5**.^{196–202} Substituted 3,4-dihydropyridinethiones **3b** can be formed by treating salts **5** with hydrochloric acid. These compounds are rather stable, although they are oxidised with atmospheric oxygen on storage in solution to form 3-cyano-1*H*-pyridine-2-thiones **6**.

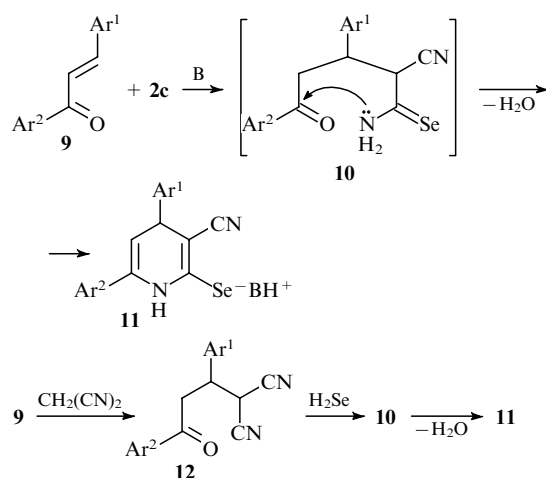


$\text{R}^1 = \text{Ph, 4-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 4\text{-FC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 3\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 3\text{-Py, 4-Py}$; $\text{R}^2 = \text{H, Me, Ph, COMe, CO}_2\text{Me, CO}_2\text{Et}$; $\text{R}^3 = \text{Me, Ph}$.

Salts **4** and **5** were also prepared by the reactions of amide **2b** with ketones **7**²⁰³ and **8**,²⁰¹ respectively.



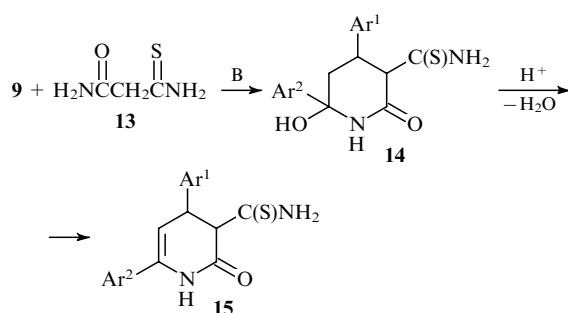
The reactions of chalcones **9** with cyanoselenoacetamide (**2c**) in the presence of an excess of *N*-methylmorpholine afforded Michael adducts **10**. Under the reaction conditions, the latter underwent cyclisation to give 1,4-dihydropyridine-2-selenolates (**11**) in 60%–90% yields.^{45, 46, 204, 205} The latter compounds were also prepared by the reactions of chalcones **9** with malononitriles followed by the reactions of the resulting δ -keto dinitriles **12** with hydrogen selenide.



Ar¹ = Ph, 3-FC₆H₄, 4-FC₆H₄, 2-thienyl;
Ar² = Ph, 4-ClC₆H₄, 2-Py; B is *N*-methylmorpholine.

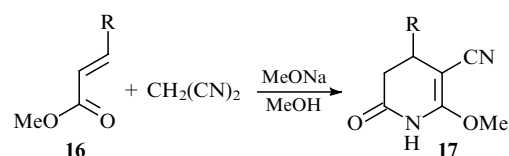
Condensation of aryl(hetaryl) chalcones with amides **2a,b** in the presence of alkali metal alkoxides or amines as catalysts was used also for the preparation of a series of 3,4-dihydro derivatives of 3-cyano-1*H*-pyridin-2-ones and -2-thiones.^{206, 207}

The reactions of ketones **9** with thiocarbamoylacetamide (**13**) in the presence of piperidine or sodium methoxide produced substituted piperidones **14**, which were transformed into pyridones **15** in an acidic medium.^{208, 209}



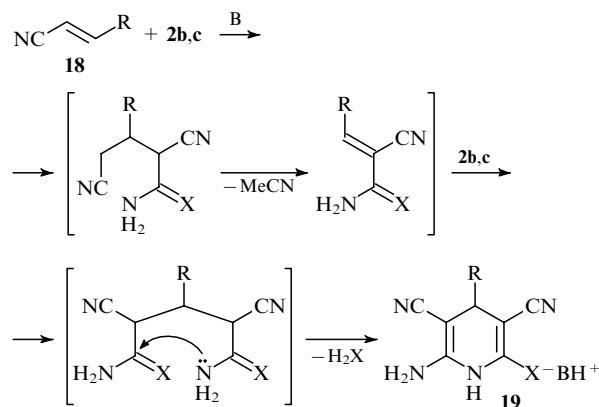
Ar¹ = Ph, 4-ClC₆H₄, 4-NO₂C₆H₄; Ar² = Ph; B = MeONa, piperidine.

The use of sodium methoxide as a catalyst in the reactions of substituted methyl acrylates **16** with malononitrile gave rise to 3,4-dihydro-1*H*-pyridin-2-ones **17** in 49%–85% yields.²¹⁰



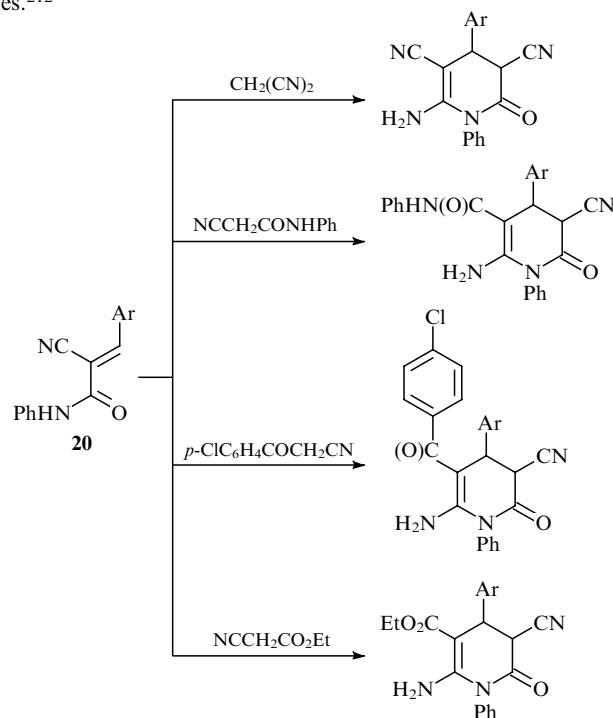
R = Alk, Ar.

The reactions of 3-phenyl- and 3-(2-furyl)acrylonitriles (**18**) with cyanothio(seleno)acetamides (**2b,c**) in the presence of a twofold excess of *N*-methylmorpholine at room temperature afforded substituted 1,4-dihydropyridine-2-thiolates (selenolates) **19**.^{45, 46, 211} The reactions of amides **2b,c** with ethyl 3-phenylacrylate and ethyl 3-(2-furyl)acrylates proceeded analogously.



R = Ph, 2-furyl; X = S, Se; B is *N*-methylmorpholine.

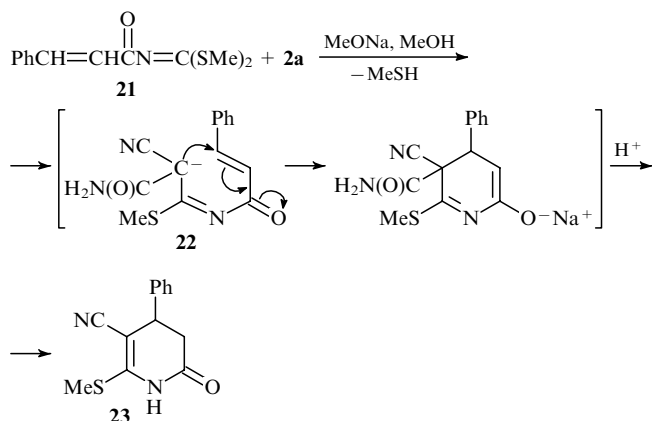
The reactions of anilides of 2-cyanoacetic acid and other 3-aryl-2-cyanoacrylic acids **20** with CH-acids were successfully used for the preparation of various 3,4-dihydro-1*H*-pyridin-2-ones.²¹²



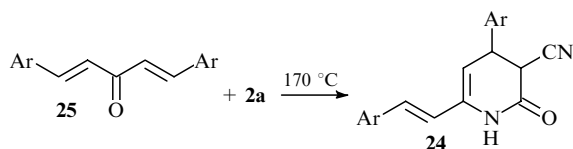
Ar = 4-MeOC₆H₄.

Condensation of α,β -unsaturated carbonyl compound **21** with amide **2a** in the presence of sodium methoxide in methanol proceeded through the intermediate formation of Michael adduct

22 with elimination of methanethiol to give 5-cyano-6-methylthio-4-phenyl-3,4-dihydro-1*H*-pyridin-2-one (**23**) in 70% yield.²¹³

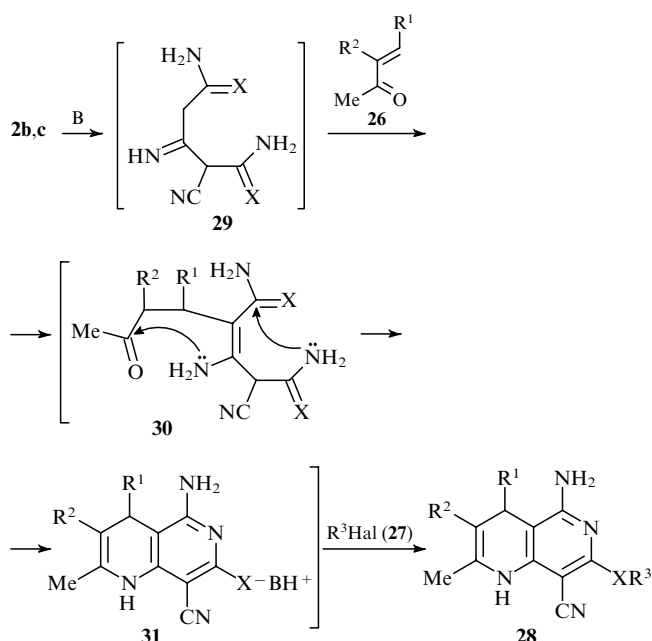


With the aim of preparing substituted 3-cyano-3,4-dihydro-1*H*-pyridin-2-ones **24**, a mixture of pentadienone **25** and cyanoacetamide (**2a**) was heated at 170 °C without a solvent in a sealed tube. Pyridones **24** were obtained in 32%–37% yields.²¹⁴



Ar = Ph, 4-MeOC₆H₄.

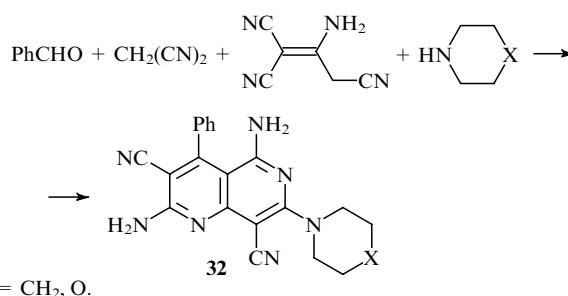
Multicomponent cascade heterocyclisation involving α,β -unsaturated ketones and amides **2b,c** was used with advantage in the synthesis of functionalised naphthyridines, which possess a broad spectrum of biological activities.^{215,216} In particular, these compounds were used for the design of drugs exhibiting cardio-tonic,⁶³ antitubercular,²¹⁷ antitumour,^{218,219} anti-HIV^{220–222} and other activities. However, available procedures for the synthesis of naphthyridines are rather complicated and involve many steps, whereas sulfur- and selenium-containing analogues remain virtually unknown. Studies performed by our research group showed for the first time that condensation of unsaturated ketones **26** with amides **2b,c** and alkyl halides **27** in the presence of *N*-methylmorpholine proceeded as cascade heterocyclisation to



R¹ = Ar, Het; R² = COMe, CO₂Et; R³ = Alk, CH₂CH=CH₂;
X = S, Se; Hal = I, Br, Cl; B is *N*-methylmorpholine.

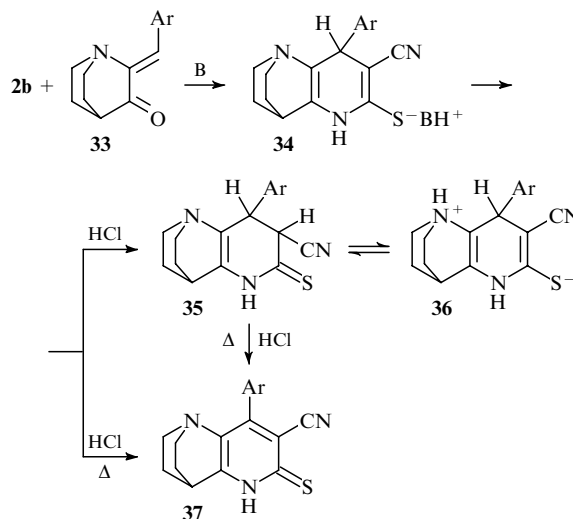
yield previously unknown polyfunctionalised 1,6-naphthyridines **28**.^{53,223–228} In the first step, amide **2** undergoes Thorpe dimerisation to form imino nitrile **29**, which is involved in the Michael addition with ketone **26** to form adduct **30**. Under the reaction conditions, the latter undergoes cyclocondensation to produce salt **31**, which is regioselectively alkylated with alkyl halides **27** giving rise to 1,4-dihydro-1,6-naphthyridines **28**.

Multicomponent cascade heterocyclisation of benzaldehyde with malononitrile and its dimer in the presence of a twofold excess of piperidine or morpholine afforded previously unknown 2,5-diamino-3,8-dicyano-4-phenyl-7-piperidino(morpholino)-1,6-naphthyridines (**32**) in high yields. The reaction not only gave rise to the complex naphthyridine system but also was accompanied by the insertion of a fragment of the saturated nitrogen heterocycle, which was used as the catalyst, into the naphthyridine system.^{53,224}



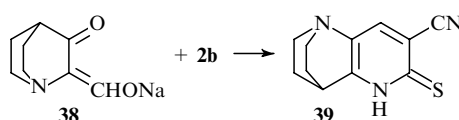
X = CH₂, O.

The reactions of 2-arylidenequinclidin-3-ones **33** with cyanothioacetamide (**2b**) in the presence of piperidine also proceeded through a mechanism of cascade heterocyclisation to form piperidinium 4-aryl-3-cyano-5,8-ethano-1,4,5,6,7,8-hexahydro-1,5-naphthyridine-2-thiolates **34**, whose treatment with hydrochloric acid gave rise to 4-aryl-3-cyano-5,8-ethano-3,4,5,6,7,8-hexahydro-1*H*-1,5-naphthyridine-2-thiones **35**, which were in tautomeric equilibrium with betaines **36**.²²⁹ Heating of salts **34** or thiones **35** in ethanol in the presence of hydrochloric acid led to their dehydrogenation to form naphthyridinethiones **37**.

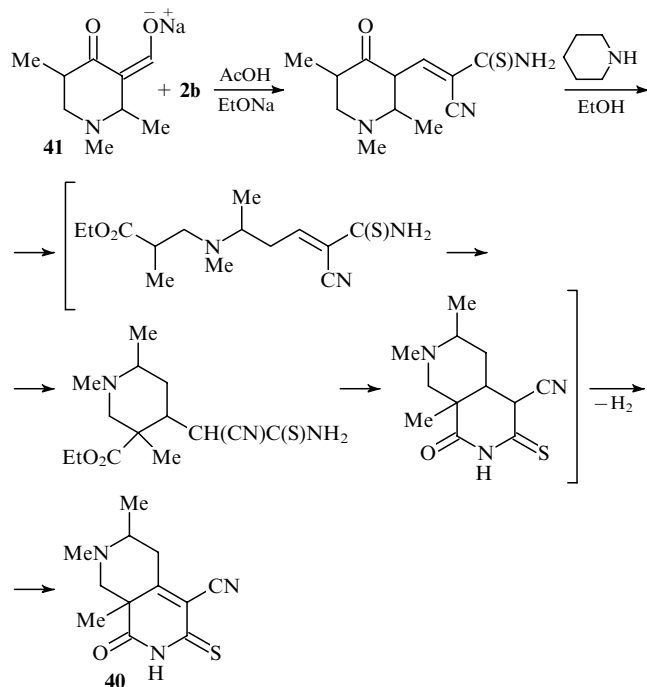


Ar = Ph, 4-FC₆H₄; B is piperidine.

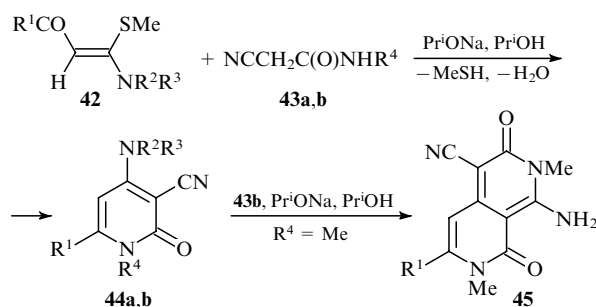
Another example of the highly regioselective synthesis of the 1,5-naphthyridine system is condensation of the sodium salt of 2-formylquinclidone (**38**) with cyanothioacetamide (**2b**) giving rise to 3-cyano-1*H*-1,5-naphthyridine-2-thione (**39**).²³⁰



4-Cyano-6,7,8a-trimethyl-3-thioxo-1,2,3,5,6,7,8,8a-octahydro-2,7-naphthyridin-1-one (**40**) was synthesised by cascade heterocyclisation of the sodium salt of 3-formyl-1,2,5-trimethyl-4-piperidone (**41**) with amide **2b**.^{45, 231}

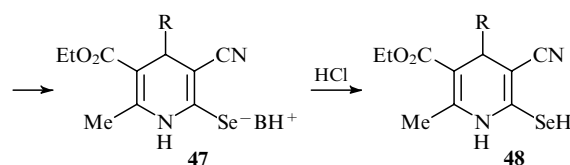
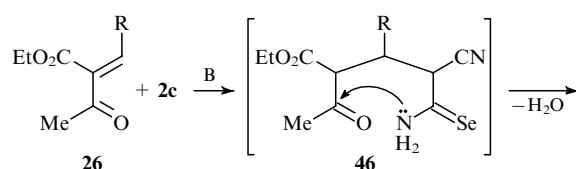


Condensation of β -enamino carbonyl compounds **42** with substituted cyanoacetamides **43a,b** proceeds through a mechanism of cascade heterocyclisation with elimination of methanethiol followed by the formation of 4-dialkylaminopyridones **44a,b** containing the β -enaminoamide fragment. Pyridone **44b** reacts with the second molecule of *N*-methylcyanoacetamide (**43b**) to give naphthyridinedione **45**.²³²



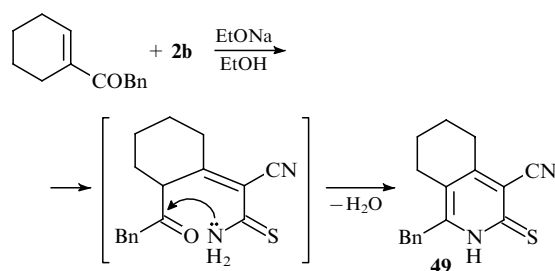
$R^1 = \text{Me, Ph, 4-ClC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4$; $R^2 = \text{Et, Ph, CH}_2\text{CH(OEt)}_2$, Bn; $R^3 = \text{H}$; $R^3 - R^4 = (\text{CH}_2)_2\text{O}(\text{CH}_2)_2$; $R^4 = \text{H (a), Me (b)}$.

Benzylidene- and 2-furfurylideneacetoacetic esters (**26**) smoothly reacted with selenoamide **2c** under mild conditions (anhydrous ethanol, 20 °C), the reagent ratio playing an essential role.^{45, 233–235} When the reagents were taken in a ratio of 1 : 1, the reaction afforded adducts **46**, which underwent cyclisation to 1,4-dihydropyridine-2-selenolates **47**. Treatment of the latter with hydrochloric acid yielded 1,4-dihydropyridine-2-selenols **48**.



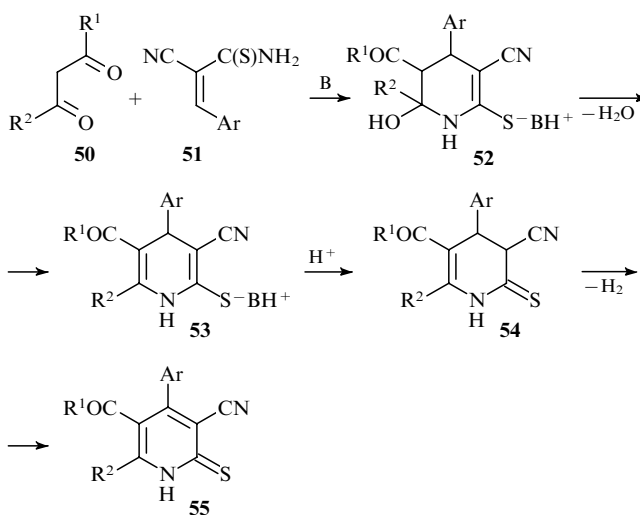
$R = \text{Ph, 2-furyl}$; B is a base.

The reaction of 1-phenylacetylcyclohexene with thioamide **2b** in the presence of sodium ethoxide in alcohol afforded pyridine-thione **49** containing a fragment of the alkaloid papaverine.²³⁶



III. Cascade heterocyclisation involving 1,3-dicarbonyl compounds

Like α,β -unsaturated analogues, 1,3-dicarbonyl compounds **50** and their enamines react with cyanothioacetamide derivatives, *viz.*, arylidenecyanothioacetamides **51**, in the presence of base catalysts to form 3-cyano-1*H*-pyridine-2-thiones or their salts.^{33, 237–254} In some cases, intermediate tetrahydropyridine-2-thiolates **52** were isolated. Subsequent elimination of water from these compounds affords 3-cyano-1,4-dihydropyridine-2-thiolates **53**. Acidification of salts **52** and **53** gave rise to 3-cyano-3,4-dihydro-1*H*-pyridine-2-thiones **54**. In solutions, the latter compounds underwent dehydrogenation to form 3-cyano-1*H*-pyridine-2-thiones **55**.

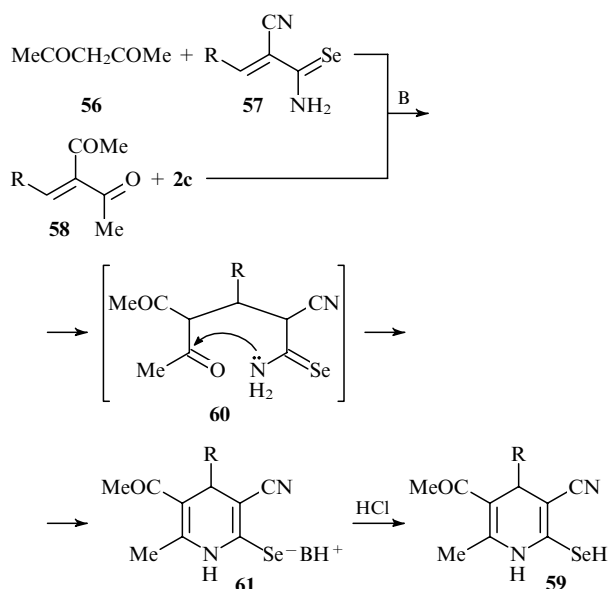


$R^1 = \text{Ph, OEt}$; $R^2 = \text{Me, CF}_3$; Ar = Ph, 3-FC₆H₄, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-NO₂C₆H₄; B is a base.

β -Enamine derivatives of 1,3-dicarbonyl compounds reacted with amides **51** also in the absence of base catalysts to produce the corresponding 1,4-dihydropyridine-2-thiolates in high yields.

The reaction of acetylacetone (**56**) with 2-furfurylideneacyano-selenoacetamide (**57**) or the reaction of an unsaturated carbonyl compound, *viz.*, 2-furfurylideneacetylacetone (**58**), with cyano-selenoacetamide (**2c**) afforded 5-acetyl-3-cyano-4-(2-furyl)-6-methyl-1,4-dihydropyridine-2-selenol (**59**) in ~80% yield.^{45, 255} These reactions proceeded through a mechanism of cascade heterocyclisation and involved the intermediate formation of

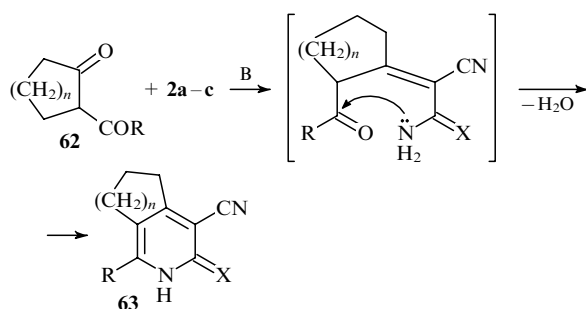
Michael adduct **60** and stable selenolate **61**, whose acidification gave selenol **59**. The reactions of amide **57** with acetoacetic ester or its enamine proceeded analogously to form 5-ethoxycarbonyl-substituted selenol of type **59**.



R is 2-furyl.

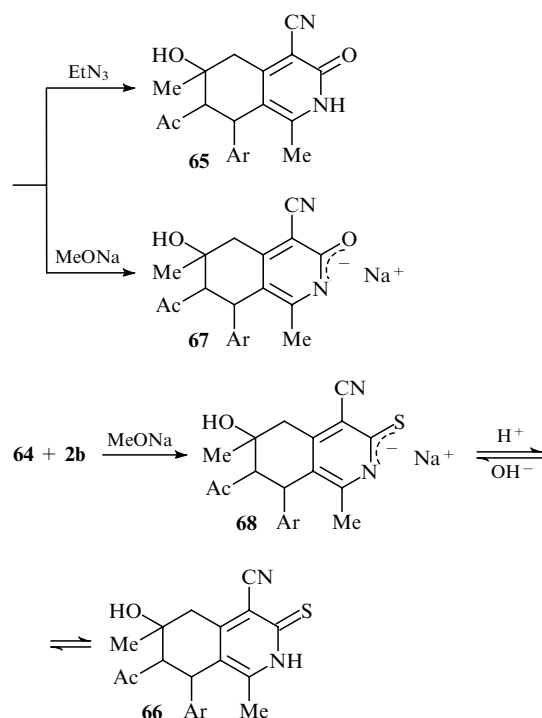
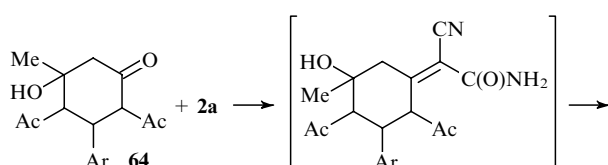
It should be emphasised that due to their diversity and high reactivity, 1,3-dicarbonyl compounds are the most convenient building blocks for the regio- and stereoselective synthesis of hydrogenated sulfur- and selenium-containing pyridines and their fused analogues that are difficult to prepare. For this purpose, acetylacetone, benzoylacetone, dibenzoylmethane, 2-thenoyltrifluoroacetone, β -keto amides (acetylacetamide, acetylacetanilides), ethyl butyrylacetate, acetoacetic and malonic esters and cyclic mono- and diketones were successfully used.^{45, 46, 256–303}

Thus, the use of 2-acylcycloalkanones **62** as substrates and cyanoacetamides **2a** as reagents made it possible to develop convenient procedures for the regioselective synthesis of fused 3-cyano-1*H*-pyridine-2-chalcogenones **63**.^{44, 188, 304–316}

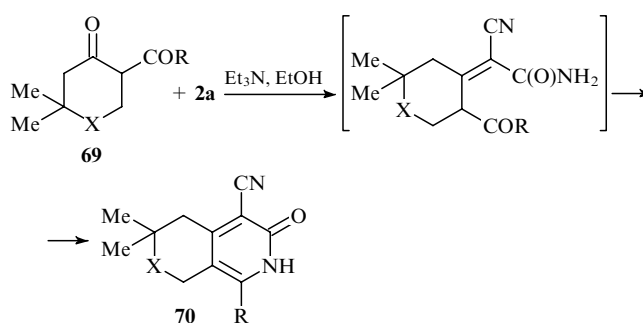


R = Alk, Ar; $n = 1, 2$; X = O, S, Se.

The reactions of amides **2a,b** with 2,4-diacetyl-3-aryl-5-hydroxy-5-methylcyclohexanones **64** afforded 7-acetyl-8-aryl-4-cyano-6-hydroxy-1,6-dimethyl-5,6,7,8-tetrahydro-2*H*-isoquinolin-3-ones **65**, corresponding thiones **66** and their sodium salts **67** and **68** in high yields.³¹⁴

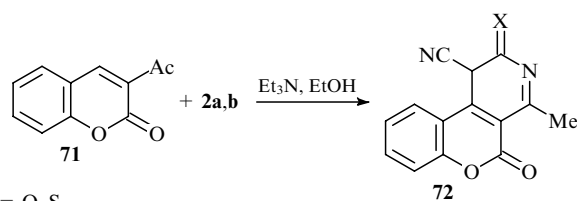


Of numerous reactions of amide **2a** with 2-acylcycloalkanones,^{269, 272, 315–318} noteworthy is the condensation with tetrahydropyrans or -thiopyrans **69** in ethanol in the presence of triethylamine giving rise to previously unknown 6-oxopyrano(thiopyrano)[3,4-*c*]pyridines **70**.^{117, 315, 316}



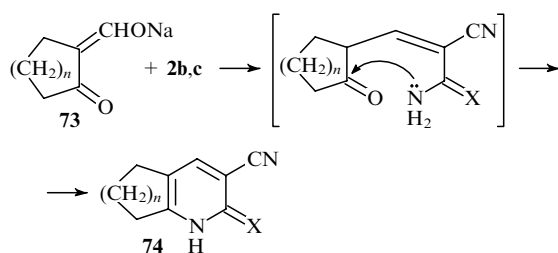
R = Alk, Ar; X = O, S.

Derivatives of coumarin or its fused analogues exhibit antibacterial, cardiovascular and hypothermal activities. Procedures for the synthesis of substituted coumarins are being developed with the aim of searching for new drugs. Thus, the reactions of 3-acetylcoumarin (**71**) with amides **2a,b** in the presence of bases giving rise to oxo and thioxo derivatives of benzopyrano[3,4-*c*]pyridine **72** have been studied.³¹⁸



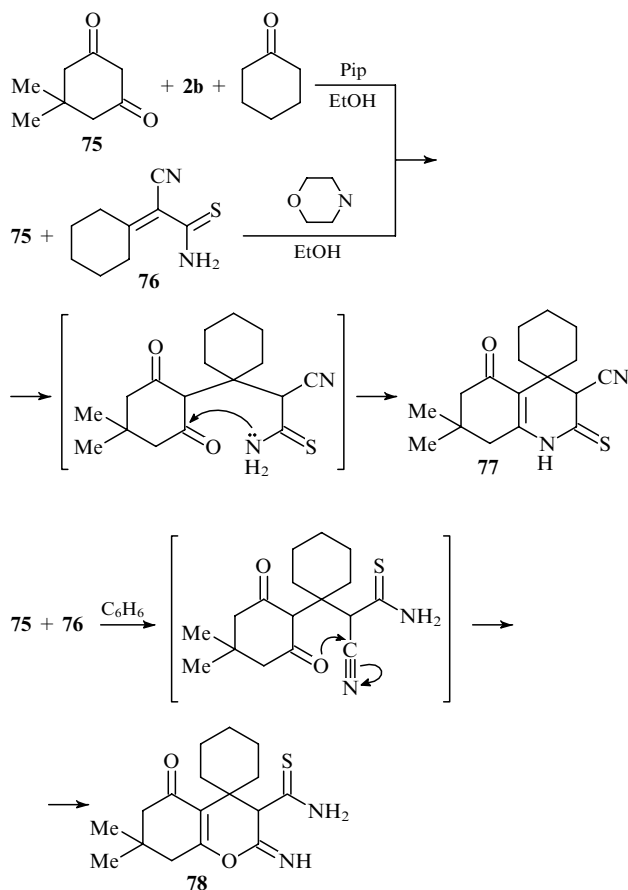
X = O, S.

Cascade heterocyclisation of amides **2b,c** with sodium salts of 2-hydroxymethylidenecycloalkanones **73** was examined. It was demonstrated that these reactions proceeded regioselectively to produce fused 3-cyano-1*H*-pyridine-2-thiones(selenones) **74**.^{44, 308, 319–326}

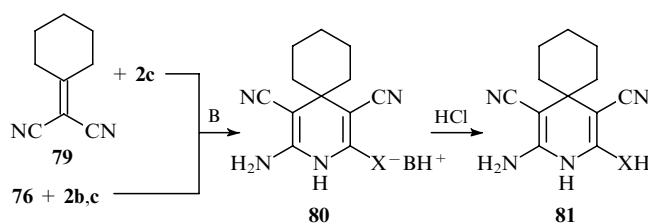


$n = 1, 2$; $X = S, Se$.

The methodology of cascade heterocyclisation is unique as can be exemplified by the synthesis of previously unknown quinoline- and pyridine-thiones containing a spiro-fused fragment. For instance, three-component condensation of dimedone (**75**), cyanothioacetamide (**2b**) and cyclohexanone in the presence of piperidine in ethanol or the reaction of diketone **75** with cyclohexylidenecyanothioacetamide (**76**) in ethanol in the presence of morpholine afforded previously unknown 3-cyano-7,7-dimethyl-5-oxospiro[cyclohexane-1,4'-octahydroquinoline]-2-thione (**77**).^{45, 293} The use of benzene as the solvent changed the direction of the latter reaction with the resulting formation of 2-iminopyran **78**.

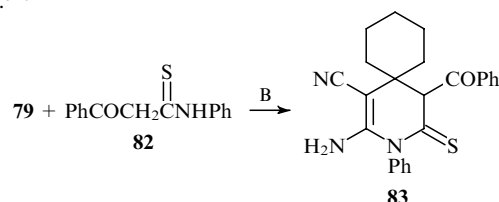


Spiro-fused partially hydrogenated pyridine-2-thiolates (sele-nolates) were also prepared with the use of other reagents. For example, the reaction of cyclohexylidenemalononitrile (**79**) with cyanoselenoacetamide (**2c**) or the reaction of cyclohexylidenecyanothioacetamide (**76**) with amides **2b,c** or malononitrile in ethanol in the presence of *N*-methylmorpholine gave rise to salts **80**, which were transformed into 6-amino-3,5-dicyanospiro[cyclohexane-1,4'-dihydropyridine]-2-thiol(selenol) (**81**) upon treatment with hydrochloric acid.^{45, 282, 327, 328}

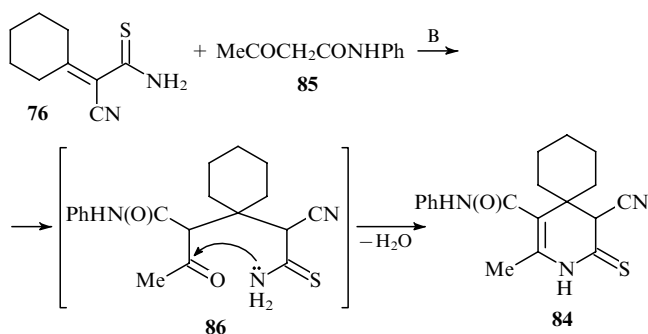


$X = S, Se$; B is *N*-methylmorpholine.

The reaction of dinitrile **79** with anilide **82** afforded partially hydrogenated polyfunctionalised spiro-fused pyridinethione **83**.³²⁸

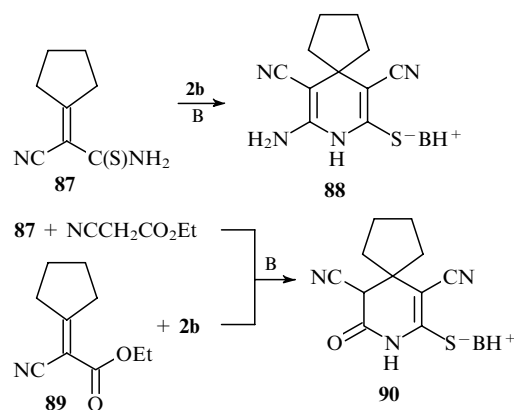


In turn, spiro[cyclohexane-1,4'-pyridine]-2-thione **84** was prepared in 87% yield by the reaction of thioamide **76** with acetoacetanilide (**85**) in ethanol in the presence of *N*-methylmorpholine.^{46, 263}

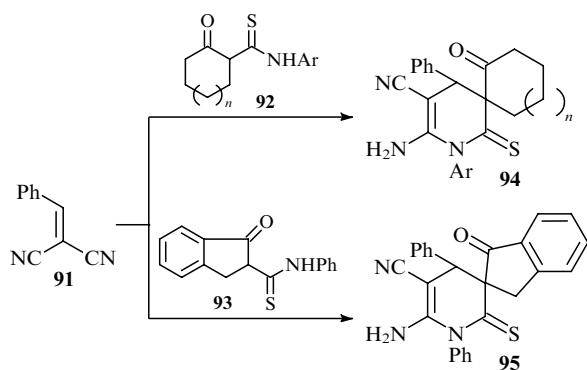


B is *N*-methylmorpholine.

An analogous reaction of cyclopentylidenecyanothioacetamide (**87**) with cyanothioacetamide (**2b**) produced 6-amino-3,5-dicyanospiro[cyclopentane-1,4'-dihydropyridine]-2-thiolate (**88**).²⁸³ The reaction of amide **87** with cyanoacetic ester or the reaction of amide **2b** with cyclopentylidenecyanoacetic ester (**89**) afforded 3,5-dicyano-6-oxospiro[cyclopentane-1,4'-tetrahydropyridine]-2-thiolate (**90**).³²⁹

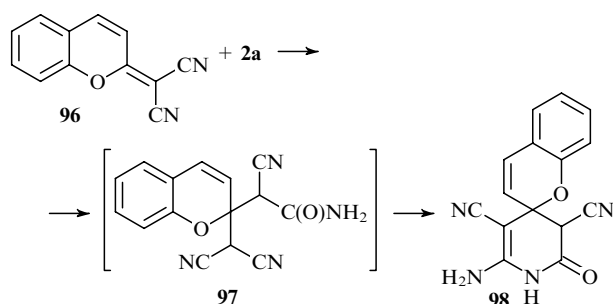


Benzylidenemalononitrile (**91**) reacted with anilides of 2-oxo-cycloalkanethiocarboxylic (**92**) and 3-oxo-2,3-dihydroindene-2-thiocarboxylic acids (**93**) to form spiro-fused pyridinethiones **94** and **95**, respectively.^{330, 331}

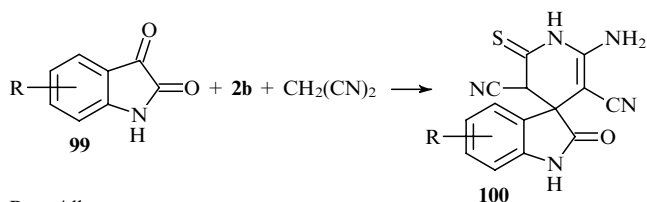


Ar = Ph, 4-MeC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄; *n* = 0–2.

On refluxing in ethanol in the presence of piperidine, cyanoacetamide (**2a**) added to chromenylidenemalononitrile (**96**) to give adduct **97**, which underwent intramolecular cyclisation *in situ* yielding spiro-fused pyridone **98**.³³¹

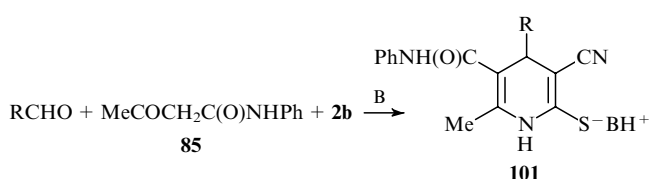


Three-component heterocyclisation of diketone **99**, amide **2b** and malononitrile in ethanol in the presence of piperidine giving partially hydrogenated pyridine-thione **100** provides another example of the synthesis of spiro-fused pyridinechalcogenones.³³²



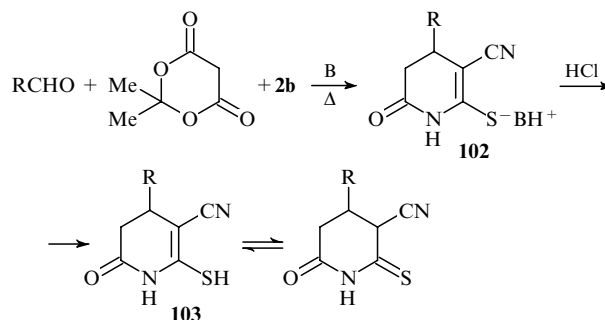
R = Alk.

It should be noted that in the last decade, three-component cascade heterocyclisation of amides of cyanoacetic acid or its thio and seleno derivatives with aliphatic, aromatic or heterocyclic aldehydes and 1,3-dicarbonyl compounds in the presence of an excess of an organic base was successfully used in the synthesis of 1*H*-pyridine-2-chalcogenones, their hydrogenated analogues and salts (see Refs 44–46, 199, 233, 241, 243, 244, 256, 257, 259, 262–268, 270, 271, 274, 276, 279, 284–286, 289–291, 293, 294, 302 and 333–339). The synthesis of salts of 4-(aryl,hetaryl)-3-cyano-6-methyl-5-phenylcarbamoyl-1,4-dihydropyridine-2-thiolates **101** from aromatic or heterocyclic aldehydes, amide **2b** and acetoacetanilide (**85**) in the presence of an excess of *N*-methylmorpholine^{257, 259, 337} provides an example.



R = Ph, 2-ClC₆H₄, 4-MeC₆H₄, 3-Py, 2-thienyl; B is *N*-methylmorpholine.

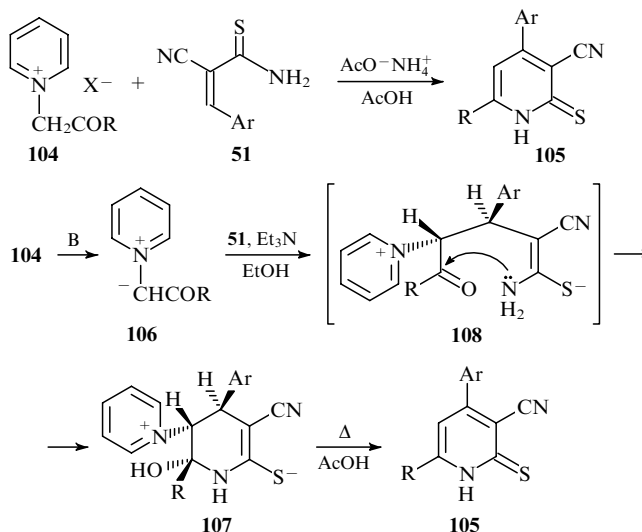
Cyclic diketones [cyclohexane-1,3-dione, dimedone, isopropylidenemalonate (Meldrum's acid)] were also used as 1,3-dicarbonyl substrates in three-component heterocyclisation.^{262, 285, 286, 295} For example, 4-(aryl,hetaryl)-3-cyano-6-oxo-1,4,5,6-tetrahydropyridine-2-thiolates **102** were prepared by refluxing an equimolar mixture of the corresponding aldehyde, amide **2b** and Meldrum's acid in alcohol in the presence of *N*-methylmorpholine for 3 h. Acidification of thiolates **102** with 10% hydrochloric acid to pH 5 afforded 4-(aryl,hetaryl)-5-cyano-6-thio-3,4-dihydro-1*H*-pyridin-2-ones **103**.²⁸⁵



R = 4-MeC₆H₄, 1-naphthyl, 2-furyl, 2-thienyl; B is *N*-methylmorpholine.

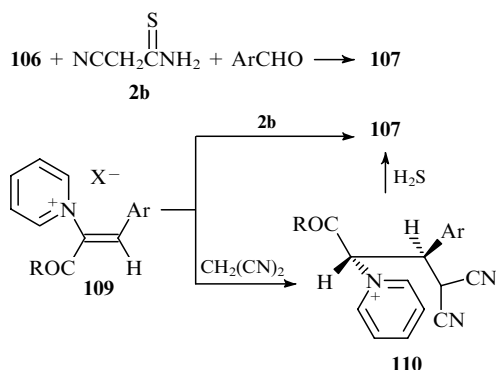
IV. Cascade heterocyclisation involving pyridinium ylides

Pyridinium ylides, which are generated *in situ* from quaternised pyridines, are widely used in fine organic synthesis.^{340–343} including the preparation of 4,6-disubstituted 3-cyano-1*H*-pyridine-2-thiones (see Refs 43, 44, 126, 327 and 344–354). It was noted that the nature of the final products depends on the reaction conditions. Thus, heating of arylidenecyanothioacetamides **51** with pyridinium salts **104** in the presence of ammonium acetate in acetic acid gave rise to 4,6-disubstituted 3-cyano-1*H*-pyridine-2-thiones **105**.³⁴⁶ By contrast, the reactions of pyridinium ylides **106** generated from salts **104** with amides **51** in ethanol in the presence of triethylamine at room temperature afforded *trans,trans*-1,4,5,6-tetrahydropyridine-2-thiolates **107**, which were isolated and characterised as stable crystalline salts.^{345–348, 351, 355–367} The high selectivity of these reactions results from the stereoselectivity of the addition of ylides **106** to amides **51**. Subsequent cyclisation of adducts **108** proceeded with retention of the *trans* arrangement of the hydrogen atoms.^{44, 346, 362} Heating of salts **107** in acetic acid in the presence of ammonium acetate afforded thiones **105**.



R = Me, OMe, NH₂, Ph, 3-Py; Ar = Ph, 3-FC₆H₄, 4-FC₆H₄, 4-ClC₆H₄, 4-NO₂C₆H₄, 3-Py; X = I, Br; B is a base.

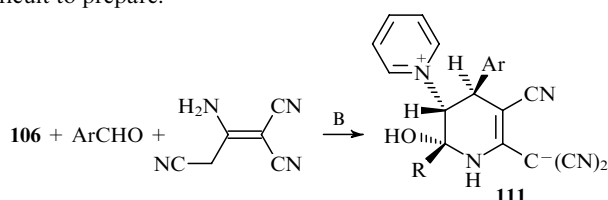
Thiolates **107** were also synthesised without the preliminary preparation of thioamides **51** by three-component condensation of pyridinium ylides **106**, cyanothioacetamide (**2b**) and aromatic aldehydes ^{346, 347, 351} as well as by the reaction of pyridinium salt **109** with amide **2b**.³⁶⁰ The use of malononitrile instead of amide **2b** in the reaction with the *E* isomer of compound **109** resulted in the formation of *trans*-adducts **110**, whose treatment with hydrogen sulfide produced *trans*-substituted tetrahydropyridines **107**.



R = Me, OMe, NH₂, Ph; Ar = Ph, 4-ClC₆H₄, 4-BrC₆H₄, 4-FC₆H₄, 4-MeOC₆H₄, 3-Py, 4-Py; X = Cl, Br.

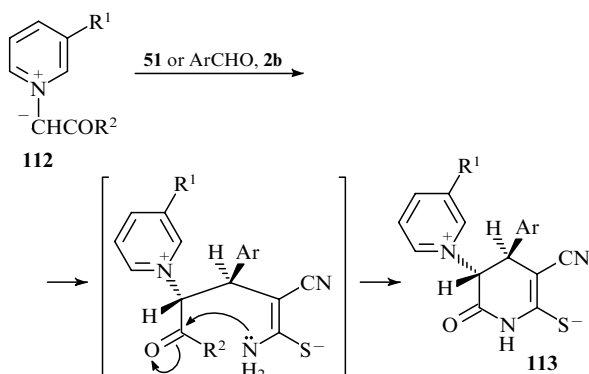
Isoquinolinium ylides also found application in the synthesis of thiolates.³⁴⁷

Stereoselective three-component condensation of pyridinium ylides **106**, aromatic aldehydes and 2-amino-1,1,3-tricyanopropene afforded *trans*-6-R-4-aryl-3-cyano-6-hydroxy-5-pyridinio-1,4,5,6-tetrahydropyridine-2-dicyanomethylides **111**, which are difficult to prepare.^{345, 346}



Ar = Ph, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-MeOC₆H₄; R = Me, OMe, NH₂, Ph, 3-Py.

The reactions of *meta*-substituted pyridinium ylides **112** with arylidenecyanothioacetamides **51** provided the basis for regio- and stereoselective procedures for the synthesis of *trans*-4-aryl-3-cyano-6-oxo-5-pyridinio-1,4,5,6-tetrahydropyridine-2-thiolates (**113**).^{44, 223, 345, 353–355} Tetrahydropyridines **113** were also syn-

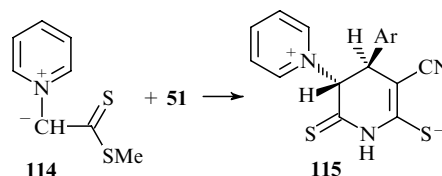


R¹ = Me, Br, NH₂; R² = Me, Ph, NH₂, OMe; Ar = Ph, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-HOC₆H₄, 4-MeOC₆H₄, 2-NO₂C₆H₄, 3-Py, 4-Py.

thesised by one-pot heterocyclisation of pyridinium ylides **112** with aromatic aldehydes and cyanothioacetamide (**2b**) without the preliminary preparation of unsaturated amides **51**.^{44, 345}

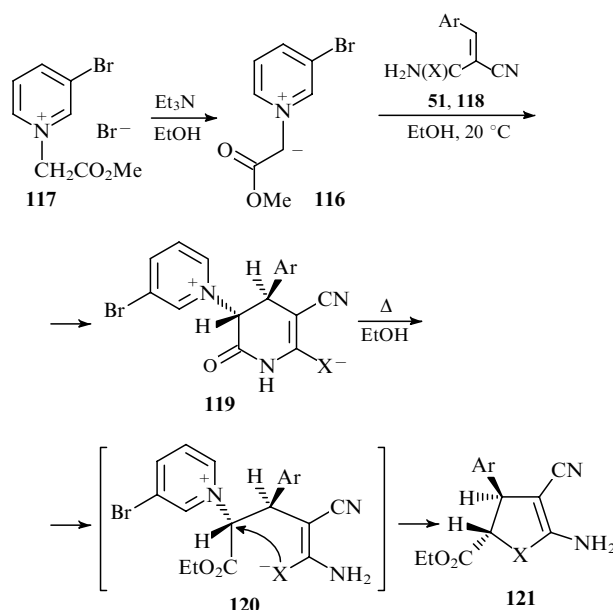
Various pyridinium ylides are used for the preparation of 4-aryl-3-cyano-6-oxo-5-pyridinio-1,4,5,6-tetrahydropyridine-2-olates.^{346, 353–356, 368}

Cascade heterocyclisation of pyridinium ylide **114** with amides **51** gave rise to *trans*-substituted 6-thioxo-1,4,5,6-tetrahydropyridine-2-thiolates **115**.^{223, 346, 353, 355}



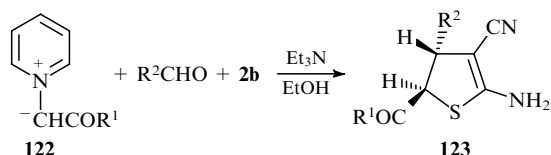
Ar = 4-HOC₆H₄, 4-MeOC₆H₄, 4-FC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 3-Py.

It was found that the direction of cascade heterocyclisation involving pyridinium ylides depends on the reaction temperature. For example, the reactions of 3-bromopyridinium ylide **116** generated from salt **117** with unsaturated nitriles **51** and **118** at room temperature in ethanol in the presence of triethylamine proceeded stereo- and atroposelectively to yield *trans*-substituted 1,4,5,6-tetrahydropyridines **119**. Heating of the latter compounds in ethanol led to alcoholysis and opening of the tetrahydropyridine ring at the amide bond to give the corresponding intermediates **120**. The subsequent intramolecular nucleophilic substitution proceeded with elimination of 3-bromopyridine and retention of the *trans*-arrangement of the hydrogen atoms and produced the corresponding *trans*-dihydrofurans and -thiophenes **121**.^{43, 44, 344, 349, 350, 354, 369} Five-membered heterocycles **121** were also generated in high yields without isolation of intermediates **119** and **120** by the reactions of ylide **116** with nitrile **51** or **118**, respectively, in ethanol at ~80 °C.



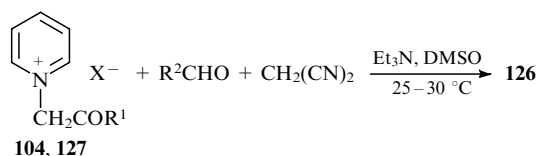
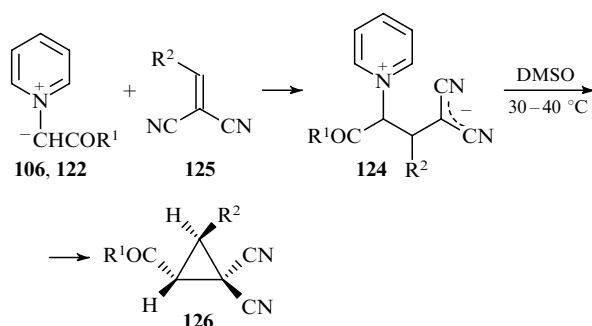
Ar = 3-Py, 4-FC₆H₄, 2-MeOC₆H₄; X = S (**51**), O (**118**).

Three-component cascade heterocyclisation of ylide **122**, aromatic aldehydes and amide **2b** in ethanol in the presence of triethylamine at room temperature gave previously unknown adamantylcarbonyldihydrothiophenes **123** in 62%–95% yields.^{43, 343, 349}



R¹ is 1-adamantyl; R² = 4-Py, 4-FC₆H₄, 4-ClC₆H₄.

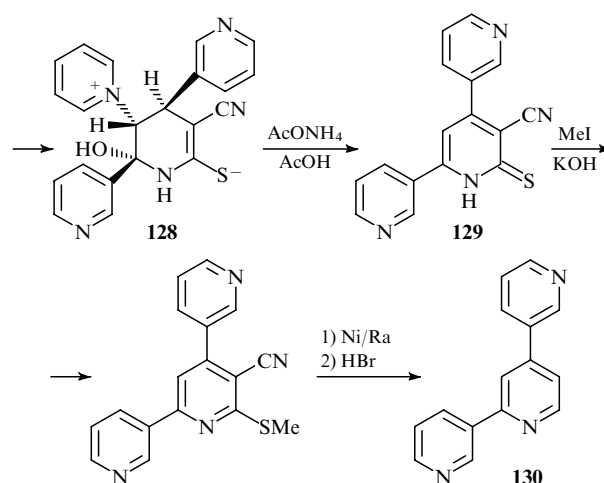
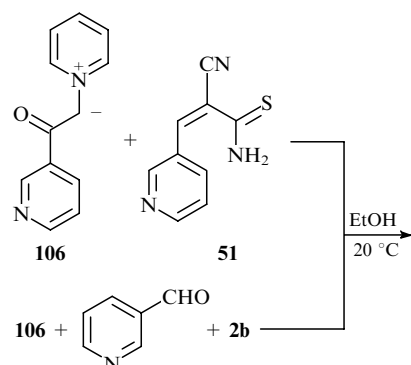
Considerable synthetic potential of pyridinium ylides enables one to use these compounds for the development of fundamentally new approaches to functionalised cyclopropanes. For example, heating of betaines **124**, which were generated by the reactions of pyridinium ylides **106** and **122** with arylidenemalononitriles **125**, in DMSO at 30–40 °C led to intramolecular 1,3-elimination of pyridine to form *trans*-cyclopropanes **126** in 80%–96% yields.^{43, 344, 357, 370, 371} Compounds **126** can also be prepared in 78%–94% yields by three-component condensation of salts **104** or **127** with aromatic aldehydes and malononitrile in DMSO in the presence of triethylamine at 25–30 °C.



R¹ = NH₂, Me (**104**, **106**), 1-adamantyl (**122**, **127**);

R² = 4-ClC₆H₄, 4-BrC₆H₄, 4-IC₆H₄, 3-Py, 4-Py, 2-thienyl.

The synthesis of nicotine, viz., 2,4-bis(3-pyridyl)pyridine, which is a minor alkaloid from tobacco *Nicotiana tabacum*,^{43, 44, 344, 351} provides yet another example of the successful use of the methodology of cascade heterocyclisation involving pyridinium ylides. Thus, the reaction of ylide **106** (R = 3-Py) with amide **51** (Ar = 3-Py) in ethanol at room temperature gave rise to 4,5-*trans*-3-cyano-6-hydroxy-4,6-bis(3-pyridyl)-5-pyridinio-1,4,5,6-tetrahydropyridine-2-thiolate (**128**) in 98% yield. This compound was also synthesised in 92% yield by three-component condensation of ylide **106** (R = 3-Py), 3-pyridinecarbaldehyde and amide **2b** under analogous conditions. Heating of thiolate **128** in acetic acid in the presence of ammonium acetate afforded thione **129** in 83% yield. The latter was transformed into nicotine **130** in 82% yield by successive alkylation, hydrogenolysis in

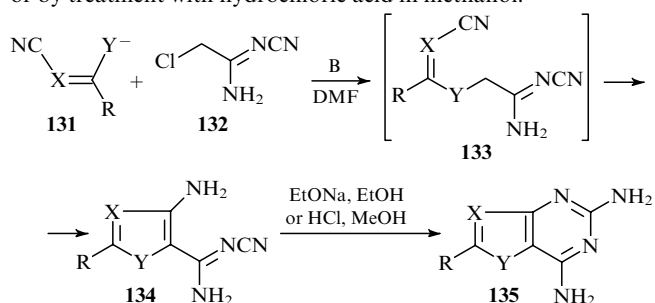


the presence of Raney nickel and decyanation in an acidic medium.

V. Cascade heterocyclisation in the synthesis of fused heterocycles

Functionalised fused heterocycles are of equal or even higher practical interest than the corresponding mononuclear heterocyclic systems. However, most of the available procedures for their synthesis are rather laborious, involve many steps and often require drastic conditions, which eventually leads to a substantial decrease in the yields and an increase in the cost of the final products. The use of the strategy of cascade heterocyclisation allows one not only to eliminate these drawbacks but also to construct polyfunctional annelated heterocycles, which are impracticable to prepare by conventional methods. The methodology of cascade heterocyclisation involving simple and available substrates and reagents provided the basis for the development of convenient procedures for the synthesis of different classes of fused heterocycles, such as thieno[3,2-*b*]pyridines, thieno[3,2-*d*]pyrimidines, thiazolo[4,5-*b*]pyridines, thiazolo[4,5-*d*]pyrimidines, pyrido[3',2':4,5]thieno[3,2-*b*]pyridines, pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines, pyrido[3',2':4,5]thieno(selenopheno)[3,2-*d*]pyrimidines, quinuclidino[2'',3'':5',6']pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines, pyrimido[4',5':4,5]thieno[2,3-*c*]-2,7-naphthyridines, pyrido[2'',3'':4',5']thieno[3',2':4,5]thieno[3,2-*b*]pyridines, etc.^{50, 52, 371–390}

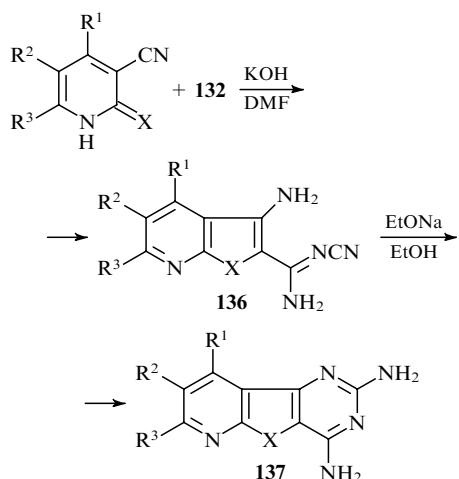
The successful application of the strategy of cascade heterocyclisation can be exemplified by regioselective procedures for the synthesis of thieno-, selenopheno- and thiazolodiaminopyrimidines on the basis of vicinal mercapto(hydroseleno)nitriles **131** and *N*-cyanochloroacetamide (**132**). The reactions start with regioselective alkylation at the chalcogen atom to form intermediates **133**, which undergo Thorpe–Ziegler cyclisation giving rise to compounds **134**. The latter are transformed into hetarylpyrimidines **135** by heating in ethanol in the presence of sodium ethoxide or by treatment with hydrochloric acid in methanol.^{50, 373, 375}



R = NHPh, NHCH₂CH=CH₂; X = N, CCN; Y = S, Se;

B is a base.

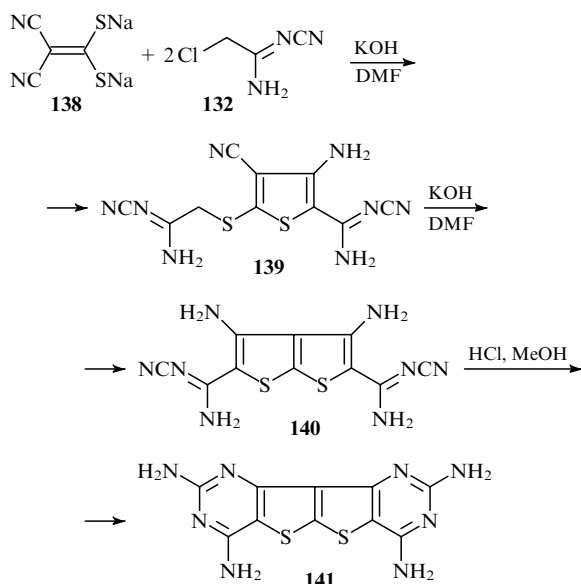
An analogous reaction of amidine **132** with 1*H*-pyridine-2-chalcogenones in DMF in the presence of an excess of KOH involved two successive steps, *viz.*, nucleophilic substitution and Thorpe–Ziegler condensation, and produced thieno(selenopheno)[2,3-*b*]pyridines **136**.³⁷³ Refluxing of the latter compounds with sodium ethoxide in ethanol afforded 2,4-diaminopyrido[3',2':4,5]thieno(selenopheno)[3,2-*d*]pyrimidines **137**. The latter compounds can also be synthesised without isolation of intermediates **136**.^{372, 373}



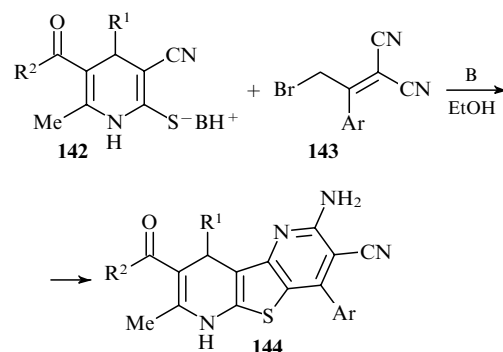
$R^1 = \text{H, Me, CF}_3, 4\text{-ClC}_6\text{H}_4$; $R^2 = \text{H}$; $R^3 = \text{Me, Ph, 4-MeC}_6\text{H}_4$;

$R^2-R^3 = \text{pyridine ring}, (\text{CH}_2)_4$; $X = \text{S, Se}$.

The reaction with the use of sodium 2,2-dicyanoethylene-1,1-dithiolate (**138**) as the nitrile component proceeded through the successive formation of compounds **139** and **140** to give tetraannelated heterocycle **141** as the final product.^{50, 373, 375}

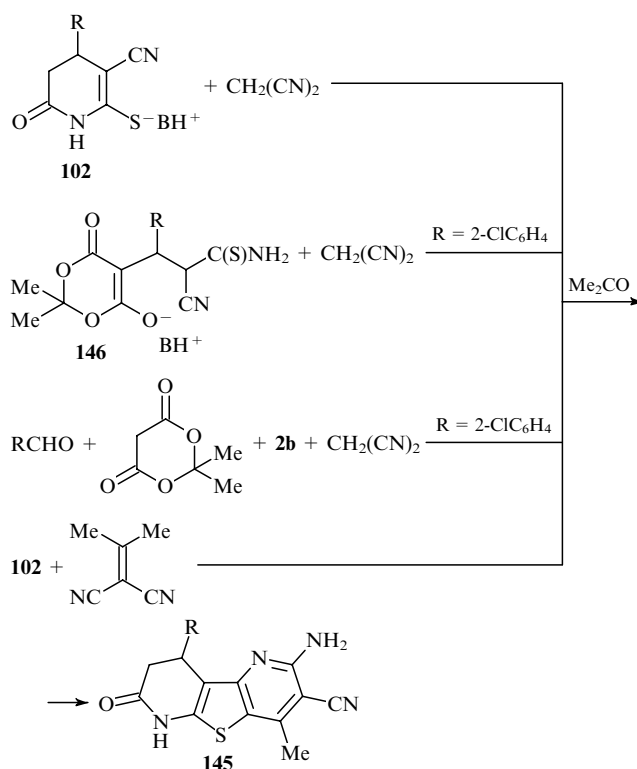


Of other numerous examples of the employment of cascade heterocyclisation in the synthesis of fused heterocyclic systems, noteworthy is the preparation of pyridothienopyridines, pyridothienopyrimidines and their hydrogenated analogues.^{52, 380–383, 387, 391, 392} For example, the reactions of piperidinium 3-cyano-1,4-dihydropyridine-2-thiolates **142** with 2-bromo-1-arylethylidenemalononitriles **143** produced 2,5-dihydropyrido[3',2':4,5]thieno[3,2-*b*]pyridines **144** in high yields.^{52, 381} This procedure can also be used for the synthesis of functionalised pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidines.



$R^1 = 4\text{-MeOC}_6\text{H}_4, 2\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-thienyl}$; $R^2 = \text{Me, OEt}$;
 $\text{Ar} = \text{Ph, 4-BrC}_6\text{H}_4$; B is piperidine.

Tetrahydropyridothienopyridines **145** were synthesised by three-component cascade heterocyclisation of tetrahydropyridine-2-thiolates **102**, malononitrile and acetone in refluxing ethanol. These compounds were also prepared by the reactions of precursors of thiolates **102**, *viz.*, the corresponding Michael adducts **146**, with malononitrile and acetone, by condensation of 2-chlorobenzaldehyde, Meldrum's acid, cyanothioacetamide (**2b**), malononitrile and acetone in the presence of *N*-methylmorpholine or by refluxing a mixture of thiolate **102**, isopropylidenemalononitrile and acetone in ethanol.^{391, 392}



$R = \text{Ph, 4-MeC}_6\text{H}_4, 2\text{-ClC}_6\text{H}_4, 2\text{-MeOC}_6\text{H}_4, 2,5\text{-(MeO)}_2\text{C}_6\text{H}_3, 3,4\text{-(MeO)}_2\text{C}_6\text{H}_3, 3,4,5\text{-(MeO)}_3\text{C}_6\text{H}_2, 4\text{-EtOC}_6\text{H}_4, 3,4\text{-(OCH}_2\text{)}_2\text{C}_6\text{H}_3, 1\text{-naphthyl, 2-thienyl}$; B is *N*-methylmorpholine.

Recent advances in cascade heterocyclisation have been discussed in the reviews^{389, 390, 393–395} and studies.^{396–405}

* * *

Due to elaboration of fundamentals of one-pot cascade heterocyclisation of carbonyl compounds and CH-acids under the conditions of base catalysis, one can easily perform the regio- and stereoselective synthesis of polyfunctional heterocycles, in particular, of substituted pyridinechalcogenones and their hydrogenated and fused analogues. An important advantage of this

approach is the simplicity and accessibility of substrates and reagents, viz., of aromatic and heteroaromatic aldehydes, cycloalkanones, acyclic and cyclic mono- and dicarbonyl compounds, α,β -unsaturated carbonyl compounds, cyanoacetamides and their thio and seleno analogues.

Undoubtedly, this methodology shows promise for the development of procedures for the preparation of new classes of heterocyclic compounds.

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Advances in the chemistry of furazano[3,4-*b*]pyrazines and their analogues

A B Sheremetev, I L Yudin

Contents

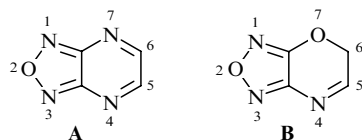
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Abstract. The published data on the methods for the synthesis of furazans fused to six-membered heterocycles with two heteroatoms in positions 1 and 4, their reactivities and practical applications are considered and systematised. The bibliography includes 89 references.

I. Introduction

The first paper devoted to the synthesis of compounds of the furazanopyrazine series was published in 1969.¹ However, intense development of this branch of chemistry began only in the mid-1980's when nitro derivatives of furazanopyrazines were recommended for use as explosives. High operating characteristics of this class of compounds attracted the attention of the specialists and gave impetus to comprehensive studies of their miscellaneous derivatives. Systematic studies of high-energy materials based on furazanopyrazine have led to the development of a vast variety of effective components of explosives and propellants. These studies provided profound insight into the chemistry and reactivities of furazanopyrazines and made accessible their polyfunctional derivatives. These achievements stimulated investigations into other properties of furazanopyrazines, *viz.*, biological activity, photosensitivity, *etc.* Obviously, furazanopyrazine analogues where one or both pyrazine nitrogen atoms are replaced by oxygen or sulfur atoms are promising candidates for medicinal drugs. However, the methods for their synthesis are still poorly studied. The lack of efficient procedures for the preparation of such compounds impedes further investigations into their properties.

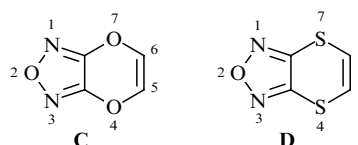
Four structural types in which the furazan (1,2,5-oxadiazole) ring is fused to a six-membered ring containing two heteroatoms in positions 1 and 4 are presently known, namely furazano[3,4-*b*]pyrazine (**A**), furazano[3,4-*b*][1,4]oxazine (**B**), 1,4-dioxino[2,3-*c*]furazan (**C**) and 1,4-dithiino[2,3-*c*]furazan (**D**).



A B Sheremetev, I L Yudin N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 938 36 51. E-mail: sab@ioc.ac.ru

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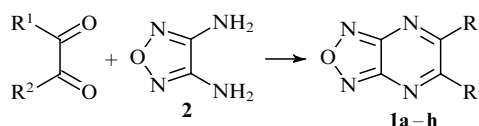
The presence of three contiguous heteroatoms in the furazan structure determines the pronounced electron-withdrawing character of this heterocycle. The bond localisation in the heterodiene fragment of furazan is strongly fixed; therefore, its derivatives are not prone to annular-group tautomerism. These features of the furazan ring determine the reactivities of all of its derivatives.^{2–5}

This review is an attempt to generalise the whole body of available data on the synthesis, properties and applications of furazanopyrazines and their analogues. The review is intended mostly for organic chemists and is aimed at stimulating further studies in this field.

II. Furazano[3,4-*b*]pyrazine derivatives

1. Synthesis

The furazanopyrazine system can be built starting from furazan or pyrazine derivatives. Condensation of α -dicarbonyl compounds with aromatic and heterocyclic *o*-diamines is the most popular procedure for the synthesis of fused pyrazines. For the first time, this reaction was used for the preparation of furazanopyrazines **1** in 1969.¹ 3,4-Diaminofurazan (**2**) was used as a diamine.

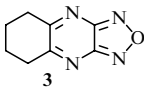
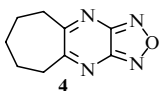
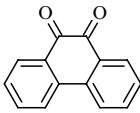
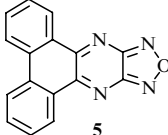
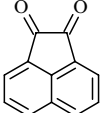
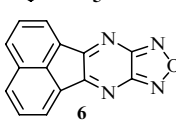
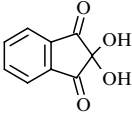
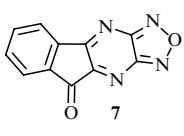
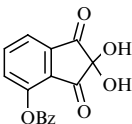
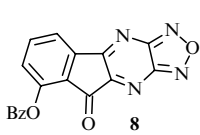
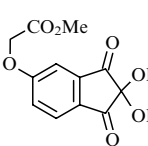
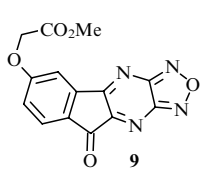
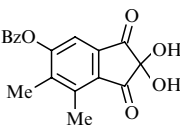
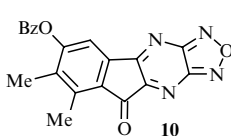


Compound 1	R ¹	R ²	Reaction conditions	Yield (%)	Ref.
a	Ph	Ph	AcOH, 110 °C	35	1
	Ph	Ph	BF ₃ ·OEt ₂ , 130 °C, 10 min	84	6
b	Me	Me	AcOH, 50 °C	51	7
c	Ph	H	AcOH, EtOH (1 : 3), Δ, 2 h	92	6
	Ph	H	AcOH, EtOH (1 : 1), Δ, 1 h	68	8
d	Ph	H	AcOH, Δ, 2.5 h	53	9
	4-ClC ₆ H ₄	H	AcOH, EtOH (1 : 1), Δ, 1 h	69	8

Compound 1	R ¹	R ²	Reaction conditions	Yield (%)	Ref.
e	4-BrC ₆ H ₄	H	AcOH, EtOH (1 : 1), Δ, 1 h	73	8
f	4-MeOC ₆ H ₄	H	AcOH, EtOH (1 : 1), Δ, 1 h	65	8
g	4-O ₂ NC ₆ H ₄	H	AcOH, EtOH (1 : 1), Δ, 1 h	78	8
h	Ph	Me	AcOH, EtOH (1 : 3), Δ, 2 h	79	6

The nucleophilicities of amino groups in compound **2** are much lower than those in aromatic *o*-diamines (e.g., *o*-phenylenediamine); therefore, more drastic reaction conditions are required. Later, this method and its modifications were used for the synthesis of the furazano[3,4-*b*]pyrazine derivatives **1a–h**.^{6–9}

Table 1. Reaction conditions and yields of the reaction products of cyclic α-diketones with the diamine **2**.

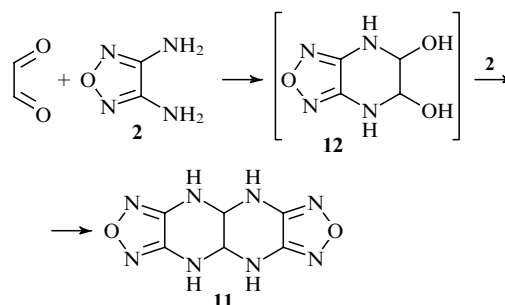
α-Diketone	Reaction conditions with the diamine 2	Product	Yield (%)	Ref.
	AcOH, ^a EtOH, Δ, 1 h		45	8
	AcOH, ^a EtOH, Δ, 1 h		39	8
	AcOH, Δ		60	1
	AcOH, Δ		80	1
	EtOH, Δ, 10 min		86 83	8 11
	AcOH, ^a EtOH, Δ, 6 h		46	10
	AcOH, ^a EtOH, Δ, 4 h		19	10
	AcOH, ^a EtOH, Δ, 4 h		33	10

^a AcOH : EtOH = 1 : 1.

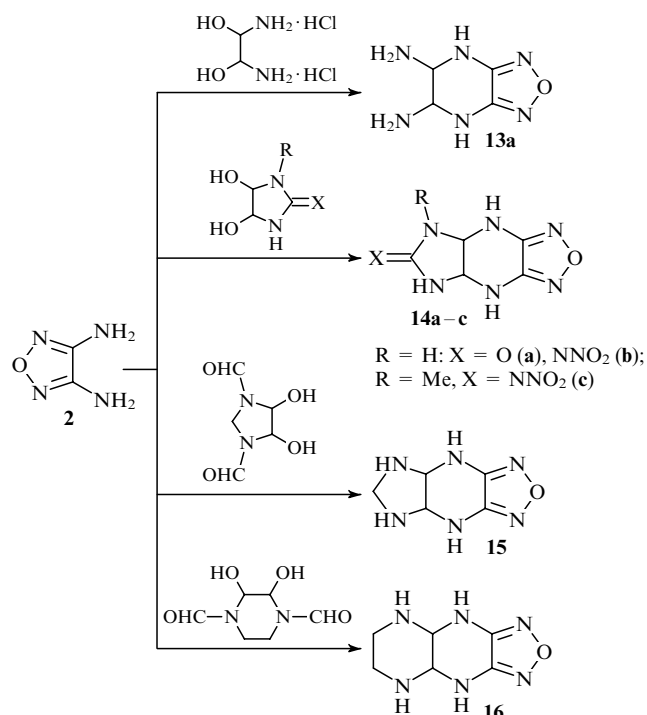
This reaction is carried out by heating the reactants in acetic acid or in a mixture of acetic acid and ethanol. The preparation of the derivative **1a** by melting of benzil with the diamine **2** in the presence of boron trifluoride etherate has been described.⁶ Under these conditions, the target product was obtained in 84% yield after 10 min. However, this single example of the use of a Lewis acid as a promoter of this reaction does not allow one to judge on the applicability of this approach to other subjects.

Cyclic α-diketones react with the diamine **2** under similar conditions to yield polycyclic derivatives **3–10** (Table 1).^{1, 8, 10, 11}

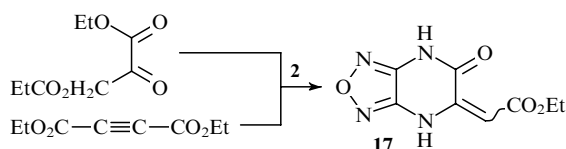
Glyoxal reacts with the diamine **2** in water in the presence of hydrochloric acid at 60 °C to give the tetracycle **11** in a quantitative yield.^{12–17} The reaction proceeds *via* intermediate dihydroxy derivative **12**.



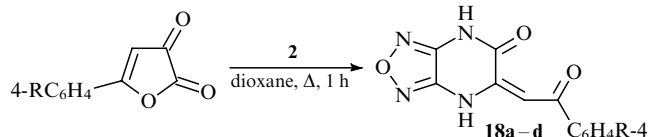
Preformed glyoxal adducts with NH₄Cl or weakly basic amines can be used in a reaction with diamine **2** in the presence of acids. This approach was used for the synthesis of partially hydrogenated furazanopyrazines **13–16**,^{16, 18, 19} however, the yields of reaction products seldom exceeded 60%. Compound **14b** was obtained in 55% yield by condensation of the dihydroxy derivative **12** with nitroguanidine.¹⁹



Heating of ethyl oxaloacetate with the diamine **2** for 1 h at 140–150 °C affords a mixture of *Z,E*-isomers of ethoxycarbonylmethylidene pyrazinone **17** (yield 54%).²⁰ If the condensation is carried out in boiling acetic acid, the product yield increases to 85%.²¹ Pyrazinone **17** was also synthesised by boiling the amine **2** with diethyl acetylenedicarboxylate (AcOH, EtOH, 45 min; yield 74%).⁸

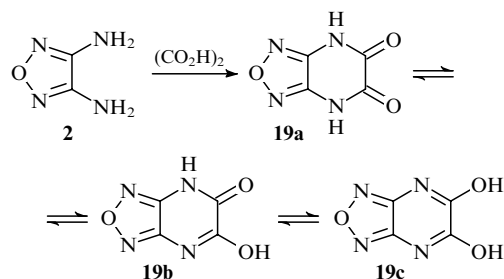


Cyclic α -keto ethers, *viz.*, 2,3-dihydrofuran-2,3-diones, condense with the diamine **2** in boiling dioxane to yield pyrazinones **18a–d**. The nature of the substituent in the phenyl ring of the starting furandione does not influence the yields of reaction products which are in the range 60%–75%.^{22,23}

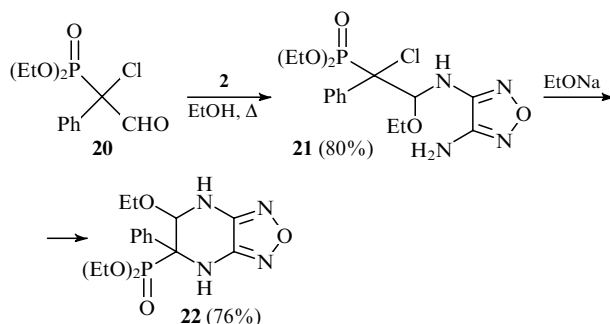


R = Me (**a**), Br (**b**), Cl (**c**), OMe (**d**).

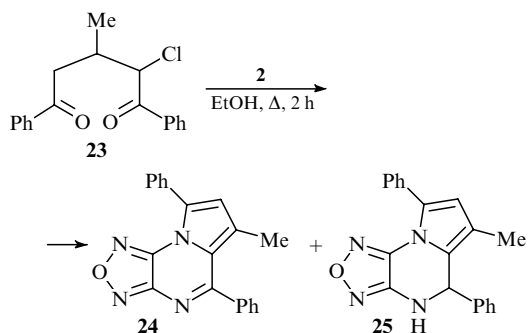
In contrast to α -keto acids used in the form of esters for the preparation of hydrogenated furazanopyrazines (furazanopiperazines), oxalic acid reacts with the diamine **2** on boiling in dilute hydrochloric acid. The reaction product (yield 30%) exists as an equilibrium mixture of tautomers **19a–c**.¹



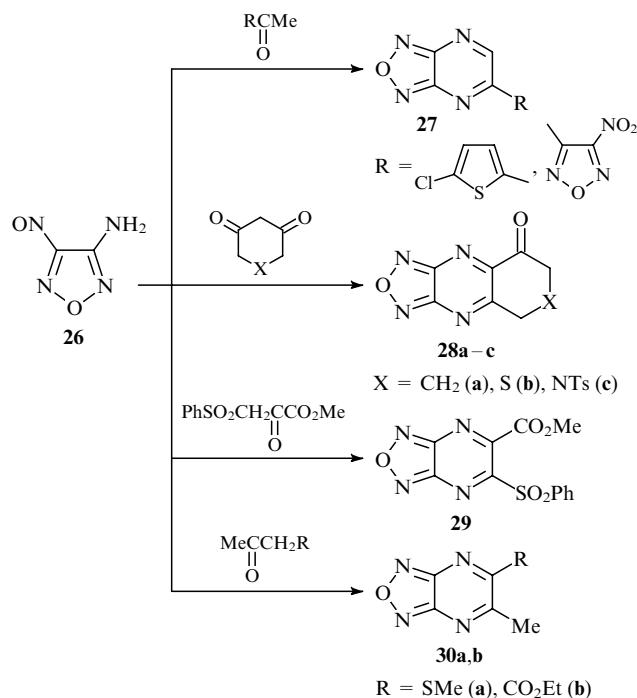
Reaction of phosphoryl-substituted chloroaldehyde **20** with the diamine **2** yields hemiaminal **21**; treatment of the latter with sodium ethoxide results in cyclocondensation to give C-phosphorylated furazanopyrazine derivative **22**.²⁴



Condensation of the amine **2** with chloro-substituted 1,5-diketone **23** gives a mixture of a tricyclic compound **24** (75%) and its dihydro derivative **25** (15%). Compound **25** is readily aromatised under the action of MnO_2 ; the yield of the reaction product **24** is 60%.²⁵

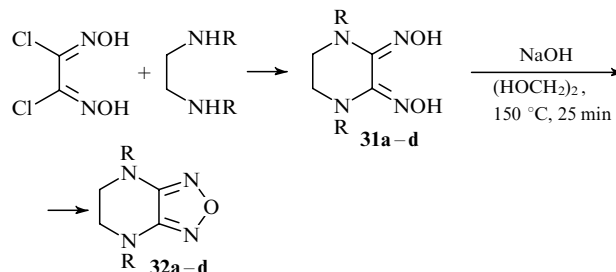


3-Amino-4-nitrosfurazan (**26**) is yet another furazan derivative suitable for the design of furazanopyrazines.²⁶ Carbonyl compounds containing a reactive methylene group, which are more accessible than α -dicarbonyl compounds, are used as the second component.²⁷ The one-pot reaction is carried out first in an alkaline medium (NEt_3 , Na_2CO_3) which is then changed to an acidic one (AcOH). The yields of furazano[3,4-*b*]pyrazines **27–30** are 50%–90%. The attempts to introduce compounds with reactive methylene groups but devoid of the ketone function (*e.g.*, malononitrile, ethyl cyanoacetate, nitroacetoneitrile, *etc.*) into the condensation did not result in the formation of the pyrazine ring.



Furazanopyrazines can also be prepared from pyrazine precursors by fusing the furazan ring. 2,3-Bis(hydroxyimino)piperazines, which are usually prepared by reaction of dichloroglyoxime with aliphatic,^{15,28,29} aromatic^{30–32} or heterocyclic^{33–35} 1,2-diamines, are the key compounds in this procedure.

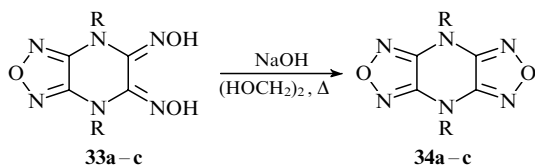
Cyclisation of the dihydroxyimine fragment involves treatment with dehydrating agents to give the corresponding furazans or with oxidants resulting in furazan *N*-oxides (furoxans). Thus heating of an equimolar mixture of dioximes **31a–d** with NaOH in ethylene glycol yields the corresponding furazanopiperazines **32a–d**.^{15,29}



R = H (**a**, 50%), Me (**b**, 52%), Pr^i (**c**, 60%), Bu^t (**d**, 75%).

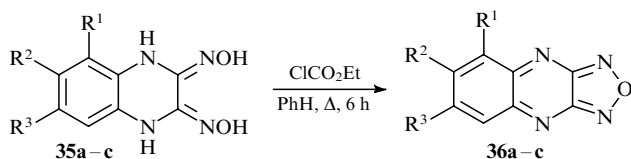
Treatment of dioximes **33a–c** with sodium hydroxide results in closure of the second furazan ring and formation of difurazanopiperazines **34a–c**. Under these conditions, unsubstituted difurazanopiperazine **34a** is formed in ~80% yield on heating of dioxime **33a** in aqueous alkali.^{35–37} Long-term treatment of the dioximes **33b,c** containing substituents at nitrogen atoms of the

piperazine ring with sodium hydroxide in ethylene glycol yields the tricyclic products **34b,c**.^{33, 34}



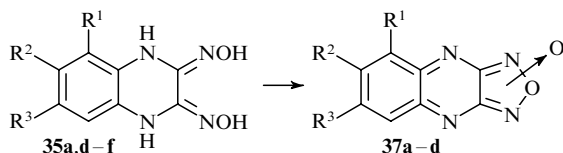
R = H (a), Bn (b), CH₂C₆H₄OMe-4 (c).

Dehydration of quinoxaline dioximes **35a-c** can be carried out by treatment with ethyl chloroformate in boiling benzene. In this case, dehydration is accompanied by aromatisation of the piperazine ring. The yields of furazanoquinoxalines **36a-c** do not exceed 50%.³⁸



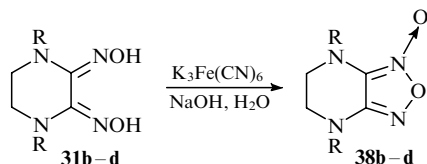
R¹ = R² = R³ = H (a); R¹ = R² = H, R³ = Me (b);
R¹ = H, R¹ = R² = Me (c).

Treatment of the dioximes **35a,d,e** with bis(trifluoroacetoxy)-λ³-iodanylbenzene results in the oxidation of both the dioxime fragment and the piperazine ring to give furoxans **37a-c**.³⁹ The dioxime **35f** is oxidised with lead tetraacetate, but the corresponding furoxan **37d** is formed in low yields.³¹ However, the position of the *N*-oxide oxygen atom in compounds **37a-d** has not been established.^{31, 39}



Com- pound 35	R ¹	R ²	R ³	Reaction conditions	Com- pound 37	Yield (%)
a	H	H	H	PhI(OCOCF ₃) ₂ , CH ₂ Cl ₂ , 20 °C	a	94
d	Me	H	H	PhI(OCOCF ₃) ₂ , CH ₂ Cl ₂ , 20 °C	b	66
e	(CH=CH) ₂	H	H	PhI(OCOCF ₃) ₂ , CH ₂ Cl ₂ , 20 °C	c	66
f	H	Cl	H	Pb(OAc) ₄	d	24

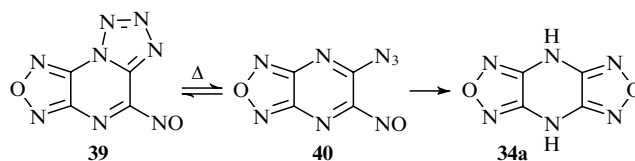
Furoxanopiperazines **38b-d** are easily prepared by oxidation of the dioximes **31b-d** with potassium ferricyanide in aqueous alkali.¹⁵ If the starting piperazine has no substituents at nitrogen atoms (as in the case of the dioxime **31a**), no furoxan is formed.



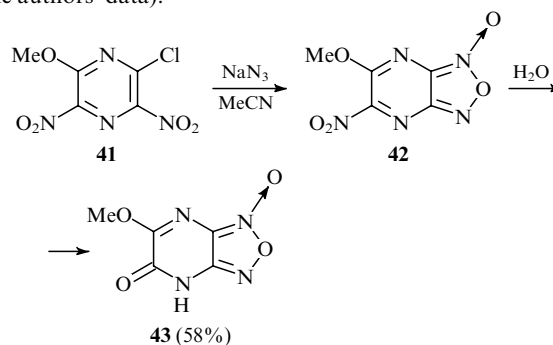
R = Me (**b**, 72%), Prⁱ (**c**, 90%), Bu^t (**d**, 98%).

Thermolysis of the nitroso tetrazolopiperazine derivative **39** in AcOH–MeOH triggers a cascade of reactions which include the tetrazole ring opening, formation of the tautomer **40**, liberation of the nitrogen molecule, cyclisation of the resulting nitrene with the

nitroso group and abstraction of hydrogen atoms from the solvent molecule. Difurazan **34a** is formed in 36% yield.⁴⁰



Until recently, thermolysis of *o*-azidonitro compounds as a method for the synthesis of fused furoxans^{4, 5, 41} has not been used for the preparation of furoxanopyrazines. However, it was found that gentle heating of chloropyrazine **41** with sodium azide in acetonitrile results in an immediate formation of furoxan **42**; no intermediate azide could be isolated. Furoxan **42** is unstable and is rapidly hydrolysed by the atmospheric moisture to pyrazinone **43** (the authors' data).



The data presented suggest that the furazanopyrazine system can be formed using different approaches. The applicability of particular approach depends on the accessibility of the starting compounds and is sometimes limited by the absence of knowledge of the processes involved.

2. Chemical reactions

The data on reactions of furazanopyrazines are scarce. It is known that furazanopiperazine **32a** reacts with copper nitrate or perchlorate to give coordination compounds with the complex-forming cation linked to the nitrogen atom of the furazan rather than of the piperazine ring.⁴²

Heating of furazanopyrazinone **17** in 4 M hydrochloric acid for 1 h leads to the destruction of the six-membered cycle; the reaction product, diaminofurazan **2**, is formed in 22% yield.⁸

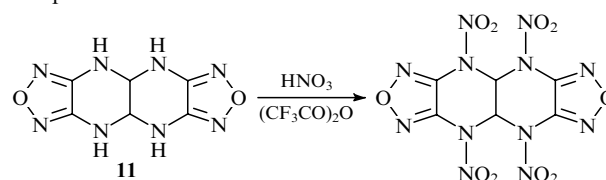
Hydrolysis of furoxanopiperazines **38b-d** is complete in 5 min upon heating in 50% ethanol. Here, the furoxan ring is opened to give the corresponding 1,4-dialkyl-2,3-dioxopiperazines.¹⁵

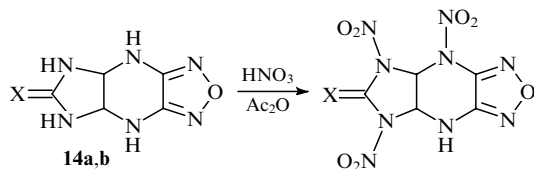
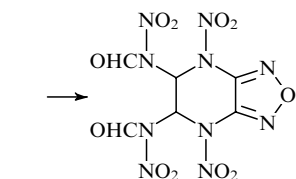
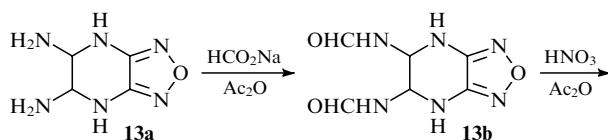
One furazan ring in difurazanopiperazine **34a** is hydrolysed to produce two carbonyl groups (Δ, HNO₃, AcOH).³⁵

Treatment of compounds **14b**,¹⁹ **32a**,⁴³ and **34a** with sodium nitrite in acidic media results in their *N*-nitrosation.³⁵

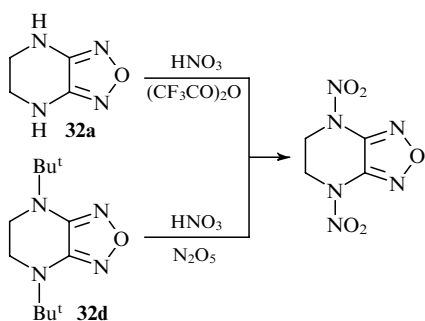
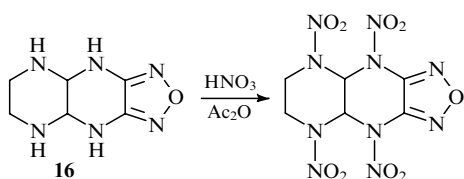
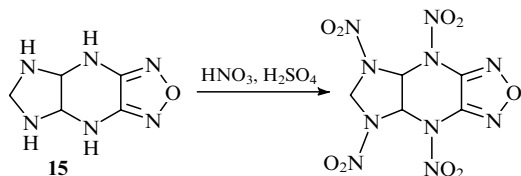
The overwhelming majority of published data are devoted to the synthesis and investigation of properties of nitro derivatives of furazanopyrazine. As mentioned above, some compounds of this series are promising components of explosives, propellants and gunpowders.

Treatment of compounds **11**,¹²⁻¹⁵ **13b**,¹⁶ **14a**,^{16, 19} **14b**,¹⁹ **15**,¹⁶ **16** and **32a,d**^{15, 29, 37} with a mixture of 100% HNO₃ and acetic or trifluoroacetic anhydride, HNO₃–H₂SO₄ or N₂O₅–HNO₃ at low temperatures results in their nitration.

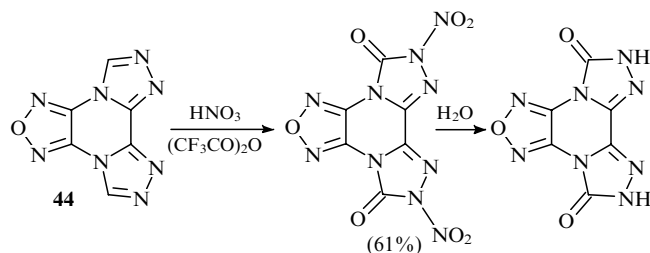




X = O (a), NNO₂ (b).

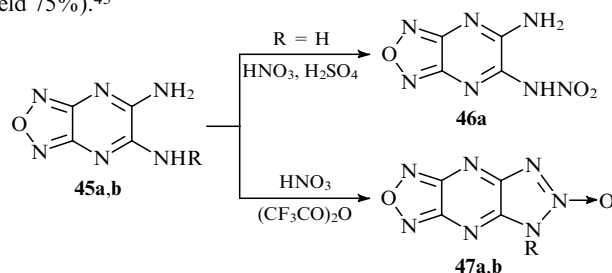


Treatment of the tetracycle **44** with an HNO₃–(CF₃CO)₂O mixture results in oxidation of the C–H fragment of the triazole rings and nitration at two nitrogen atoms to give *N*-nitrotriazolone.⁴⁴ Like the aforementioned nitro compounds, this nitro derivative is easily hydrolysed.



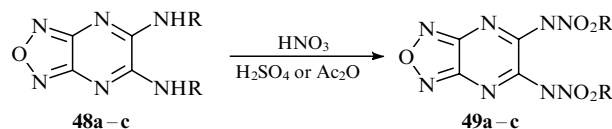
It should be noted that the diamine **13a** when treated with nitric acid forms a salt and is not nitrated.¹⁸ At the same time,

treatment of the corresponding aromatic diamine **45a** with a nitrating mixture results in its conversion into the mononitro compound **46a**. Reactions of the diamines **45a,b** with HNO₃–(CF₃CO)₂O or BF₄NO₂ lead to the triazole ring closure and the formation of tricyclic *N*-oxides **47a** (yield 92%) and **47b** (yield 75%).⁴⁵



R = H (a), Me (b).

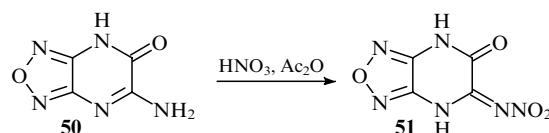
Treatment of bis(alkylamino)-substituted compounds **48a–c** with a mixture of HNO₃ and sulfuric acid or acetic anhydride gives *N,N'*-dinitro derivatives **49a–c**.^{44,45} The yields of the reaction products do not depend on the nature of the substituent R. In the case of the hydroxymethyl derivative **48b**, the nitration affects both the nitrogen and the oxygen atoms.



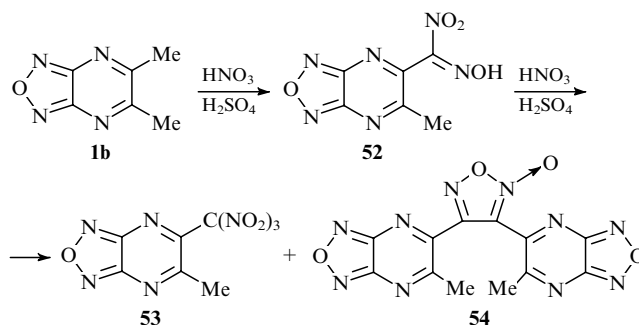
48: R = Me (a), CH₂OH (b), CH₂C(NO₂)₃ (c);

49: R = Me (a, 79%), CH₂ONO₂ (b, 82%), CH₂C(NO₂)₃ (c, 79%).

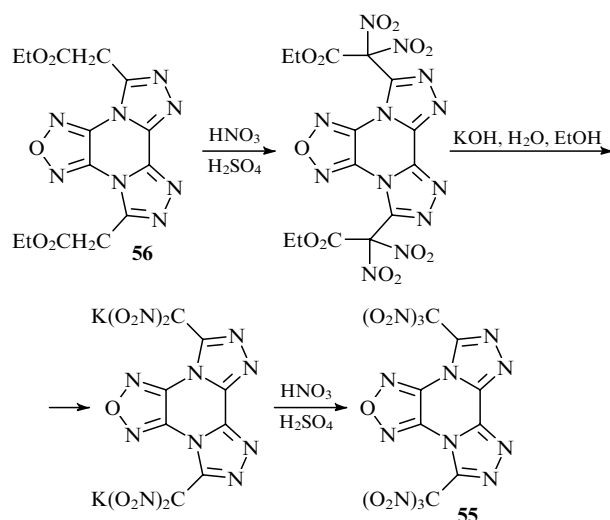
The nitration of compound **50**, containing an amino and a carbonyl group in the pyrazine ring, with an HNO₃–Ac₂O mixture gives *N*-nitroimine **51** (yield 37%). The starting compound **50** is mostly converted into dioxopiperazine **19**.⁴⁶



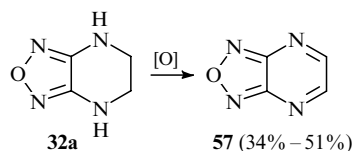
Upon treatment with an HNO₃–H₂SO₄ mixture, compound **1b** is nitrated and nitrosylated at the methyl group of the pyrazine ring to give nitrolic acid **52** which either undergoes further nitration with HNO₃–H₂SO₄ to give the trinitromethyl derivative **53** or eliminates the HNO₂ fragment to give furoxan **54**.⁷ The ratio of the products **52–54** depends on the concentrations of the acids and the temperature; however, the total yields of the three compounds do not exceed 40%.⁷



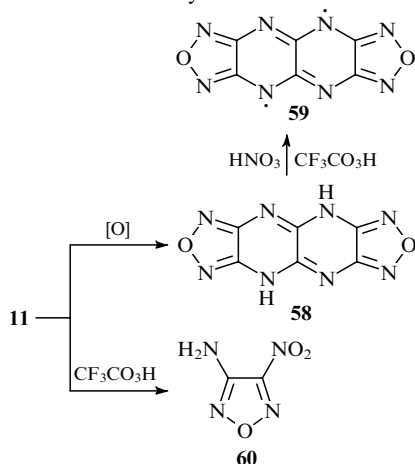
Compound **55** containing two trinitromethyl groups is prepared in three steps by stepwise introduction of nitro groups into the derivative **56**.⁴⁷



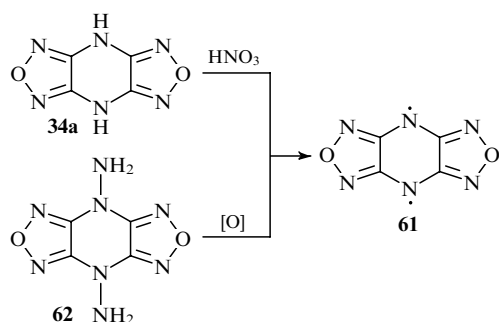
Dehydrogenation of furazanopiperazines results in their aromatisation. Thus oxidation of compound **32a** resulted in the first member of this series, viz., furazano[3,4-*b*]pyrazine **57**. PhIO, AgO, PbO₂ or MnO₂ are used as oxidants (the authors' data).



The oxidation of the tetracycle **11** by such oxidising agents as K₃Fe(CN)₆, KMnO₄ and SeO₂–H₂O₂ in water gives the dihydro derivative **58**; treatment of the latter with a nitrating mixture affords the biradical **59** in a total yield of ~ 50%. Treatment of the tetracycle **11** with trifluoroacetic acid leads to the destruction of the six-membered cycles and the formation of furazan **60**.⁴⁸

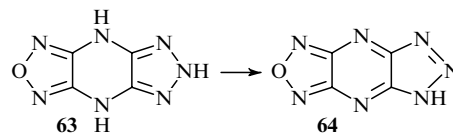


The stable biradical **61** is formed in quantitative yield by treatment of the tricycle **34a** with nitrating agents of any kind.^{35, 48}

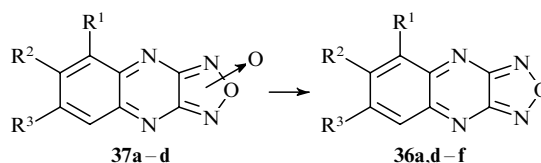


Special mention should be made of an unusual reaction of diamine **62** with oxidants which also yields the biradical **61**.⁴⁹

Treatment of compound **63** with MnO₂ or 60% nitric acid results in the aromatisation of the piperazine ring and formation of furazanopyrazinotriazole **64**, whereas various nitrating mixtures cause the destruction of the triazole ring to the dioxo derivative **19**.⁵⁰

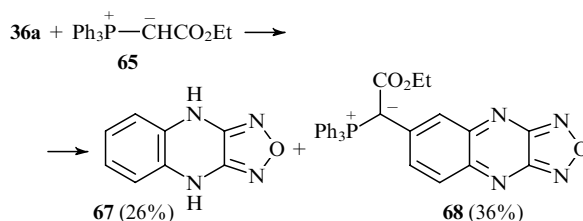
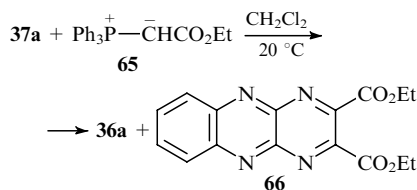


Furazanopiperazine derivatives undergo reduction. Thus furoxanoquinoxalines **37a–c** are converted into the corresponding furazans **36a,d–f** upon boiling with triethyl phosphite in ethanol.³⁹ Triphenylphosphine in CH₂Cl₂ causes rapid reduction of furoxan **37d** to furazan **36d**.³¹ A mixture of furazans **36a** and **36d** is formed from furoxan **37a** in boiling chloroform.³¹

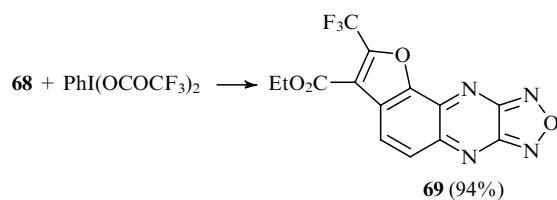


Compound 37	Reaction conditions	Product	R ¹	R ²	R ³	Yield (%)
a	P(OEt) ₃ , EtOH, 4 h	36a	H	H	H	35
	PCl ₃ , CHCl ₃ , Δ, 5 h	36a	H	H	H	22
		36d	H	Cl	H	16
b	P(OEt) ₃ , EtOH, 4 h	36e	Me	H	H	35
c	P(OEt) ₃ , EtOH, 4 h	36f	(CH=CH) ₂	H	H	50
d	PPh ₃ , CH ₂ Cl ₂ , 20 °C	36d	H	Cl	H	35

Reaction of furoxanoquinoxaline **37a** with ethoxycarbonyltriphenylphosphoniomethanide (**65**) yields a mixture of the furazan **36a** and the tricyclic derivative **66**.⁵¹ In turn, the furazan **36a** reacts slowly with the ylide **65** to yield dihydro derivative **67** and a novel ylide **68**.³¹ The formation of dihydro derivatives of the type **67** is the main reaction for furazanoquinoxalines **36d–f** containing substituents in the phenyl nucleus.³¹

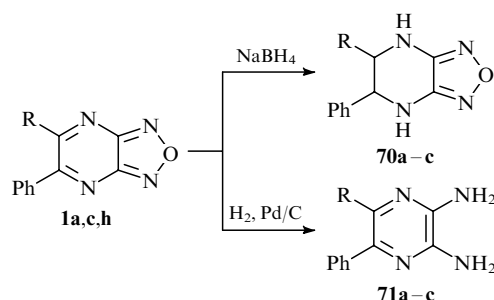


It is of note that treatment of compound **67** with bis(trifluoroacetoxy)-λ³-iodanylbenzene results in its aromatisation and the formation of the starting furazan **36a** (yield 75%), whereas the reaction of the ylide **68** with the same reagent affords tetracyclic derivative **69** containing a fused furan ring.³¹



Electrochemical reduction of the furoxan ring in compounds **37a,b** has been studied.⁵² The dioximes **35a,d** are readily formed; they can undergo more profound reduction.

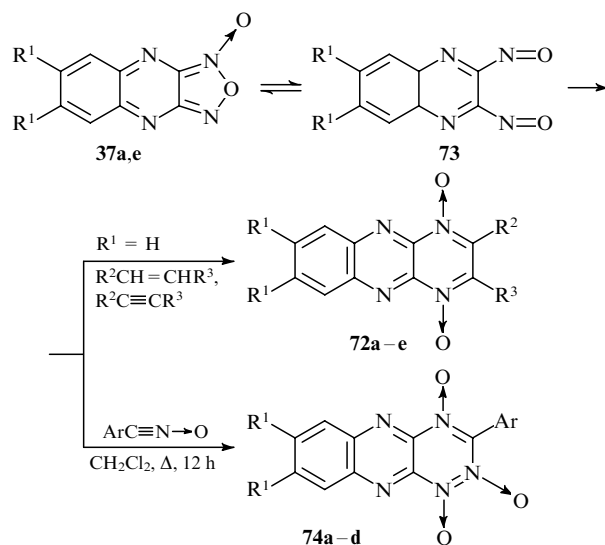
Treatment of compounds **1a,c,h** with sodium borohydride in boiling ethanol for 1 h leads to selective reduction of the pyrazine ring. The yields of piperazines **70a–c** are 84%–87%. Higher yields of compounds **70a–c** were obtained using LiAlH_4 as the reducing agent in boiling THF.⁶ Catalytic reduction of compounds **1a,c,h** (10% Pd/C, H_2 , 1 atm, ethyl acetate, 20 °C, 20 h) results in furazan ring opening and the formation of diaminopyrazines **71a–c** in 65%–97% yields.⁶



R = H (**1c**, **70a**, **71a**), Me (**1h**, **70b**, **71b**), Ph (**1a**, **70c**, **71c**).

Hydrogenolysis (PtO_2 , H_2 , ~50 atm, AcOH, 7 days) of N- CH_2Ph bonds in compound **34b** competes with hydrogenation of the phenyl (but not furazan) rings.³⁴

Furoxanoquinoxaline **37a** reacts with alkenes and alkynes upon long-term (up to 80 h) boiling in CHCl_3 to yield the same



37: $\text{R}^1 = \text{H}$ (**a**), Me (**e**);

72: $\text{R}^2 = \text{R}^3 = \text{Ph}$ (**a**, 22–31%); $\text{R}^2 = \text{Ph}$, $\text{R}^3 = \text{H}$ (**b**, 41%);

$\text{R}^2 = \text{R}^3 = 4\text{-MeOC}_6\text{H}_4$ (**c**, 47%);

$\text{R}^2 = \text{Ph}$, $\text{R}^3 = 4\text{-MeC}_6\text{H}_4$ (**d**, 19%);

$\text{R}^2 = \text{Ph}$, $\text{R}^3 = 4\text{-MeOC}_6\text{H}_4$ (**e**, 20%);

74: $\text{R}^1 = \text{H}$, Ar = 2,4,6- $\text{Me}_3\text{C}_6\text{H}_2$ (**a**, 46%);

$\text{R}^1 = \text{H}$, Ar = 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$ (**b**, 72%);

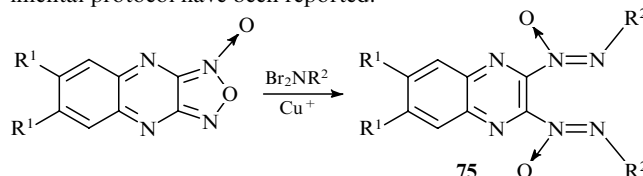
$\text{R}^1 = \text{Me}$, Ar = 2,4,6- $\text{Me}_3\text{C}_6\text{H}_2$ (**c**, 54%);

$\text{R}^1 = \text{Me}$, Ar = 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$ (**d**, 63%).

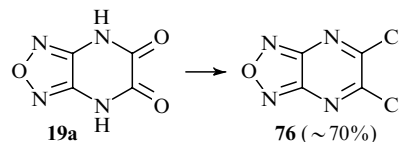
products, viz., di- N,N' -oxides **72a–e**.⁵³ This transformation proceeds in accordance with the so-called Beirut reaction⁴¹ where the *o*-dinitroso compound **73**, a valent tautomer of furoxan, plays the role of an intermediate.

Unusual tri- N,N',N'' -oxides **74a–d** were prepared by reaction of furoxans **37a,e** with arenecarbonitrile oxides. This reaction also involves the dinitroso intermediate **73**. A feasible mechanism of the formation of compounds **74a–d** has been proposed.⁵⁴

Presumably, the formation of bis(azoxy)quinoxalines **75** (yields ~50%) in the reaction of furoxans with N,N -dibromoamines catalysed by Cu(I) ions proceeds *via* the corresponding dinitroso intermediates.⁵⁵ Unfortunately, no details of the experimental protocol have been reported.

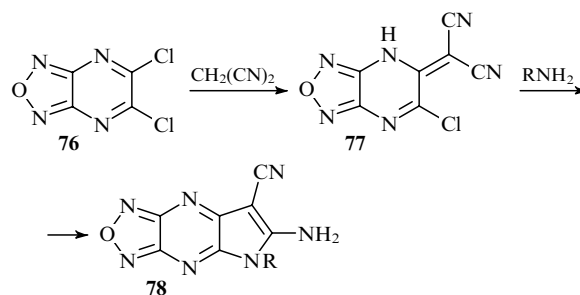


Of special interest is the use of the dichloro derivative **76** in the synthesis of various furazano[3,4-*b*]pyrazines. Compound **76** is prepared on heating of the diketone **19a** with thionyl chloride,^{47,56} POCl_3 in the presence of a catalytic amount of DMF or a $\text{POCl}_3\text{--PCl}_5$ mixture.⁵⁶



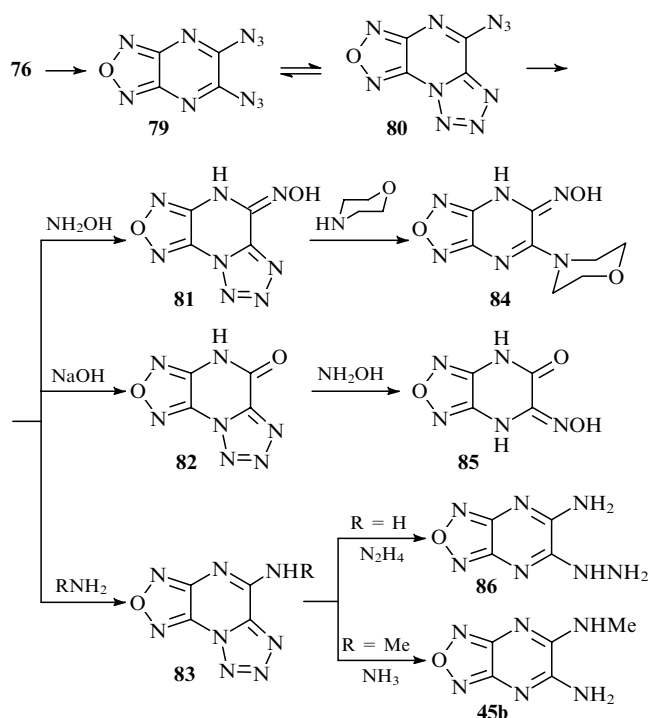
Since the furazano[3,4-*b*]pyrazine system is a typical π -acceptor, the halogen atoms in compound **76** manifest high activity towards nucleophiles. The reactivity of the dichloride **76** exceeds markedly those of its analogues containing 1,2,5-thiadiazole and triazole rings instead of the furazan ring as well as 2,3-dichloroquinoxaline and tetrachloropyrazine.⁵⁶

Thus reactions of dichloride **76** with ammonia, alkyl- and arylamines,⁵⁶ hydroxylamines,^{35,36,56} hydrazines,^{47,56} azide ion,⁵⁷ alcohols,^{56,58} phenols,⁵⁶ hydroxyfurazans⁵⁸ and thiols^{56,59} proceed smoothly with substitution of both chlorine atoms. The corresponding products are formed in high yields. Selective substitution of only one chlorine atom can sometimes be achieved by varying reaction conditions^{40,56} and using weak or sterically hindered nucleophiles.^{56,60–62} The second chlorine atom in the monosubstitution products can be replaced by another nucleophile.^{40,56,60,61} Thus the one-pot reaction of the dichloride **76** with the malonodinitrile anion yields dicyanomethylidene derivative **77** which cyclises into tricyclic aminonitriles **78** upon treatment with amines.^{60,61} The yields of compounds **78** are 90%–95%.



R = Alk, Ar, Het *etc.*

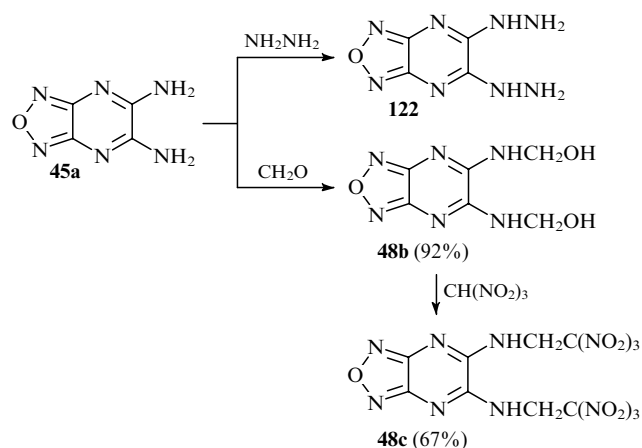
An original procedure for the synthesis of non-symmetrical furazanopyrazine derivatives involves the substitution of the azido groups for the chlorine atoms in compound **76** and subsequent reaction of the azido derivative **79** with nucleophiles.^{57,63}



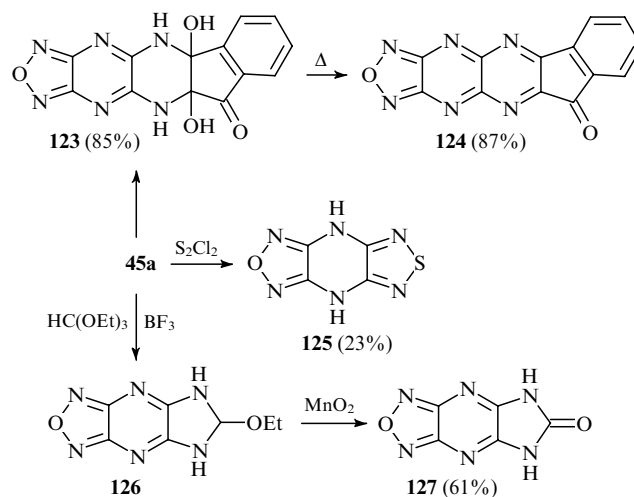
Owing to azido–tetrazole tautomerism, one of the azido groups in compound **79** exists in a cyclic form. This stabilises the remaining azido group of the tautomer **80** and makes it less mobile than the chlorine atoms in the dichloride **76**. Replacement of one azido group is complete in ~ 1.5 h at 20 °C. Incubation of the reaction mixture for ~ 24 h results in replacement of the second azido group. The yields of monosubstitution products, such as compounds **81–83**, are 76%–85%.^{57,63} Subsequent long-term (~ 24 h) treatment with another nucleophile yields non-symmetrical compounds **45b**, **84–86**, which can be difficult to synthesise by other methods.

High reactivities of both the chlorine atoms in compound **76** were employed in the synthesis of polycyclic heterocycles incorporating a furazanopyrazine fragment. Thus reactions of the dichloride **76** with 1,3- and 1,4-dinucleophiles, such as diamines, amino and mercapto alcohols, aminothiols, thiourea, 2-aminoazoles, 2-aminoazines and *N*-benzoylglycine in acetonitrile at 20 °C yield polycyclic compounds **87–121** (Table 2). In the majority of cases, these reactions occur in the absence of a base (method A). However, the use of weakly nucleophilic reagents requires addition of triethylamine or other analogous bases (method B). The yields of reaction products depend on the nucleophilicities and steric characteristics of the starting reagents.

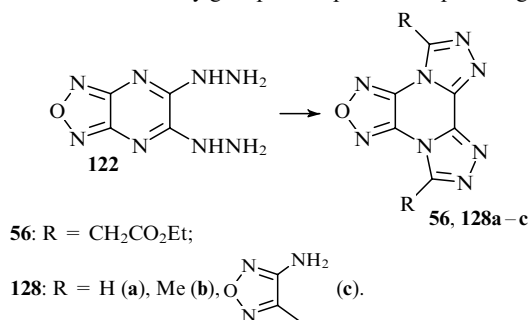
The amino groups of the diamine **45a**, which is readily prepared from the dichloride **76**,⁵⁶ are deactivated owing to the electron-withdrawing effect of the fused ring system. Attempts at alkylation of the amine **45a** with alkyl and aryl halides, halogeno ketones, diethyl carbonate and dichloroglyoxime were unsuccessful. This amine does not form stable salts even with strong acids.⁴⁴ Its treatment with oxidising mixtures based on H₂O₂ causes its degradation. At the same time, the electron-withdrawing nature of the ring allows replacement of the amino groups upon treatment with hydrazine to give bishydrazine **122**. Treatment of the diamine **45a** with formaldehyde yields the bis(hydroxymethyl) derivative **48b** which is stable owing to the electron-withdrawing character of the bicyclic fragment. Treatment of compound **48b** with trinitromethane gives the Mannich base **48c**.⁴⁴ Analogous Mannich bases were prepared from cyclic compounds containing NH groups.⁴⁶



A series of fused furazanopyrazine derivatives were synthesised from the diamine **45a**. Its reaction with ninhydrin in AcOH results in the dihydroxy derivative **123**.¹¹ Heating of compound **123** in ethanol, DMF or H₂SO₄ for more than 3 h is accompanied by dehydration and formation of a pentacyclic product **124**. Thiadiazole **125** was prepared by treating the amine **45a** with sulfur monochloride.⁴⁴ Condensation of the amine **45a** with triethyl orthoformate in the presence of a Lewis acid gives tricyclic compound **126** which is converted into imidazolone **127** on oxidation with MnO₂.⁴⁴



Treatment of the bishydrazine **122** with HNO₂ gives the tetrazole **80**,⁵⁷ while its heating with acids, acid anhydrides⁴⁴ or imidates⁴⁷ results in simultaneous formation of two triazole rings. The tetracyclic derivatives **56** and **128a–c** are formed in 60%–90% yields. The methyl groups in compound **128b** were oxidised to carboxy groups with potassium permanganate.⁴⁴

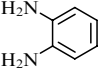
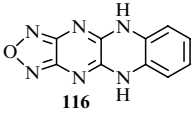
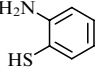
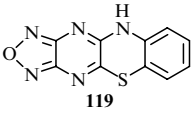
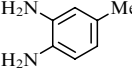
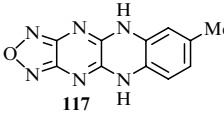
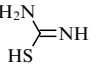
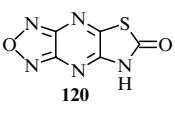
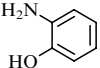
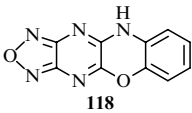
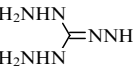
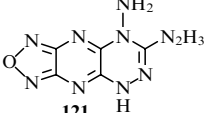


An unusual polycyclic system **129** was obtained upon oxidation of amine **130** with subsequent thermolysis of azo derivative **131**.⁶³ However, the total yield of compound **129** did not exceed 20%.

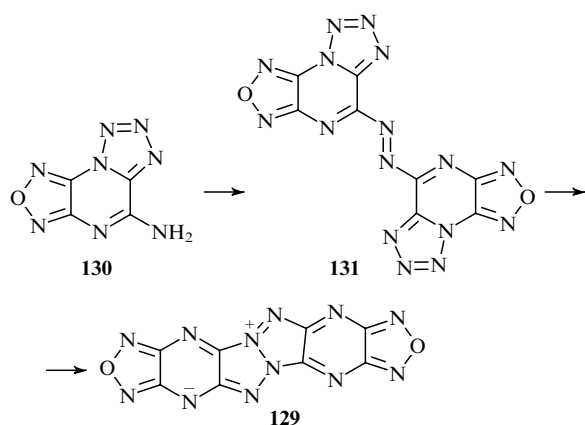
Table 2. The reaction of 5,6-dichlorofurazano[3,4-*b*]pyrazine with dinucleophiles.

Dinucleophile	Reaction conditions	Structure	Yield (%)	Ref.	Dinucleophile	Reaction conditions	Structure	Yield (%)	Ref.
	A		58	64		A B		58 89	see ^a
	B		62	64		A		66	64
	A		73	64		A		36	64
	B		64	60		B		28	63
	B		46	64		B		24	63
	A		72	64		A		62	64
	B		83	64		A		58	64
	A		32	64		A		55	64
	B		48	64		A		81	64
	A		92	64		B		41 77	see ^a
	A		18	64		A B		12 35	see ^a
	A		80	64		A B		23	see ^a
	A		75	64		B		18 67	see ^a
	A		47	64		A B		18	see ^a
	A		42	64		B		18	see ^a

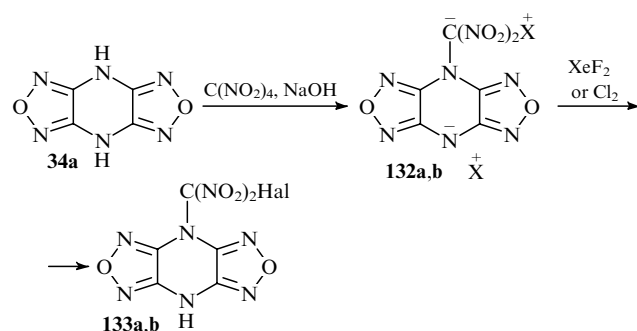
Table 2 (continued).

Dinucleophile	Reaction conditions	Structure	Yield (%)	Ref.	Dinucleophile	Reaction conditions	Structure	Yield (%)	Ref.
	B		93	64		A		81	64
	A		87	64		B		28	64
	A		72	64		A		43	63

Note. A, in the absence of a base; B, in the presence of a base. ^a The authors' data.



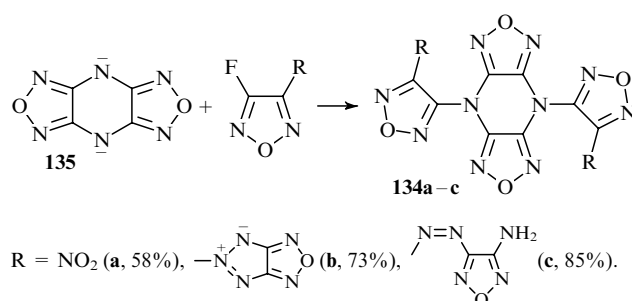
Polycyclic compounds containing NH groups represent acids of moderate strength. For example, pK_a^1 for the difurazanopiperazine **34a** is 6.96, whereas pK_a^2 is 10.17.^{35, 48} It is acylated^{35, 48} or alkylated (arylated)^{35, 48, 50} under ordinary conditions. Compound **34a** reacts specifically with tetranitromethane in an alkaline medium to give disodium salt of dinitromethyl derivative **132** in 75% yield.³⁵ Trinitromethyl reagents react in a similar way.



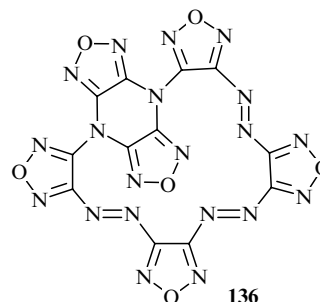
$X^+ = Na$ (**132a**), K (**132b**); Hal = F (**133a**, 78%), Cl (**133b**, 90%).

Reaction of the disodium salt **132a** with XeF_2 or Cl_2 gives the corresponding halogen derivatives **133a,b**.³⁵ Compound **133a** is also formed upon treatment of the dipotassium salt **132b** with XeF_2 .⁴⁷

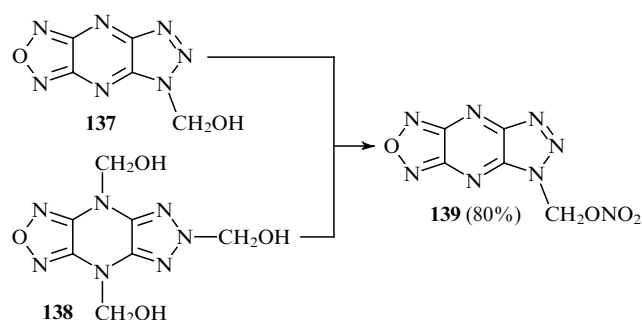
Compounds **134a–c** containing two furazanylamine fragments were prepared by a reaction of a dianion **135** with the corresponding fluorofurazans.^{65, 66} By varying the reaction conditions, one can direct the reaction to the predominant formation of the monoaddition product.



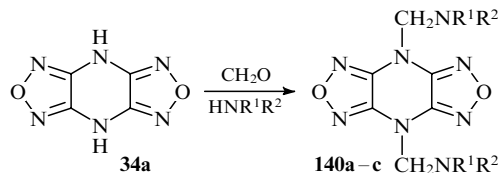
Oxidation of the diamine **134c** with dibromoisocyanurate results in intramolecular crosslinking of the amino groups into an azo group to yield macrocycle **136**.^{65, 66}



Reactions of polycyclic compounds containing NH groups with formalin give *N*-hydroxymethyl derivatives; treatment of the latter with HNO_3-Ac_2O or $HNO_3-(CF_3CO)_2O$ results in their conversion into the corresponding nitroxymethyl derivatives.^{44, 48, 50} It should be noted, however, that both mono- (**137**) and tris(hydroxymethyl) derivatives (**138**) yield the same nitrate **139**.⁵⁰

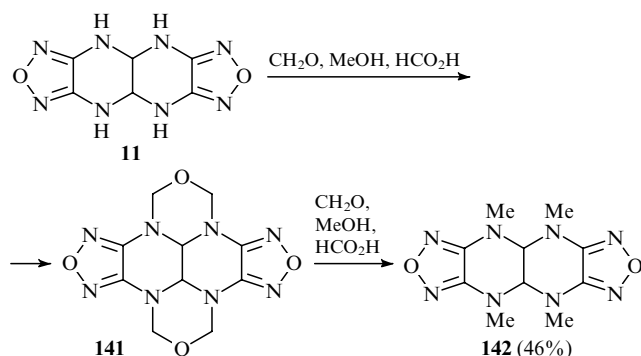


N-Hydroxymethyl derivatives are acylated with acetic anhydride; their treatment with SOCl_2 yields chloromethyl derivatives. The chlorine atom in the latter can be substituted for the azido group under the action of sodium azide.⁴⁸ Mannich bases **140a–c** were obtained in nearly quantitative yields using a three-component reaction of the difurazanopiperazine **34a** with CH_2O and amines.⁴⁸

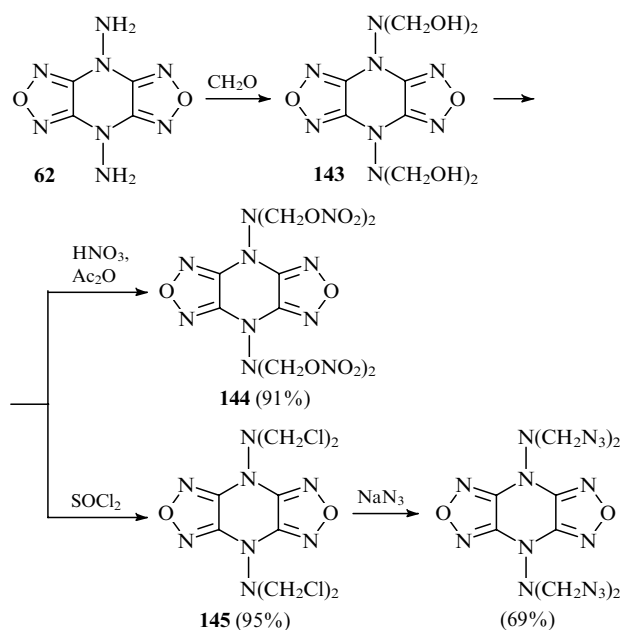


$\text{R}^1\text{R}^2\text{N} = \text{NH}(\text{CH}_2)_2\text{SH}$ (**a**), $\text{NHC}_6\text{H}_4\text{Cl-4}$ (**b**), N (c).

Short-term heating of the tetracyclic compound **11** with formaldehyde in a methanol–formic acid mixture results in the polycycle **141** in quantitative yield. Boiling of the reaction mixture for 36 h results in partial reduction of compound **141** to the tetramethyl derivative **142**.⁶⁷

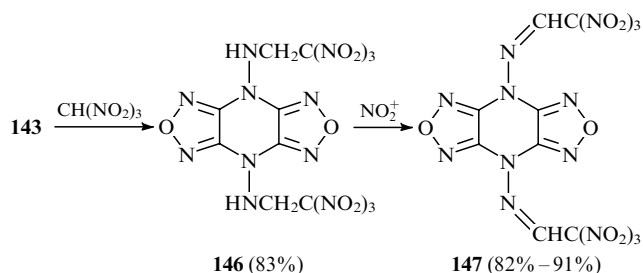


Polycyclic compounds containing NH groups are aminated upon treatment with hydroxylaminosulfonic acid to give *N*-amino derivatives.^{48, 49, 63} *N,N'*-Diaminopiperazine **62** reacts with aldehydes to yield bishydrazones; its acylation gives a *N,N,N',N'*-tetraacetyl derivative.⁴⁸ The conversions of bis(bishydroxymethylamino)piperazine **143** prepared in the reaction of the diamine **62** with formaldehyde have been studied.⁴⁸

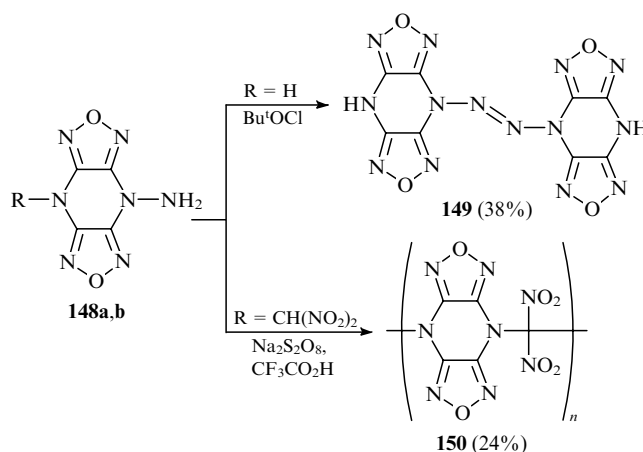


Thus nitration of compound **143** with an HNO_3 – Ac_2O mixture gave nitrate **144**. Reaction with thionyl chloride yields

tetrachloride **145**, the chlorine atoms in which are reactive enough to be substituted by the azide ion.⁴⁸ Reaction of the hydroxymethyl derivative **143** with nitroform results in splitting of two hydroxymethyl groups to give bis(trinitroethylamino)piperazine **146**, which affords trinitroacetaldehyde **147** instead of nitramine upon nitration with various nitrating reagents.^{48, 63}



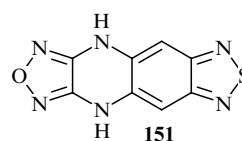
In contrast to oxidation of the diamine **62**, which generates the biradical **61**, treatment of monoaminopiperazine **148a** with *tert*-butyl hypochlorite affords an unstable tetrazene **149**.⁴⁹ A similar monoamine **148b** undergoes oxidation by sodium persulfate in trifluoroacetic acid to the oligomer **150**.⁴⁹



$\text{R} = \text{H}$ (**a**), $\text{CH}(\text{NO}_2)_2$ (**b**).

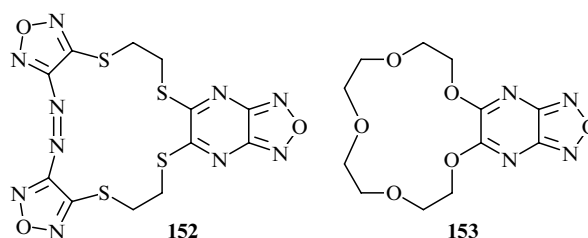
3. Properties and applications

The biological activities of furazano[3,4-*b*]piperazines have been little studied. Compound **1c** has been patented as a herbicide.⁹ The oxo derivatives **18a–d** have been recommended as tranquilizers.²³ Furazanopiperazine **151** and its derivatives were found to possess biocidal activities.⁶⁸



The macrocyclic compound **136** was used as an inhibitor of the soluble form of guanylate cyclase.⁶⁵

The sulfur-containing macrocycle **152** was regarded as a candidate complexone,⁵⁹ but compound **153** proved to be more efficient. The latter forms adducts with alkali metal nitrates and perchlorates as well as with dinitramine salts (the authors' data).

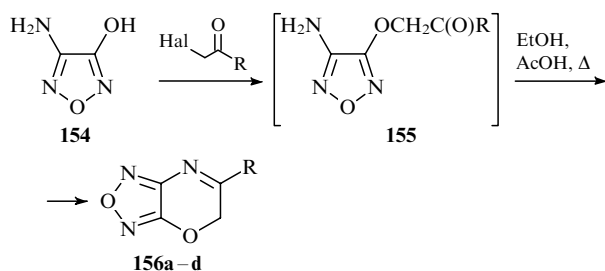


Furazanopiperazine **32a** possesses interesting photoelectric properties which are manifested as specific effects during electron movements in thin layers.^{69–71}

However, nitro and other polynitrogenous furazanopyrazane derivatives attract the most attention. Various thermochemical and explosive properties of their derivatives have been studied. Although most of these data are known to specialists only, some evidence can be found in popular literature. Characteristics of some compounds, *viz.*, detonation rate;^{12, 13, 16, 29, 37} shock, friction and flame sensitivity;^{12, 14, 16, 29} enthalpy;^{14, 29, 27, 72} thermal stability and thermal degradation^{16, 63, 72–78} and combustion,^{46, 63} have been established and documented. Such parameters as density,^{12, 13, 29, 33, 37, 46, 79} enthalpy,^{37, 46, 79, 80} detonation rate,^{12, 13, 29, 33, 79} detonation pressure,^{12–14, 29, 33} temperature and other combustion characteristics have been studied using computer methods.^{46, 63} The possibility of using nitro derivatives as components of explosive and pyrotechnical compositions and propellants has been considered.^{12–14, 16, 29, 37, 46, 63, 80, 81}

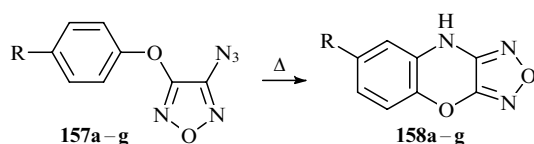
III. Furazano[3,4-*b*][1,4]oxazine derivatives

Both methods presently employed in the synthesis of furazanoxazine derivatives are based on the use of compounds of the furazan series. Thus 3-amino-4-hydroxyfuran **154** reacts with α -halogeno ketones in the presence of NEt_3 to give the intermediates **155** which undergo *in situ* cyclisation upon heating in an ethanol–AcOH mixture to give bicyclic derivatives **156a–d**.²

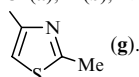


R = Me (**a**), CH_2Cl (**b**), Ph (**c**),  (**d**).

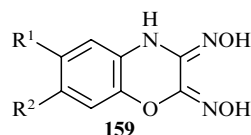
Thermolysis of 4-aryloxy-3-azido-furazans **157a–g** in decalin was used to obtain tricyclic compounds **158a–g** (the authors' data). It is of note that cyclisation occurs smoothly only with the *para*-substituted derivatives **157a–g**; reaction products are formed in 43%–72% yields. Attempts to use compounds with an *ortho*- or *meta*-substituent in the phenyl ring resulted in a complex mixture of products. The possibilities of this method are also limited by accessibility of the starting azides **157a–g**.



R = Cl (**a**), F (**b**), NMe_2 (**c**), Me (**d**), OMe (**e**), Ph (**f**),



The structural similarity of phenoxazine derivatives endowed with physiological activities and compounds of the type **158** makes them attractive targets for synthesis. However, attempts to fuse the furazan ring to the benzoxazine ring by treatment of dioximes **159** with ethyl chloroformate (which has been employed in the synthesis of the furazanoquinoxalines **36a–c**) were unsuccessful.³⁸

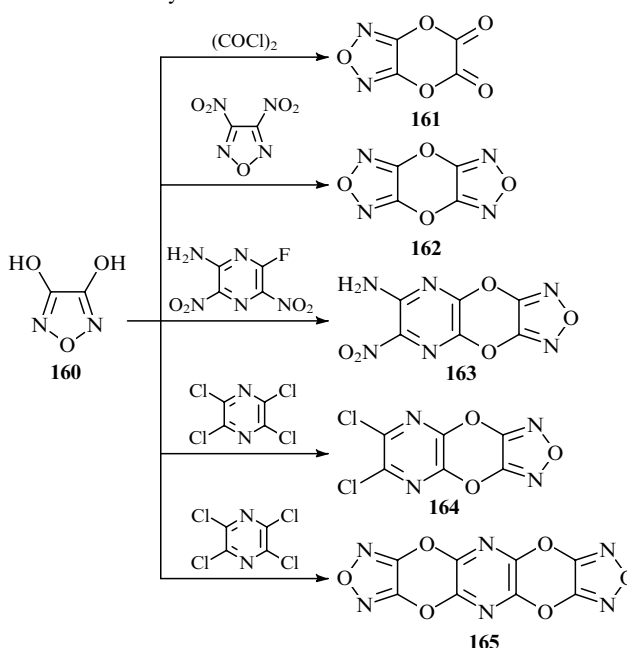


$\text{R}^1, \text{R}^2 = \text{H}, \text{Me}, \text{Cl}$.

There is still no information on the reactivities of furazanoxazine derivatives in the literature.

IV. 1,4-Dioxino[2,3-*c*]furazan derivatives

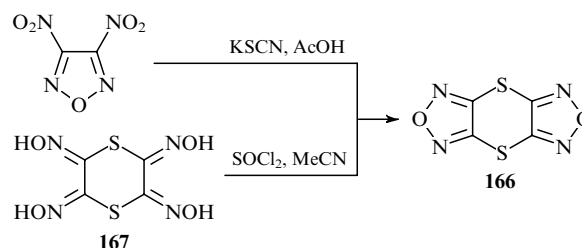
Only one method for the construction of 1,4-dioxino[2,3-*c*]furazan derivatives is known. The key building block is 3,4-dihydroxyfuran **160**.^{58, 82} Its treatment with oxalyl chloride in the presence of triethylamine in CH_2Cl_2 gives dioxo derivative **161**.⁶³ Reaction of compound **160** with 3,4-dinitrofurazan affords a mixture of products from which the tricyclic derivative **162** was isolated in 12% yield.⁸³



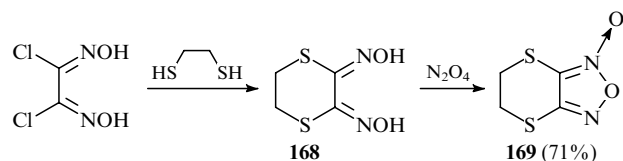
Compounds **163–165** were synthesised by the reaction of salts prepared from compound **160** with the corresponding halogeno pyrazines under conditions of phase-transfer catalysis.^{58, 84–86} The pyrazine ring in compound **163** was oxidised to di-*N,N'*-oxide upon treatment with peroxy acids.⁸⁴

V. 1,4-Dithiino[2,3-*c*]furazan derivatives

1,4-Dithiino[2,3-*c*]furazan derivatives were prepared starting from compounds of both the furazan and dithiine series. Both approaches were used for the synthesis of dithiinodifurazan **166**. This is the reaction product of 3,4-dinitrofurazan with potassium thiocyanate (yield 27%).⁸⁷ Dehydration of tetroxime **167** with thionyl chloride also yields compound **166**.⁸⁸



Oxidation of dioxime **168** (prepared from dichloroglyoxime and 1,2-ethanedithiol) with nitrogen oxides affords furoxan derivative **169**, which is recommended as a cardiostimulator along with acyclic thio-substituted furoxans.⁸⁹



No other data on the possible applications and reactivities of heterocyclic derivatives are available.

* * *

The data presented suggest that the most impressive success has been achieved in the chemistry of furazanopyrazine derivatives, whereas furazans fused to other six-membered heterocycles with two heteroatoms in positions 1 and 4 have been little explored. Further efforts in this branch of chemistry will be aimed at the search for useful properties of furazan fused to pyrazines, oxazines, dioxines and dithiines which, in turn, will stimulate the development of convenient methods for their synthesis. We hope that this review will be helpful for both chemists and specialists in other fields.

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Technetium: behaviour during reprocessing of spent nuclear fuel and in environmental objects

N N Popova, I G Tananaev, S I Rovnyi, B F Myasoedov

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Abstract. The review surveys main chemical properties of technetium, methods of its isolation and determination and its behaviour during reprocessing of spent nuclear fuel and in environmental objects. Methods for extraction and isolation of technetium as a hazardous long-lived radionuclide are described. Prospects of using technetium in industrial processes and in medicine are considered. The bibliography includes 276 references.

I. Introduction

Technetium is a Group VII element, which was first prepared by nuclear synthesis in the mid-twentieth century. The characteristic feature of technetium is that all its isotopes with mass numbers from 90 to 110 are radioactive. Technetium is an artificial element and does not occur in nature. However, more than 60 tonnes of Tc have accumulated in the world because spent nuclear fuel (SNF) has a high Tc content (0.6 g per kilogram of ^{235}U in the case of 50% burn-up).¹ Large amounts of fission products (FP), including Tc, were released into the environment from nuclear weapon production and nuclear power engineering. Since the ^{99}Tc isotope has a long half-life, it is a very hazardous radioactive element. Besides, technetium shows a high migration ability and some of its compounds are volatile.

The main chemical and physicochemical properties of technetium are well known and were described in monographs and reviews^{2–9} as well as in the handbook published in 1999.¹⁰ However, many new studies published in recent years require generalisation. Besides, progress in nuclear power engineering has generated a need for additional studies of the behaviour of Tc

during reprocessing of spent nuclear fuel and in environmental objects. The lack of the necessary information on important radiochemical properties and behaviour of technetium in natural objects has already led to contamination of the environment by a large amount of Tc.

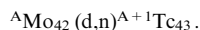
The present review surveys the main properties of technetium responsible for its behaviour during reprocessing of SNF and in environmental objects. These data may be of use for improvements in present-day technologies for reprocessing of SNF from the viewpoint of optimisation and complete extraction of Tc as well as for the prediction of its behaviour in natural objects.

II. Discovery, methods of preparation and main properties of technetium

D I Mendeleev was the first to suppose that a chemical element with the atomic mass of 99 should be present between manganese and rhenium in the Periodic Table (and gave it the name ekamanganese).^{11,12} However, the discovery of this element in manganese-containing ores and minerals appeared to be a difficult problem. All attempts to isolate the new element with the atomic number 43 failed. The Russian chemist Shchukarev¹³ and German physicist Mattauch¹⁴ formulated the ‘prohibition rule’ stating that the isobars of two adjacent elements in the Periodic Table cannot be stable, *i.e.*, one of these elements is necessarily radioactive. This led to the conclusion that the element with the atomic number 43 could not have stable isotopes and, consequently, could not occur in nature.

1. Preparation and nuclear properties of technetium isotopes

In 1937, Perrier and Segre^{15,16} carried out the first experiments on isolation of the element with the atomic number 43 from a molybdenum target bombarded with deuterons on a cyclotron according to the reaction



The new element was named technetium (for the Greek word ‘τεχνηος’, which means artificial).

Later on, another procedure was developed for the preparation of Tc by irradiation of molybdenum-containing samples in slow neutron flux¹⁷



N N Popova, I G Tananaev, B F Myasoedov V I Vernadsky Institute of Geochemistry and Analytical Chemistry, Russian Academy of Sciences, ul. Kosygina 19, 119991 Moscow, Russian Federation. Fax (7-095) 938 20 54. Tel. (7-095) 939 70 07. E-mail: popova@geokhi.ru (N N Popova). Tel. (7-095) 939 70 98. E-mail: tananaev@geokhi.ru (I G Tananaev). Tel. (7-095) 237 80 81. E-mail: bf@geokhi.ru (B F Myasoedov)
S I Rovnyi State Scientific Centre of the Russian Federation ‘Mayak Plant’, ul. Lenina 31, 456780 Ozersk, Chelyabinsk Region, Russian Federation. Fax (7-351) 712 69 45. Tel. (7-351) 712 89 45. E-mail: rel@envc.chel-65-chel.su

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Kilogramme amounts of either spectrally pure MoO₃ or molybdenum metal are used as a target. The target is irradiated in a reactor for one year and kept until the parent ⁹⁹Mo isotope completely decays. Irradiation of 1 kg of molybdenum with a flux of 8×10^{13} neutrons cm⁻² s⁻¹ makes it possible to accumulate up to 60 mg of Tc. Isolation of technetium must be carried out in 'hot' chambers operating under remote control at a hot laboratory, whereas the yields remain low.

In this connection, isolation of technetium in the course of SNF reprocessing is presently a more convenient procedure, because technetium is a fission product accumulated upon irradiation of nuclear fuel in a reactor. The accumulation of Tc depends on the nature of the fissionable nuclide and the depth of burn-up and reaches ~1 kg per tonne of fuel in fast-neutron reactors.¹⁸ The yield of ⁹⁹Tc during fission of ²³⁵U or ²³⁹Pu is about 6.1%.¹⁹ Other Tc isotopes with the mass numbers from 99 to 110 inclusive were also found among fission products of uranium. These isotopes are produced through β⁻-decay or neutron capture.⁸ However, nuclear reactors produce these isotopes in insignificant yields.

Of technetium isotopes, the long-lived ⁹⁹Tc isotope ($\tau_{1/2} = 2.14 \times 10^5$ years) is of particular importance. This isotope serves as a β-ray emitter with the energy $E_{\beta\text{max}} = 292$ keV, and its decay is not accompanied by γ-radiation.²⁰ The ^{99m}Tc isotope ($\tau_{1/2} = 6.6$ h) is widely used in medicine. This radionuclide is most commonly isolated with the use of chromatographic,²¹ extraction²² or sublimation^{23,24} generators based on ⁹⁹Mo. Generators based on sublimation separation of Tc outperform generators of other types in many respects. Their construction assumes heating of MoO₃ to 850 °C in a flow of O₂. The yield of ^{99m}Tc obtained by sublimation of volatile technetium oxide and its condensation in a cooled receiver followed by dissolution of the condensate reaches 1 Ci ml⁻¹. The type of ^{99m}Tc decay is the isomeric transition of the nucleus from a metastable state to a lower-energy level. In studies of ^{99m}Tc, it was demonstrated that the chemical state of the element has only a slight effect on the rate of decay of an unstable nucleus. Thus, the half-life of technetium metal is 1.003 times longer than that of K₂TcO₄.²⁵

For technetium, 21 isotopes with the mass numbers from ⁹⁰Tc to ¹¹⁰Tc are known, seven of these isotopes being isomers. Most Tc isotopes have short half-lives (from 0.81 s for ¹¹⁰Tc to 61.2 days for ^{97m}Tc). The exceptions are the above-mentioned ⁹⁹Tc isotope and two long-lived isotopes, viz., ⁹⁷Tc ($\tau_{1/2} = 2.6 \times 10^6$ years) and ⁹⁸Tc ($\tau_{1/2} = 4.2 \times 10^6$ years), which are prepared by irradiation of molybdenum with deuterons or protons.

2. Technetium metal

The main properties of technetium metal were studied predominantly in the 1960s. It was demonstrated that it has a hexagonal close-packed structure with the parameters $a = 2.7409$, $c = 4.3983$ Å.^{19,26} In polycrystalline films prepared by ion deposition at liquid nitrogen temperature, technetium has a face-centred cubic structure with the lattice parameter $a = 3.68 \pm 0.05$ Å.²⁷

The hexagonal crystal lattice of technetium has a small number of easy-slip planes due to which the as-cast metal is brittle and cracks even at small degrees of reduction upon rolling at 20 °C. Nevertheless, technetium was prepared as rods, strips, foil and wire by the corresponding technological processing.²⁸

Technetium is a refractory metal with the melting point of >2000 °C.²⁹ It forms continuous series of solid solutions with metals, which crystallise in the hexagonal system, viz., with ruthenium, osmium and rhenium (analogue of Tc).³⁰ Technetium is a superconductor ($T_c = 8.24$ K). The magnetic susceptibility of Tc remains constant in the temperature range of 80–1300 K and is close to that of rhenium.³¹

Technetium metal is generally prepared by thermal decomposition of pertechnetates with organic cations under a stream of inert gas^{32,33} or thermolysis of other Tc compounds (for example, of NH₄TcO₄) in a reducing medium.^{34–37}

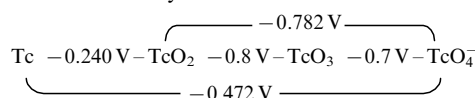
The metal thus prepared is insoluble in HCl or H₂SO₄. However, it is readily oxidised with nitric acid.



3. Behaviour of technetium in solutions

The electronic structure of the Tc atom ([Rn]3d¹⁰4s²4p⁶4d⁶5s¹) is responsible for its transition-metal properties. Due to such an electron shell structure, technetium can exist in a wide range of oxidation states from +7 to -1 and has a tendency to disproportionation. Besides, equilibrium systems containing Tc in different oxidation states can occur in solutions. This is manifested in the behaviour of technetium in chemical reactions and different technological processes.

The scheme of the Latimer potentials in an acidic medium was reported in the study:³⁸



The formal oxidation potentials of technetium [relative to the normal hydrogen electrode (NHE)] in acidic and alkaline media are given below.³⁹

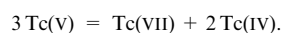
Medium	+7/+6	+6/+5	+6/+4	+5/+4	+4/0	-1/0
HClO ₄ (1 mol litre ⁻¹)	0.56	—	1.39	0.71	0.28	-0.5
NaOH (1 mol litre ⁻¹)	-0.64	-0.1	—	-0.88	-1.35	—

The standard oxidation potential E for the Tc(VII)/Tc(IV) pair is 0.738 V (vs. NHE).⁴⁰

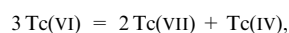
In HNO₃ solutions, the stability of Tc ions increases in the following series: Tc(VII) > Tc(IV) > Tc(V) > Tc(VI).⁴¹

In acidic media, Tc(IV) is stable only in the presence of complex-forming compounds. For example, Tc(IV) forms the well-studied TcCl₆²⁻ complex in HCl solutions (6 mol litre⁻¹).⁴²

Technetium(V) is unstable and undergoes disproportionation in acidic media according to the following scheme:



In the HCl + NaCl system (ionic strength $\mu = 1.0$), the reaction rate is proportional to the square of the Tc(V) concentration.¹⁸ Although prone to disproportionation, pentavalent technetium is more stable than hexavalent technetium and its compounds can be isolated from aqueous solutions.^{43–44} Technetium(VI) also undergoes disproportionation according to the reaction



the reaction proceeding with a very high rate (at 25 °C, the rate constant is $\sim 3 \times 10^6$ litre mol⁻¹ s⁻¹).¹⁸ The stability of technetate ions in aprotic solvents provides evidence that its disproportionation proceeds with the involvement of protons.⁴⁵

The pertechnetate ion is stable in solutions. This ion acts as a rather strong oxidising agent and can be reduced with a number of reducing agents, such as ascorbic acid,^{46–49} hydroxylamine,^{50,51} urea⁵² and the chloride, bromide and iodide ions.^{53–55} In an alkaline medium, the TcO₄⁻ ion is catalytically reduced in the presence of PdCl₂ (0.001 mol litre⁻¹) to Tc(IV) at 65 °C during 4 days.⁵⁶

Reduction of pertechnetate ions with different reagents in the presence of complex-forming agents is used in many procedures for the qualitative and quantitative determination of Tc.⁵⁷

Only Tc(VII) and Tc(IV) compounds are of practical importance, because these ions are thermodynamically stable and can exist in solution. It is in these oxidation states that technetium can be present both in wastes of radiochemical production facilities and in environmental objects. Unstable and reactive intermediate

forms, viz., Tc(V) and Tc(VI), cannot exist under normal conditions but can be involved in redox reactions.

4. Chemical and physicochemical properties of selected technetium compounds

Abundant data on the synthesis, investigation and use of a number of simple and complex technetium compounds are available in the literature (see, for example, the recent review⁵⁸). Hence, we shall take a quick look at the properties of technetium compounds, which determine the behaviour of technetium in nuclear technology and environmental objects. Special attention is given to technetates and Tc(IV) compounds.

The TcO_4^- anion is stable in acidic, neutral and alkaline media.⁴¹ Pertechnetates MTcO_4 belong to a class of ionic crystals stabilised primarily through Coulombic interactions between ions.⁵⁹ Since the electronic structure of TcO_4^- and its size are similar to those of ReO_4^- , pertechnetates are analogues of perrhenates and, in some cases, these compounds are isostructural. Pertechnetates are more similar to permanganates in thermal stability rather than to perrhenates. The physicochemical properties of polycrystalline MTcO_4 depend substantially on the nature of the M cation. Probably, this is partially associated with a distortion of the tetrahedral symmetry of the pertechnetate ion and the type of the crystal system. According to the data from vibrational spectroscopy and ^{17}O and ^{99}Tc NMR spectroscopy, the pertechnetate ion in aqueous and non-aqueous solutions has a regular tetrahedral symmetry regardless of the nature of the cation.⁶⁰ According to the results of vibrational spectroscopy and X-ray diffraction studies, the island anionic polyhedron TcO_4^- in crystals is distorted, the degree of distortion being decreased with increasing cation radius.

Pertechnetates may be divided into three groups.^{60–62}

1. Pertechnetates of alkali metals (Na, K, Rb) whose crystals have scheelite-like structures and are characterised by a small angular distortion of the TcO_4^- anion ($1–2^\circ$).

2. Ammonium pertechnetate whose tetragonal lattice is built from the isolated TcO_4^- and NH_4^+ groups linked through hydrogen bonds. The unit cell parameters of NH_4TcO_4 vary substantially in the temperature range of $100–340\text{ K}$.

3. Pertechnetates with onium cations whose structures are poorly known (except for Me_4NTcO_4 , in which the anionic polyhedron TcO_4^- is strongly distorted); the Tc–O bond lengths in these compounds differ by 0.04 Å and the bond angles are 105.5 and 111.7° .⁶⁰

Alkali metal pertechnetates are readily soluble in water. Thus, the solubility of NaTcO_4 is $11.3\text{ mol litre}^{-1}$ at 20°C .³⁹

Technetium(IV) dioxide TcO_2 , which is the most important and stable Tc(IV) compound, occurs as a paramagnetic black powder with a density of 6.9 g cm^{-3} . At 298.16°C , this compound is characterised by the following thermodynamic parameters: $-\Delta H_{\text{form}} = 434.59\text{ kJ mol}^{-1}$; $S^\circ = 62.5\text{ J mol}^{-1}\text{ deg}^{-1}$; $-\Delta S^\circ = 173.9\text{ J mol}^{-1}\text{ deg}^{-1}$; $-\Delta G_{\text{form}} = 382.76\text{ kJ mol}^{-1}$. Technetium(IV) dioxide TcO_2 crystallises in the monoclinic system with the following unit cell parameters: $a = 5.53$, $b = 4.79$, $c = 5.53\text{ Å}$, $\beta = 120^\circ$.⁶³ According to the results of EXAFS measurements, the Tc–Tc distance in the structure of TcO_2 is 2.61 Å .⁶⁴

Technetium(IV) dioxide is quite stable in air at 20°C . In deaerated neutral and acidic aqueous solutions, this compound is stable, whereas in aerated aqueous solutions, TcO_2 rapidly oxidises with subsequent dissolution (with a rate of $\sim 1\text{ mass \%}$ during 10 days) to give $\text{Tc}^{\text{VII}}\text{O}_4^-$.⁶⁵

Technetium(IV) dioxide occurs in two forms, viz., non-hydrated (TcO_2) and hydrated ($\text{TcO}_2 \cdot n\text{H}_2\text{O}$). The hydrated form is less stable (compared to TcO_2) both in solutions and in air.

In alkali solutions, TcO_2 dissolves to give $\text{Tc}(\text{OH})_6^{2-}$ ions, which have a characteristic orange colour. The hydroxo technetate ions, whose solutions absorb light at $\lambda = 410\text{ nm}$, are readily oxidised with atmospheric oxygen to Tc(VII).

The solubility of $\text{TcO}_2 \cdot n\text{H}_2\text{O}$ at pH 7–10 in the absence of oxidising and complex-forming agents is close to $10^{-8}–10^{-9}\text{ mol litre}^{-1}$ and increases substantially as the pH of the solutions increases. In air, the solubility of $\text{TcO}_2 \cdot n\text{H}_2\text{O}$ in a NaOH solution ($1–3.6\text{ mol litre}^{-1}$) containing N_2H_4 ($0.02\text{ mol litre}^{-1}$) is $(1.1 \pm 0.1) \times 10^{-5}\text{ mol litre}^{-1}$. Under the same conditions, the solubility of $\text{Tc}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ is $6.1 \times 10^{-6}\text{ mol litre}^{-1}$.^{41,66}

III. Methods of isolation of technetium from solutions

1. Liquid–liquid extraction

Liquid-liquid extraction is most commonly used for the isolation of technetium from solutions with different compositions. Abundant data on the extraction properties of Tc(VII) have been accumulated. Different extractants were proposed for extracting technetium from acidic, neutral and alkaline solutions, among which are alcohols, ketones, ethers, nitro compounds, organophosphorus compounds,^{67,68} nitriles, amines,⁶⁹ etc.^{70–72}

The extractants characterised by the best distribution coefficients of Tc(VII) in acidic media are listed in Table 1.

Table 1. Distribution coefficients of Tc(VII) (D_{Tc}) in acidic media.

Extractant	Acid	Concentration /mol litre ⁻¹	D_{Tc}	Ref.
Triisooctylamine ($0.2\text{ mol litre}^{-1}$) in syntin	HNO_3	1	270	39
Acylidimethylbenzylammonium chloride	H_2SO_4	1	105	73
Diisopentyl methylphosphonate	HNO_3	0.1	117	39
Tri-n-octylamine ($0.1\text{ mol litre}^{-1}$) in cyclohexane	H_2SO_4	1	110	73
Tri-n-octylphosphine oxide ($0.5\text{ mol litre}^{-1}$)	HNO_3	0.1	78	39
Cyclohexanol	H_2SO_4	1	32	73

A solution of tetraphenylarsonium chloride in chloroform ($10^{-4}\text{ mol litre}^{-1}$) is the most efficient extractant in neutral and weakly alkaline media. The distribution coefficient $D_{\text{Tc(VII)}}$ for this agent is 106 (Na_2CO_3 , pH 10).^{74,75}

α -Picoline ($D = 1840$), 5-ethyl-2-methylpyridine ($D = 1000$), 2,4-dimethylpyridine ($D = 700$) and quinoline ($D = 523$) are the most promising extractants for the extraction of technetium from alkaline solutions ($0.5\text{ mol litre}^{-1}\text{ NaOH} + 1\text{ mol litre}^{-1}\text{ Na}_2\text{CO}_3$).⁷⁵

2. Sorption and extraction chromatography

Data on sorption extraction of technetium(VII) by both synthetic organic sorbents and inorganic materials are available in the literature.

It was demonstrated that Tc(VII) as the TcO_4^- ion has a high affinity for different granulated anion-exchange resins. Strongly basic anion-exchange resins of the AV-17 type, Dowex-1 $\times 8$ or vinylpyridine ion-exchange resins show the highest efficiency for absorption of Tc(VII). Polyfunctional ion-exchange resins, for example, EDE-10, are less efficient for absorption of Tc(VII).⁷⁶ The plot of the distribution coefficient $[K_d^{\text{Tc(VII)}}]$ vs. the pH of the solution for sorption of Tc(VII) with the AV-17 anion-exchange resin⁷⁷ is shown in Fig. 1.

The distribution coefficient $K_d^{\text{Tc(VII)}}$ for sorption of TcO_4^- from NaOH solutions ($0.25\text{ mol litre}^{-1}$) by the Dowex-1 $\times 8$ ion-exchange resin is $4500\text{ cm}^3\text{ g}^{-1}$, but this coefficient decreases substantially as the salt background increases. Thus, an increase in the concentration of NaNO_3 from 0.5 to $5.0\text{ mol litre}^{-1}$ leads

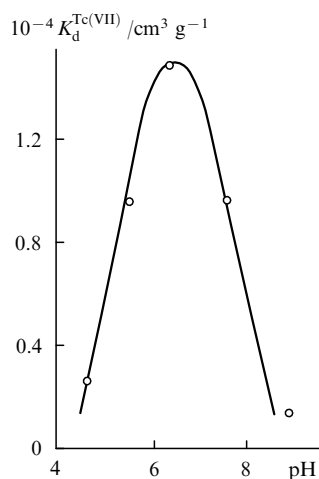


Figure 1. Plot of $K_d^{Tc(VII)}$ vs. pH upon sorption on the AV-17 anion-exchange resin in the Cl form.⁷⁷

to a decrease in $K_d^{Tc(VII)}$ from 575 to 122 $\text{cm}^3 \text{g}^{-1}$, all other factors being the same. In the case of sorption of Tc(VII) on the VP-1AP anion-exchange resin, the distribution coefficient $K_d^{Tc(VII)}$ changes from 6233 to 5193 $\text{cm}^3 \text{g}^{-1}$ in the range of the NaOH concentrations from 1 to 4 mol litre^{-1} .³⁹

Sorption of technetium(VII) from aqueous solutions with pH 2–12 by granulated monofunctional AV-17-based anion-exchange resins containing amine and amide functional groups or nitrogen heterocycles was studied. It was demonstrated that the AV-17 anion-exchange resin and resins containing different functional groups can be arranged in the following order of increasing affinity for the pertechnetate ion: AV-17 > NC(O)Et₂ > NC(O)Bu₂ⁿ > S(CH₂)₂NMe₂ > NMe₂. The pH of solutions providing the maximum sorption of technetium increases in the same order. Thus, the maximum distribution coefficients of Tc(VII) (in $\text{cm}^3 \text{g}^{-1}$) corresponding to the maximum pH are as follows: 1.3×10^4 at pH 5 [NC(O)Et₂], 1.2×10^4 at pH 4 [NC(O)Bu₂ⁿ], 1.1×10^4 at pH 3 [S(CH₂)₂NMe₂] and 0.4×10^4 at pH 2.5 (NMe₂).⁷⁷

Sorption of TcO_4^- from acidic solutions should be considered as an acid–base interaction according to the reaction



where R~ is the functional group of the resin.

Sorption of technetic acid by basic anion-exchange resins is accompanied by localisation of the proton at the functional group giving rise to $\text{RH}^+ \cdots \text{TcO}_4^-$ ion pairs. The logarithm of the constant of proton association in the HCl–LiCl system ($\mu = 5$) is 0.033.^{77, 78}

Sorption of the TcO_4^- ions was studied⁷⁹ on the radiation-stable styrene–vinylpyridine anion-exchange resin ReillenTM–HPQ (30–60 mesh granules) containing 75% of highly basic methylated ion-exchange amino groups and 25% of weakly basic non-methylated ion-exchange amino groups. If the equilibrium was established within 30 min, the distribution coefficients $K_d^{Tc(VII)}$ in HNO₃ solutions with concentrations of 10, 5 and 1 mol litre^{-1} were estimated at 11.5, 55.7 and 415 $\text{cm}^3 \text{g}^{-1}$, respectively. These values are substantially higher than the corresponding values for the commercial Dowex-1 $\times 8$ anion-exchange resin (under the same conditions, 5, 15 and 135 $\text{cm}^3 \text{g}^{-1}$, respectively). The ReillenTM–HPQ sorbent can also be used for the extraction of technetium(VII) from salt solutions. Thus, the distribution coefficients K_d of TcO_4^- with the use of this sorbent at an HNO₃ concentration of 0.001 mol litre^{-1} are 162 $\text{cm}^3 \text{g}^{-1}$ (in a solution containing 4 mol litre^{-1} of NaNO₃), 515 $\text{cm}^3 \text{g}^{-1}$ (1 mol litre^{-1} of NaNO₃) and 138 $\text{cm}^3 \text{g}^{-1}$ (4 mol litre^{-1} of LiNO₃). At an HNO₃ concentration of 0.5 mol litre^{-1} , K_d are 109 $\text{cm}^3 \text{g}^{-1}$ (4 mol litre^{-1} of NaNO₃), 553 $\text{cm}^3 \text{g}^{-1}$

(1 mol litre^{-1} of NaNO₃) and 423 $\text{cm}^3 \text{g}^{-1}$ (1 mol litre^{-1} of LiNO₃).⁷⁹

Not only granulated ion-exchange resins but also fibrous complex-forming sorbents are used in procedures for isolation and extraction of technetium. The latter sorbents exhibit high selectivity for particular ions. Such sorbents have advantages over granulated materials, because they not only possess high selectivity for metal ions but also have a large surface, which ensures their good kinetic properties. In addition to traditional fibrous complex-forming sorbents prepared by a modification of the starting matrices, fibrous materials filled with powdered complex-forming sorbents also show promise. The latter sorbents are composed of fine porous polyacrylonitrile fibers (30–40 μm in diameter), within which a complex-forming sorbent or an ion-exchange agent (filling agent) is held. Fibrous complex-forming sorbents are used for the extraction of rare and noble metals^{80–82} as well as of transuranium elements.^{83, 84} Fibrous complex-forming agents of the POLYORGS type, which were developed at the V I Vernadsky Institute of Geochemistry and Analytical Chemistry of the Russian Academy of Sciences, were also used for the sorption of Tc(VII) from acidic, neutral and alkaline media.⁸⁵ Data on extraction of technetium from solutions with different compositions are given in Table 2. The filled fibrous complex-forming sorbents AV-17 and POLYORGS-17 virtually completely absorb trace amounts of Tc both from acidic and alkaline solutions. Other known sorbents also extract technetium from acidic solutions, though to a lesser degree. Under the optimum conditions, the equilibrium distribution coefficients [$K_d^{Tc(VII)}$] for the filled fibrous sorbents of choice are $\geq 10^4 \text{ cm}^3 \text{g}^{-1}$, and these sorbents are highly competitive with commercial granulated materials (Table 3).

Table 2. Sorption of Tc(VII) by various fibrous ‘filled’ sorbents.⁸⁵

Sorbent	Functional groups	Degree of sorption (%)	
		HNO ₃ (see ^a)	NaOH ^a
AV-17	quaternary ammonium	92	91
AN-31	secondary and tertiary amine	88	23
POLYORGS-17	1,(3)5-dimethylpyrazole	96	96
POLYORGS-33	amidoxime and hydrazide	67	6
POLYORGS-35	hydrazide	79	0

Note. $V/m = 100 \text{ cm}^3 \text{g}^{-1}$, 20 °C, the contact time was 2 h.

^a The concentration was 0.1 mol litre^{-1} .

Table 3. Sorption of Tc(VII) by fibrous ‘filled’ sorbents.⁸⁵

Solution	Concentration / mol litre^{-1}	$K_d^{Tc(VII)} / \text{cm}^3 \text{g}^{-1}$	
		AV-17	POLYORGS-17
HNO ₃	10^{-3}	3.7×10^4	1.0×10^3
	10^{-2}	1.3×10^4	2.5×10^3
	0.1	1.2×10^3	2.2×10^3
	0.5	382	189
NaOH	0.1	1.0×10^3	277
	1.0	900	—
NaNO ₃	0.1	861	432

Note. $V/m = 100 \text{ cm}^3 \text{g}^{-1}$, 20 °C, the contact time was 2 h.

Fibrous sorbents of the POLYORGS type were used for the extraction of technetium from water samples from the Karachai Lake (Russia) located in the territory of the Mayak Production Association and also from wells located in the neighbourhood of this lake.⁸⁶

It was noted that Tc(VII) is efficiently sorbed by activated carbon from acidic solutions, which model compositions of high-level radioactive waste.⁸⁷ The distribution coefficient $K_d^{\text{Tc(VII)}}$ in solutions containing HNO_3 at a concentration of $0.5 \text{ mol litre}^{-1}$ is $\sim 10^3 \text{ cm}^3 \text{ g}^{-1}$. For comparison, the sorption of Tc(VII) on other inorganic sorbents, including SiO_2 , Al_2O_3 and aluminosilicates, was also studied. Activated carbon appeared to be the sorbent of choice, the use of activated carbon being most efficient in strongly acidic media. The mechanism of sorption and the possibility of the recovery of activated carbon were discussed.⁸⁷ The authors of the cited study believed that activated carbon acts as an ion-exchange agent, anion-exchange centres being formed on its surface in solutions with pH 2–5 resulting in an increase in $K_d^{\text{Tc(VII)}}$. An increase in the salt background leads to a ~ 100 -fold decrease in the sorption of Tc.⁸⁷

Sorption of Tc(VII) and Tc(IV) on aluminium hydroxide was investigated.⁸⁸ The experiments were carried out under an atmosphere of N_2 . Under experimental conditions, the sorption of technetium was insignificant and K_d decreased to zero at pH > 7. In hydrochloric solutions, Tc(IV) is sorbed on $\text{Al}(\text{OH})_3$ as the TcCl_6^{2-} anions. The sorption maximum is observed in neutral media.

The distribution coefficient $K_d^{\text{Tc(VII)}}$ for extraction of Tc(VII) from a solution of HNO_3 ($0.05 \text{ mol litre}^{-1}$) with the use of a solid extractant, which is composed of a Polysorb-1 or Chromosorb-W matrix incorporating a solution of trioctylphosphine oxide in cyclohexanone, is $\sim 3500 \text{ cm}^3 \text{ g}^{-1}$. An increase in the concentration of HNO_3 to 1 mol litre^{-1} causes a decrease in the distribution coefficient to $1060 \text{ cm}^3 \text{ g}^{-1}$. In solutions containing HCl (1 mol litre^{-1}) and SnCl_2 ($0.03 \text{ mol litre}^{-1}$), $K_d^{\text{Tc(VII)}}$ is 2.8. The distribution coefficient $K_d^{\text{Tc(VII)}}$ of Tc(IV) in solutions containing HCl (5 mol litre^{-1}) and SnCl_2 ($0.3 \text{ mol litre}^{-1}$) is even lower (<1). In neutral and alkaline media, $K_d^{\text{Tc(VII)}}$ are $110 \text{ cm}^3 \text{ g}^{-1}$ (pH 6.4) and $10 \text{ cm}^3 \text{ g}^{-1}$ ($0.5 \text{ mol litre}^{-1}$ of NaOH + $2.5 \text{ mol litre}^{-1}$ of NaNO_3).⁷⁰

With the aim of isolating technetium from plant materials, the sorption of the following anions was studied: TcO_4^- , technetium diethylenetriaminepentaacetate as well as the $[\text{Tc}^{\text{VO}}_2(1,4,8,11\text{-tetraazacyclotetradecane})]^+$ cationic complex on polydextran gel Sephadex G-25, hydrophilic silica gel Zorbax GF-250 and polymeric gel HEMA-SEC BIO1000. It was found that HEMA-SEC BIO1000 is the matrix of choice for isolation of Tc(VII). In solutions of NaCl with a concentration of $0.04 \text{ mol litre}^{-1}$, $K_d^{\text{Tc(VII)}}$ for these ions have close values (4, 1.5 and $0.8 \text{ cm}^3 \text{ g}^{-1}$, respectively).⁸⁹

The sorption of Tc on TiO_2 , cadmium sulfide, zirconium phosphate and complex inorganic materials⁹⁰ was studied upon contact between a sorbing material (1 g) and a solution of Tc(VII) (10 ml) at 20°C (Table 4). At pH 6.5, Termoxid-34 and GSK (see Table 4) are the most efficient sorbents. After irradiation of samples using a ^{60}Co γ -source ($\sim 10^7 \text{ rad}$) at 20°C for 20 h, their total sorption capacity was almost halved.

Table 4. Distribution coefficients $K_d^{\text{Tc(VII)}}$ for different composites.⁹⁰

Sorbent	$K_d^{\text{Tc(VII)}} / \text{cm}^3 \text{ g}^{-1}$		
	pH 1.27	pH ~ 6.5	pH 12.7
GSK (crystalline CdS)	11.0	13.4	2.16
Termoxid-34 (high-density crystalline TiO_2)	5.3	31.3	0.73
SPSK ($\text{Sb}_2\text{O}_5 \cdot n \text{ SiO}_2 \cdot m \text{ P}_2\text{O}_5$)	4.7	9.4	<0.1
ISMA ($n \text{ LiO} \cdot m \text{ MnO}_2 \cdot l \text{ Al}_2\text{O}_3 \cdot k \text{ H}_2\text{O}$)	4.0	10.25	~ 1

Sorption methods are being developed for the extraction of technetium from alkaline wastes (pulp) of radiochemical production facilities. It is known that high-level radioactive wastes were accumulated during 50 years as a result of weapon plutonium

production and still remain unprocessed both in Russia (Mayak Production Association, Ozersk)⁹¹ and abroad, particularly, in the USA (Hanford Site, Savannah River Site, Idaho National Engineering and Environmental Laboratory, West Valley Staffing Group and Oak Ridge National Laboratory).^{92–94} Thus, thousands of tonnes of alkaline pulps, which have the overall activity of $\sim 2 \times 10^5 \text{ Ci}$ and contain Np (50–100 kg), Pu (540–860 kg), Am ($\sim 30 \text{ kg}$) and Tc ($\sim 2 \text{ t}$), were accumulated at the Hanford Site of the Westinghouse Hanford Company (Richland, USA).^{92–94} It is also necessary to extract technetium during reprocessing of alkaline pulps followed by burial of hazardous long-lived radionuclides. Main problems associated with the development of sorption methods for the extraction of technetium from these wastes are a high concentration of alkali ($[\text{OH}^-] \approx 1\text{--}4 \text{ mol litre}^{-1}$), high salt background ($[\text{Na}^+] \approx 2\text{--}5 \text{ mol litre}^{-1}$, $[\text{Al}^{3+}] \approx 0.8 \text{ mol litre}^{-1}$; $[\text{K}^+] \approx 0.1 \text{ mol litre}^{-1}$; $[\text{NO}_3^-] \approx 1.6 \text{ mol litre}^{-1}$; $[\text{NO}_2^-] \approx 1 \text{ mol litre}^{-1}$), high density of the liquid phase ($\approx 1.1\text{--}1.3 \text{ cm}^3 \text{ g}^{-1}$) and high radiation background.

Selective organic granulated anion-exchange resins and inorganic materials (including metals) are used for the extraction of technetium from alkaline solutions with high salt concentrations.

The SuperLig 639 sorbent was specially constructed for the extraction of technetium from alkaline high-level radioactive waste stored at the Hanford Site (USA). This sorbent was tested on real solutions from the waste tanks AN-103 ($[\text{Na}^+] \approx 4.9 \text{ mol litre}^{-1}$, $[\text{NO}_3^-] \approx 1.6 \text{ mol litre}^{-1}$, $[\text{OH}^-] \approx 1.9 \text{ mol litre}^{-1}$), AZ-102 ($[\text{Na}^+] \approx 2.7 \text{ mol litre}^{-1}$, $[\text{NO}_3^-] \approx 0.27 \text{ mol litre}^{-1}$, $[\text{OH}^-] \approx 0.1 \text{ mol litre}^{-1}$) and AN-102 ($[\text{Na}^+] \approx 5.3 \text{ mol litre}^{-1}$, $[\text{NO}_3^-] \approx 1.5 \text{ mol litre}^{-1}$, $[\text{OH}^-] \approx 1.25 \text{ mol litre}^{-1}$).⁹⁵ This sorbent occurs as 20–70 mesh granules (200–800 μm) and is made up of the groups of crown ether DCH-18-C-6 covalently bonded to a polystyrene matrix. The distribution coefficients $K_d^{\text{Tc(VII)}}$ for sorption of technetium from radioactive wastes from the tanks AN-103, AZ-102 and AN-102 with the use of this anion-exchange resin are 530, 886 and $287 \text{ cm}^3 \text{ g}^{-1}$, respectively.

Extraction chromatography was applied to the isolation of technetium from alkaline wastes with the use of the ABECTM-5000 ion-exchange resin made up of monomethylated poly(ethylene glycol) (PEG-5000) covalently bonded to a polystyrene support, which efficiently adsorbed TcO_4^- from solutions. Sorption of Tc(VII) was carried out from NaOH solutions ($2\text{--}4 \text{ mol litre}^{-1}$). The desorption of Tc followed by its concentration were performed with the use of distilled water. The addition of the NO_3^- and NO_2^- ions to the eluent leads to an increase in the rate of elution of TcO_4^- from a sorbent layer. By contrast, the citrate, carbonate and aluminate ions facilitate the retention of TcO_4^- by the resin. An increase in the temperature from 25 to 40°C has only a slight effect on this process. The ABECTM-5000 ion-exchange resin appeared to be resistant to ^{60}Co γ -irradiation up to the dose of 131 mrad .⁹⁶

3. Currentless electrochemical deposition

The static contact between granulated Zn metal and solutions containing 0.5, 2.0 or $3.5 \text{ mol litre}^{-1}$ of NaOH and $(6 \pm 3) \times 10^{-5} \text{ mol litre}^{-1}$ of Tc(VII) in the presence of complex-forming agents led to sorption of technetium on the metal surface with $K_d^{\text{Tc(VII)}}$ of 1.4, 3.9 and $5.7 \text{ cm}^3 \text{ g}^{-1}$, respectively.⁹⁷ In the dynamic mode, the distribution coefficients $K_d^{\text{Tc(VII)}}$ were 1.9, 4.7 and $8.9 \text{ cm}^3 \text{ g}^{-1}$, respectively (Fig. 2). The sorption of technetium from NaOH solutions with concentrations from 0.5 to $3.5 \text{ mol litre}^{-1}$ with the use of Cr or Sn metals both in the static or dynamic modes in the presence of complex-forming agents is characterised by low distribution coefficients $K_d^{\text{Tc(VII)}}$ ($< 1.2 \text{ cm}^3 \text{ g}^{-1}$). The authors of the cited study⁹⁷ believed that interactions of Zn, Cr or Sn with Tc in alkaline solutions caused reduction of Tc(VII) to Tc(IV) followed by sorption of the resulting $\text{TcO}_2 \cdot n \text{ H}_2\text{O}$ on the metal surface. The solubility of $\text{TcO}_2 \cdot n \text{ H}_2\text{O}$ thus precipitated in a deaerated NaOH solution (4 mol litre^{-1})

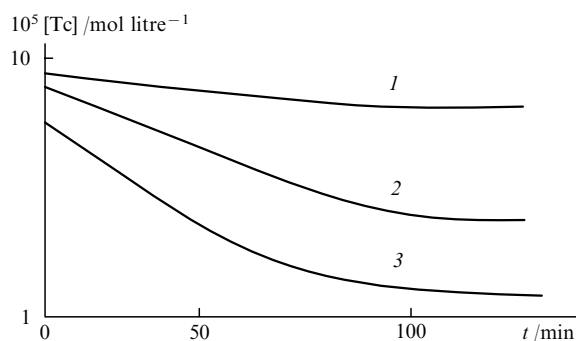


Figure 2. Sorption of Tc(VII) on zinc granules depending on the duration of the contact between the granules and a NaOH solution.⁹⁷ (1) 1M NaOH, (2) 2M NaOH, (3) 4M NaOH.

was nearly 6×10^{-7} mol litre⁻¹, which is 50 times lower than the solubility of $\text{TcO}_2 \cdot n\text{H}_2\text{O}$ prepared by reduction of Tc(VII) with hydrazine. The high reactivities of the metals used (Zn, Cr, Sn, Pb and Sb) are associated with the fact that these metals do not form oxide films (which hinder the contact) in alkaline media. Because of this, the oxidation potentials of these metals are sufficient for reduction of Tc(VII) to $\text{TcO}_2 \cdot n\text{H}_2\text{O}$. The degree of Tc deposition (contrast to actinides) increases with increasing NaOH concentration. An increase in the temperature from 20 to 60 °C and the removal of dissolved O_2 have virtually no effect on the final results.

4. Electrochemical separation

Electrochemical methods are used along with traditional chemical methods for the preparation of solutions with the aim of stabilising technetium and actinides in the desired oxidation states when using the extraction technology of reprocessing of spent nuclear fuel.^{98,99} It was demonstrated that the rate of electrolytic oxidation of Pu(0) to Pu(IV) and the yield of the product increased in the presence of technetium(VII) ions. Thus, the addition of Tc(VII) (70 mg litre⁻¹) to a solution containing Pu(III) and hydrazine caused acceleration of oxidation of plutonium by a factor of ~1.5 due, apparently, to catalytic decomposition of hydrazine with technetium ions.¹⁸ Electrolysis of solutions of Tc(VII) in H_2SO_4 (1 mol litre⁻¹) in a diaphragm cell led to reduction of technetium partially to metal that deposited on the cathode and partially to Tc(IV) accumulated in the electrolyte as a colloidal suspension of TcO_2 .

Data on the electrochemical separation of technetium from solutions which model compositions of liquid radioactive wastes were reported in the study.¹⁰⁰ In HNO_3 solutions (0.1–1.0 mol litre⁻¹), electrochemical reduction of Tc(VII) to Tc(III) involves two electrode reactions. The first reaction proceeds at 0.069 to –0.205 V (relative to SHE) and is associated with reduction of technetium. The second reaction proceeds at –0.71 V and results in decomposition of nitric acid catalysed by Tc(III) cations. Electrochemical reduction of the pertechnetate ions by polarographic methods on a mercury electrode in an acetate buffer (pH 3.5–6.0) was studied. It was noted that the Tc(VII)/Tc(III) reduction proceeded through the formation of Tc(V) followed by its disproportionation to give water-insoluble suspensions of Tc(IV) compounds. Technetium(IV) present in precipitates adsorbed on the electrode was reduced to Tc(III). An original scheme of separation of technetium from solutions which model wastes from the PUREX process ($[\text{Tc(VII)}] = 200$ mg litre⁻¹, $[\text{HNO}_3] = 2\text{--}4$ mol litre⁻¹) was proposed in the study.¹⁰⁰ This method involves denitration of the starting solution with formic acid on heterogeneous platinum catalysts followed by electrolytic reduction of technetium on a graphite electrode at -1.3 ± 0.1 V to give $\text{TcO}_2 \cdot n\text{H}_2\text{O}$ (pH 6.0–7.5, the ionic strength was 0.5–1.0 mol litre⁻¹, the yield was 92%–95%).¹⁰⁰

5. Precipitation and coprecipitation

It is known that Tc(VII) is efficiently precipitated with hydrazine in the presence of FeCl_3 . The presence of complex-forming agents (for example, of sodium phosphate or sodium ethylenediaminetetraacetate at concentrations of 0.01 and 0.1 mol litre⁻¹, respectively) leads to a decrease in the degree of precipitation of technetium.¹⁰¹ Reduction of Tc(VII) with hydrazine can be accompanied by sorption of technetium on metals, such as Zn or Al.⁴¹ Up to 99.5% of Tc was precipitated in alkaline media (0.5–4.0 mol litre⁻¹ of NaOH) in the presence of $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ (0.17 mol litre⁻¹) and FeCl_3 (0.025–0.15 mol litre⁻¹). However, only 76% of Tc was extracted from model solutions of high-level radioactive wastes under analogous conditions, which indicates that Tc(VII) is only partially reduced in the presence of salts.¹⁰¹ In some cases, technetium was successfully isolated as Tc(IV),(V) hydroxides.¹⁰²

In wastes of radiochemical production facilities, Tc is present together with platinum-group elements. A procedure was developed for the separation of Tc from these elements using denitration of a solution of nitric acid with formic acid.^{87, 103, 104} Under these conditions, Pd and Rh are reduced with formic acid to metals, and Tc is reduced to Tc(IV) and is isolated as hydrated dioxide. It was found that more than 90% of Tc was precipitated in the presence of Pd and Rh (> 0.005 mol litre⁻¹) at a concentration ratio $\text{HCOOH}/\text{HNO}_3 > 1.8$. Then technetium(IV) dioxide is dissolved in the presence of different oxidising agents. Refluxing of technetium(IV) dioxide in the presence of O_2 , O_3 , H_2O_2 or HNO_3 afforded Tc(VII) in 23%, 34%, 76% or 90% yields, respectively. Storage with sodium hydroxide during 24 h afforded Tc(VII) in only 6% yield. Hence, nitric acid proved to be the most efficient oxidising agent.

The coprecipitation of Tc(VII) and Re(VII) with FeS belonging to the tetragonal system was studied.¹⁰⁵ In this process, TcO_4^- was reduced to Tc(IV) to give a TcS_2 -like phase.

The separation of technetium from Mo and Ru was achieved by its coprecipitation in the presence of tetraphenylarsonium.⁴¹ It was also demonstrated that technetium(VII) was reduced to Tc(IV) and Tc(V) and coprecipitated with the latter upon contact with $\text{Mn}(\text{OH})_2$, $\text{Co}(\text{OH})_2$ or $\text{Cr}(\text{OH})_3$, which allowed one to separate ⁹⁹Tc from impurities of ¹³⁷Cs.

IV. Methods of determination of technetium

1. Radiometry

Generally, ^{95m}Tc and ^{99m}Tc are detected from their γ -activity.¹⁰⁶ In a number of studies, ⁹⁹Tc was determined from the β -activity on a Packard 2750 TR/LL scintillation counter.^{106–108} A scheme was proposed for the determination of ⁹⁹Tc in natural samples. This scheme involves annealing of a sample at 550 °C and treatment of the residue with solutions of nitric acid followed by extraction of technetium with a 5% solution of tri-*n*-octylamine in xylene. In an aqueous reextract, Tc is concentrated by the anion-exchange method, the concentrate is dissolved in a scintillation cocktail and the ⁹⁹Tc content is determined from its β -activity in the sample.

At low concentrations in natural samples, Tc is isolated with the use of carriers (generally, ^{99m}Tc). The radiometric determination of the initial ⁹⁹Tc is performed only after the complete decay of the carrier within two weeks. The sensitivity of the method is 1.7 Bq kg⁻¹. The sample weight necessary for the determination of Tc is ~10 g.

2. Spectrophotometry

Spectrophotometry is used for the determination of the oxidation state of technetium. Thus, the state of Tc(V) in complicated complex compounds was studied by spectrophotometry.^{109, 110} The spectrophotometric determination of technetium as complexes with thiourea after separation on a strongly basic anion-exchange resin was described in the studies.^{111, 112}

To determine the concentration of technetium in sea water, it is concentrated in aqueous samples by coprecipitation with $\text{Fe}(\text{OH})_3$. After two purification cycles, *viz.*, the extraction and chromatographic purification, Tc is determined in the raffinate by spectrophotometry.¹¹³

A combination of photocalorimetry and potentiometry was used for calculating the thermodynamic characteristics of technetium and its compounds. The heat of formation of Tc_2O_7 was determined ($1115.0 \pm 10.9 \text{ kJ mol}^{-1}$) and the standard oxidation potential of the $\text{TcO}_4^-/\text{TcO}_2$ pair was measured ($-0.782 \pm 0.011 \text{ V}$).³⁸

3. Other methods

The X-ray fluorescence method is used for the detection of technetium in different technological solutions. The sensitivity of serial X-ray fluorescence instruments to Tc is $\sim 2 \text{ mg litre}^{-1}$. The level of sensitivity to technetium is increased to $90 \text{ } \mu\text{g litre}^{-1}$ with the use of a paper backing. However, this leads to an increase in the time of analysis.¹¹⁴

A method for the crystalless X-ray fluorescence determination of technetium was described in the study.¹¹⁴ This method has a substantially lower threshold of sensitivity due to scattering of the exciting radiation in the analysed sample. The sample volume is 3.5 cm^3 . Technetium cannot be detected in the presence of a large amount of plutonium due to overlapping of the peaks of the excited radiation of these elements. In mixtures with uranium, Tc is reliably determined up to the U/Tc concentration ratio of ~ 100 .

The technetium concentrations of an order of several $\mu\text{Bq litre}^{-1}$ are determined by inductively coupled plasma mass spectrometry (ICP-MS).^{115, 116} The concentrations of stable ruthenium in samples are generally much higher than the concentrations of Tc, which hinders the determination of the latter element. Hence, the complete removal of ^{99}Ru as well as of ^{98}Mo and ^{100}Mo is essential for the successful determination of Tc. Initially, technetium is concentrated by chromatography using the TEVATM Spec resin sorbent and then Tc is determined by ICP-MS. The limit of determination of technetium in samples is $0.3 \text{ } \mu\text{Bq g}^{-1}$.^{115, 117}

Electrothermal vaporisation inductively coupled plasma mass spectrometry (ETV-ICP-MS) holds the most promise for determining the Tc concentrations in samples. The main advantage of this method is that ultrasmall volumes of samples ($10\text{--}100 \text{ } \mu\text{l}$) are required for the determination of Tc, which is of particular importance in the analysis of biological objects or high-level radioactive samples. This method allows one to determine technetium without separation of ^{99}Ru . After the addition of modifying agents, such as aqueous solutions of HNO_3 (1%) or NaClO (0.7%), to analysed samples, the limit of determination of Tc is 1.4 pg ml^{-1} (0.9 mBq ml^{-1}) in the presence (which is particularly important) of a more than a thousand-fold excess of Ru.¹¹⁸

The properties of the $\text{Zn}[\text{Tc}(\text{OH})\text{Cl}_3]$ complex were studied by IR and NMR spectroscopy, powder X-ray diffraction analysis, ESR spectroscopy and thermal analysis and it was demonstrated that this compound is paramagnetic and contains Tc in the oxidation state IV.¹¹⁹

A Waters Quanta 4000 capillary electrophoresis system was developed for studying the effect of γ -radiolysis on the oxidation state of technetium in the $\text{K}^{99}\text{TcO}_4$ compound in solutions modelling groundwaters. This system consists of two electrolytic cells joined to a capillary column $75 \text{ } \mu\text{m}$ in diameter and 60 cm long (the potential difference is 30 kV). This method enables one to perform the quantitative separation of $\text{Tc}(\text{VII})$ and $\text{Tc}(\text{IV})$ in solution.^{120, 121}

To establish the crystal structures of pertechnetates with different compositions, the dependence of the quadrupole coupling constant on the temperature in the ^{99}Tc NMR spectra was studied.^{59, 122, 123}

The *in situ* behaviour of technetium in radioactive wastes was investigated by Mössbauer absorption spectroscopy.^{124, 125} This method was also used to establish the correlation between the

observed chemical shifts of technetium in the NMR spectra and its oxidation states. It was noted that the chemical shift of technetium depends on its formal oxidation state.⁶⁴

The state of technetium in a cement matrix, which is used for the isolation of radioactive wastes from the environment, was studied by XAFS Mössbauer absorption spectroscopy. This method not only enables one to determine the oxidation state of Tc in the solid state but also makes it possible to identify the compositions and structures of the resulting technetium-containing compounds. The advantage of this method is that it allows one to determine the element directly without its pre-isolation from the matrix regardless of its crystal structure.¹²⁵

In some cases, the Tc concentrations in natural objects can be estimated from the ^{137}Cs concentrations in the same materials, because these fission products are generated in close yields ($\sim 6\%$) upon uranium fission. Thus, the levels of technetium contamination in the irradiated exclusion zone surrounding the Chernobyl reactor were estimated from the ^{137}Cs concentration.^{126, 127}

V. Behaviour of technetium during reprocessing of spent nuclear fuel

1. Distribution of technetium in the PUREX process

In Russia, spent nuclear fuel is reprocessed with the use of the so-called PUREX process (Fig. 3). This process involves dissolution of irradiated fuel in nitric acid and coextraction of U and Pu with a 30% solution of tributyl phosphate (TBP) in synthetic saturated hydrocarbons followed by reductive reextraction of Pu into an aqueous phase. The process is carried out in a series of mixer-settlers with pulse or mechanical mixing of the phases. Plutonium and uranium are isolated as dioxide and uranyl nitrate, respec-

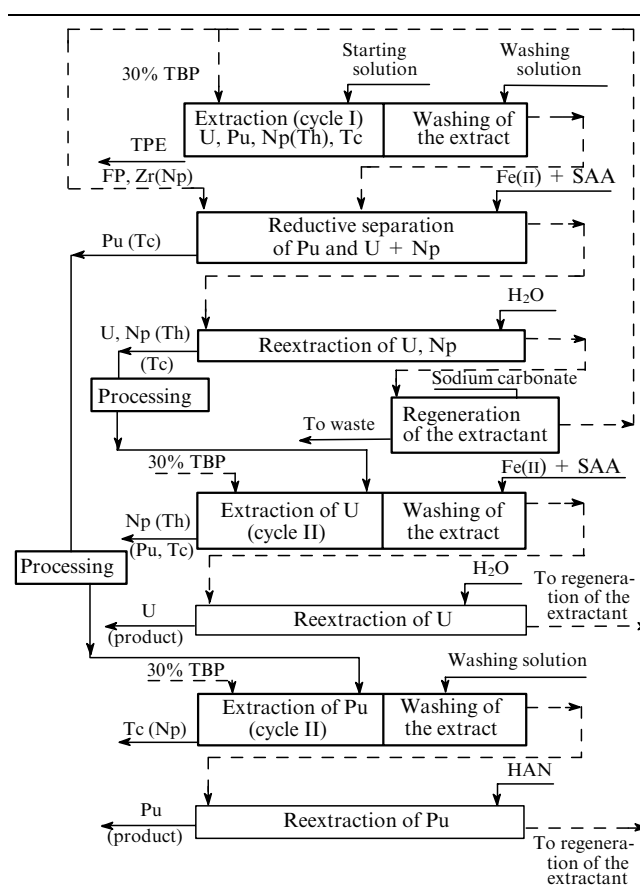


Figure 3. Scheme of the classical strongly acidic PUREX process; SAA is sulfamic acid and HAN is hydroxylamine nitrate.¹²⁸ Flows of aqueous and organic solutions are indicated by solid and dashed arrows, respectively.

tively.⁹¹ The process can be performed in two structurally identical modifications ('weakly acidic' and 'strongly acidic').¹²⁸

Upon dissolution of spent nuclear fuel in nitric acid, technetium passes into solution as pertechnetate ions. In the first step of extraction of uranium and plutonium under the conditions of the technological scheme used, technetium(VII) goes into the organic phase. In the Japanese modification of the PUREX process, the degree of extraction varies from 30% (see Ref. 129) to 80% (see Refs 111, 114 and 130) depending on the conditions of the extraction process. In the process performed according to the scheme of the RT-1 plant (Mayak Production Association, Russia), the degree of extraction reaches 94%–98%.¹³¹ Due to coextraction of Tc(VII) and U(VI), technetium goes into the organic phase as the $\text{UO}_2(\text{TcO}_4)(\text{NO}_3)(\text{TBP})_2$ complex.¹³² Data on the extraction of technetium into the organic phase depending on the concentration of nitric acid and composition of the aqueous phase are presented in Fig. 4.⁶⁵

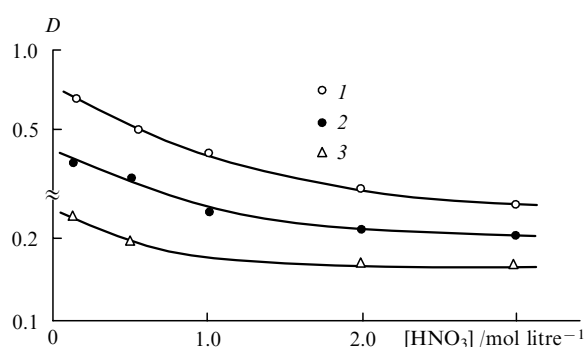
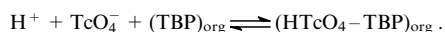


Figure 4. Plots of distribution coefficients D of Tc(VII) vs. the HNO_3 concentration and the composition of the aqueous phase upon the extraction with 30% TBP in *n*-dodecane.⁶⁵

(1) 1M $\text{UO}_2(\text{NO}_3)_2$, (2) 1M $\text{UO}_2(\text{NO}_3)_2 + 1\text{M}$ NH_4NO_3 ;
(3) 1M $\text{UO}_2(\text{NO}_3)_2 + 2\text{M}$ NH_4NO_3 .

Technetium forms mixed solvates not only with uranium but also with Pu and Zr.¹²⁹ The calculated distribution coefficients of Tc change in parallel with the experimental values, which indicates that coextraction proceeds by the hydration–solvation mechanism.

Technetium also forms a complex with tributyl phosphate

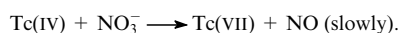
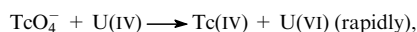


The stability and structural transformations of the latter complex were described in the study.¹³³

In the second step of the extraction process, plutonium and uranium are separated from each other. For this purpose, plutonium is subjected to reductive reextraction, generally, with U(IV) or Fe(II) in the presence of hydrazine. This process affords Pu(III), which goes into the aqueous phase, while uranium(VI) remains in the organic phase. In this step, it is very important to choose adequate conditions for stabilisation of U(IV) and Pu(III) in the presence of technetium in the organic phase and, consequently, to calculate the required amount of the reducing agent.^{133, 134}

If an aqueous solution of U(IV) is used as the reducing agent, Tc is partially reextracted together with Pu into the aqueous phase and partially remains in the organic phase. The Tc(VII) ions have a strong effect on the stability of low-valence forms of uranium and plutonium in media of nitric acid.

The TcO_4^- anions oxidise U(IV).

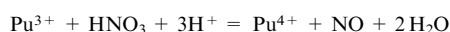


The Tc(VII) ions oxidise Pu(III) according to a reaction, whose rate is described by the following equation:

$$-\frac{d[\text{Pu(III)}]}{d\tau} = k [\text{Pu(III)}] [\text{Tc(VII)}] [\text{H}^+]^{2.3},$$

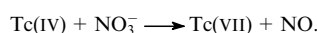
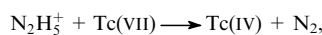
where $k = (3.82 \pm 0.11) \times 10^{-2} \text{ litre}^{3.3} \text{ mol}^{-3.3} \text{ at } 50^\circ\text{C}$ and $\mu = 4$.¹³⁵

In addition, the technetium(VII) ions catalyse oxidation of Pu^{3+} with nitric acid according to a reaction described by a first-order equation with respect to both Pu(III) and Tc(VII).¹³⁶



This reaction proceeds also in the presence of hydrazine nitrate ($\sim 0.1 \text{ mol litre}^{-1}$). It was demonstrated that Tc(VII) serves as the catalyst also for oxidation of U(IV) with nitric acid.^{133, 134}

Technetium(VII) ions have been proved to catalyse the decomposition of hydrazine used for stabilisation of Pu(III) and U(IV) in the course of the technological process.^{134, 137} In solutions, technetium(VII) is successively reduced with hydrazine to Tc(V) and Tc(IV), which are again oxidised with nitric acid to the initial state.¹³⁸



In this process, the concentration of Tc(VII) remains constant, while hydrazine is completely consumed.

For decomposition of hydrazine in the presence of Tc(VII) ions at concentrations of 0.4×10^{-2} , 1.0×10^{-2} and $2.0 \times 10^{-2} \text{ mol litre}^{-1}$, the apparent zero-order rate constants k_0 are 0.0140, 0.0415 and $0.0800 \text{ h}^{-1} \text{ litre}^2 \text{ mol}^{-1}$, respectively, and the formal rate constants $k_c = k_0/[\text{Tc(VII)}]$ are 3.5, 4.1 and $4.0 \text{ h}^{-1} \text{ litre}^2 \text{ mol}^{-1}$, respectively.

The reaction is zero order with respect to hydrazine and first order with respect to technetium, which indicates that oxidation of Tc is, most likely, the rate-determining step of this process.

The rate of Tc oxidation sharply increases with time, and the process becomes autocatalytic. The autocatalytic mechanism assumes that certain products, which accelerate oxidation of hydrazine, are accumulated in the course of the reaction. Apparently, intermediate forms, *viz.*, Tc(V) and Tc(VI), serve as such products. A mathematical model was considered and kinetic calculations were performed for oxidation of hydrazine in solutions of nitric acid catalysed by technetium ions.¹³⁹

Apparently, the above-mentioned reactions proceeding in a heterogeneous system exert an effect on the completeness of reductive reextraction of plutonium by uranium(IV).

If Fe(II) is used as a reducing agent in the step of reextraction of plutonium(III), Tc is virtually completely reextracted together with Pu into the aqueous phase. The concentration of the reducing agent has a substantial effect on the extraction ability of technetium. For example, the yield of the extracted forms of Tc decreases from 28% to 6% as the concentration of Fe(II) increases from 0 to $0.1 \text{ mol litre}^{-1}$, respectively. Under these conditions, technetium is virtually not retained in the uranium-containing organic phase. In the next step of purification of plutonium extracted, Tc passes into aqueous medium-level radioactive wastes, from which Tc can be quantitatively extracted. Thus, from 94% to 98% of Tc is separated in the step of plutonium refining involved in the technology which is employed at the RT-1 plant.¹³¹

It should be noted that the PUREX process has been initially developed and used instead of the REDOX process for reprocessing of irradiated uranium metal produced for military purposes. The drawback of the REDOX process was accumulation of large quantities of high-salt wastes, which cannot be subjected to reprocessing and utilisation. The aims and problems of reprocessing changed substantially when spent nuclear fuel from nuclear power stations appeared. At nuclear power stations, spent nuclear fuel burns up to a substantial degree (from 0.5–1 to 40–100 GW days t^{-1}).¹²⁸ An increase in the degree of burn-up complicates the extraction and separation of components with the

use of TBP solutions. In the course of the extraction reprocessing of spent nuclear fuel from nuclear power stations, the behaviour of Tc (and Np) in the extraction and redox processes is of importance. Hence, the necessity of achieving the completeness of separation of actinides extracted in the presence of technetium dictates both the modern technological schemes of reprocessing of spent nuclear fuel from nuclear power stations and trends in their development.

The elaboration of the modified PUREX process that met this requirement gave rise to different technological schemes both in Russia and abroad. One of the main aims is to separate and concentrate technetium in a single flux. Of new technologies, noteworthy is a process providing the complete extraction of U, Pu, Tc and the major portion of Np, while Zr passes into a high-level radioactive raffinate due to extensive washing of the extractant.^{140, 141} The characteristic feature of this scheme is the involvement of the step of pre-reextraction of Tc with strong acid, in which 80%–85% of Tc is removed. This makes it possible to perform reductive reextraction of plutonium under the conditions of complete removal of Np together with U followed by their separation in the uranium cycle II.

The technological scheme employed at the RT-2 plant (Russia) holds promise.^{142–144} This scheme involves the coextraction of U, Np, Pu, Tc and Zr with TBP solutions as the first step, reextraction of Zr (with a portion of Np and Tc), reextraction of Pu and Np with strong acid (Tc remains in the organic phase together with uranium), reductive separation of Pu and Np with the use of U(IV) in the cycle I, reextraction of Np and Tc into a single flux using a salt-free complex-forming agent, *viz.*, acetohydroxamic acid (AHA), followed by reextraction of uranium. This is the first scheme of such a type. However, this scheme has some drawbacks, because it is rather cumbersome and has a large number of links within the cycle.

Further progress in these investigations was achieved in the study,¹⁴⁵ in which the authors proposed that the coextraction of U, Pu, Np and Tc with dilute TBP should be followed by reductive reextraction of Np and Tc with *n*-butanol and separation of Pu and U.

However, actual success was achieved only in the SuperPUREX scheme^{128, 146} (Fig. 5) involving the extraction of U, Pu, Np and Tc as well as Zr followed by reextraction of Zr together with Tc and Np under the action of hydrazine at the corresponding concentration of HNO₃. This scheme allows one to perform any modification of isolation of uranium and plutonium, *viz.*, either their deep separation and purification within a one-cycle scheme or their simultaneous reextraction in the course of processing of plutonium – uranium fuel for fast-neutron reactors.

It should be noted that the extraction of Zr together with Tc and Np provides the basis for their subsequent incorporation into matrices for radioactive waste immobilisation.¹²⁸

With the aim of intensifying the extraction reprocessing of spent nuclear fuel, scientists are looking into the possibility of using equipment with a high specific output, *viz.*, centrifugal extractors and vibrating columns, in the key operations of fuel reprocessing.

Thus, some aspects of the behaviour of U, Tc and Zr in the extraction of uranium from solutions in nitric acid with 30% TBP solutions in *n*-alkanes were examined on a column-type vibrating extractor. It was demonstrated that the uranium front was shifted to the middle part of the column in the presence of zirconium and the concentration of uranium in the raffinate increased. It was hypothesised that the hydrodynamics of the process in extractors of this type are impaired due to formation of a structure-mechanical barrier on the drop surface and retardation of coalescence. The behaviour of Tc in this process is adequately described by the mechanism of coextraction with uranium and zirconium and by the hydration–solvation mechanism. The degree of Tc extraction was ~80%. The use of hydrogen peroxide in this process leads to a decrease in the degree of Tc extraction

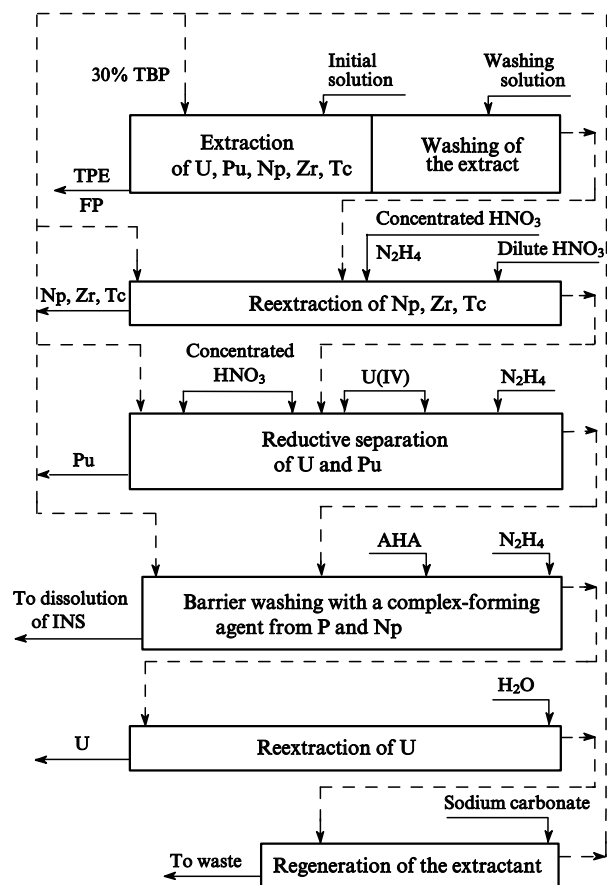


Figure 5. Scheme of the cycle I of reprocessing of spent nuclear fuel from nuclear power stations in the SuperPUREX process.¹²⁸

and reduces the influence of zirconium on the uranium extraction.¹¹¹

2. Isolation of technetium during fractionation of radiochemical wastes

All countries that develop their civil nuclear industry face the problem of fractionation of high-level radioactive wastes and separation of long-lived radionuclides. Many procedures were proposed for the extraction fractionation of wastes. Since most of the technologies developed in the last decade have been oriented primarily toward the deep separation of transuranium elements, not all processes of extraction fractionation of high-level radioactive wastes involve the step of separation of the technetium fraction. In this connection, studies of the behaviour of technetium in methods developed for the fractionation of high-level radioactive wastes are of interest.

a. Partitioning of high-level radioactive wastes using organophosphorus acids

The most well-known process of fractionation of high-level radioactive wastes involving organophosphorus acids is the technology developed at the Japan Atomic Energy Research Institute. This technology is based on the use of diisodecylphosphoric acid [(iso-C₁₀H₂₃O)P(O)OH, DIDPA] as the extractant.

This extractant is an analogue of the widely known di-2-ethylhexylphosphoric acid (D2EHPA), but it allows one to perform the process in more acidic media.

The recent version of the technological process with the use of DIDPA,¹⁴⁷ whose development was started 24 years ago, provides a way of separating the following fractions from radioactive wastes: transuranium elements (TUE); ⁹⁹Tc + platinum metals (PM); ¹³⁷Cs + ⁹⁰Sr and the remaining radionuclides.

This process involves the step of the preliminary correction of the composition of high-level radioactive wastes in the course of which the concentration of nitric acid is decreased from 2–3 mol litre⁻¹ to 0.5 mol litre⁻¹ by denitration with formic acid. This makes it possible to extract tervalent transplutonium elements (TPE). Then actinides and lanthanides are extracted with a mixture of DIDPA and TBP in *n*-dodecane. Hydrogen peroxide is added to a solution to improve the extraction of neptunium. Fission and stable elements, including technetium, platinum metals, caesium and strontium, remain primarily in the raffinate. Americium, curium and lanthanides are reextracted from the organic phase with nitric acid (4 mol litre⁻¹). Plutonium and neptunium are reextracted with oxalic acid. Uranium is extracted with sodium carbonate. The acidity of the reextract containing Am, Cm and lanthanides is again decreased from 4 mol litre⁻¹ to 0.5 mol litre⁻¹ by denitration and then these elements are extracted with a mixture of DIDPA and TBP in *n*-dodecane. Americium and curium are washed away with a mixture of diethylenetriaminepentaacetic acid (DTPA) and lactic acid. Lanthanides are washed away with nitric acid. In another modification, U and Pu are extracted with tributyl phosphate in the early step of the process and then the acidity is decreased. Then Am and Cm are extracted as described above followed by separation of lanthanides and TPE involving the reextraction of the latter with a mixture of DTPA and lactic acid. The extraction scheme is supplemented by the extraction of ⁹⁹Tc and platinum metals from the first raffinate after the extraction of all TUE by sorption on a column with activated carbon and subsequent extraction of strontium-90 and caesium-137 by inorganic ion-exchange resins (titanic acid and zeolite, respectively). The extraction affords 99.99% of Am, Cm, Pu and U and 99.95% of Np. After sorption, 99.90% of technetium and more than 99.9% of Cs and Sr are extracted. The overall volume of four fractions is 3.3 times smaller than the volume of vitrified wastes without partitioning.^{148, 149}

In the technological CTH process developed in Sweden,^{150, 151} D2EHPA is used and another way of decreasing the solution acidity is employed. Initially, U, Pu, Np and major portions of Zr, Nb, Mo and Fe are extracted with a solution of D2EHPA in a hydrocarbon diluent from a solution of high-level radioactive wastes pre-acidified to the HNO₃ concentration of 6 mol litre⁻¹. The organic phase is washed with a solution of a mixture of HNO₃ and HF to remove Zr and Nb. Then actinides are removed by ammonium carbonate. The reextract is concentrated and acidified. Then U, Pu and Np are extracted. The acidity of the first raffinate is decreased from 6 to 0.1 mol litre⁻¹ by removing nitric acid with the use of a solution of TBP in the same diluent, Pd, Ru and Tc being removed together with nitric acid. The latter elements are extracted by the ion-exchange method. Thereafter Am, Cm and lanthanides are extracted with a solution of D2EHPA followed by their reextraction with a solution of nitric acid with a rather high concentration. Caesium and strontium are isolated from the raffinate by sorption on inorganic ion-exchange resins. There is also a modification of the process, in which americium and curium are washed away by a mixture of DTPA and lactic acid, while lanthanides are washed away by nitric acid. When this scheme was tested on real high-level radioactive wastes, the factors of purification from α - and β -emitters were $\sim 10^5$ and $\sim 3 \times 10^4$, respectively.

With the aim of excluding the steps of denitration and neutralisation of a raffinate, which are involved in the two above-described processes to decrease the acidity of the high-level radioactive raffinate, a technological scheme was proposed¹⁵² for reprocessing of high-level radioactive wastes with the use of *n*-alkyl phenylphosphonic acids [PhP(O)(OH)OR, where R = *n*-C₈H₁₇–C₁₀H₂₁, (APPA)] and their zirconium salts.

The latter scheme includes two cycles. In the first of them, transplutonium and rare-earth elements are extracted from high-level radioactive wastes containing nitric acid at a concentration of 2 mol litre⁻¹ with a solution of APPA (0.9 mol litre⁻¹) in the RED-1 diluent (preferentially, 0.5 mol litre⁻¹). Transplutonium

elements are reextracted with a solution of DTPA in lactic acid. Rare-earth elements are reextracted with HNO₃ (3–5 mol litre⁻¹). In the second cycle, ⁹⁰Sr and Ca are extracted from solutions of nitric acid with a concentration of 0.1 mol litre⁻¹ by zirconium salt of APPA. It is known that zirconium improves the extraction of metals by alkylphosphonic acids.¹⁵³ Reextraction of ⁹⁰Sr and Ca is carried out using HNO₃ solutions (3–4 and 7 mol litre⁻¹, respectively). Data on the behaviour of molybdenum are lacking in the literature.

The use of APPA instead of D2EHPA made it possible to prevent the precipitation in the organic phase in the course of extraction of iron.

b. Partitioning of high-level radioactive wastes by neutral organophosphorus compounds

Mono- and bidentate neutral organophosphorus compounds (MNOPC and BNOPC, respectively) allow one to extract a series of long-lived radionuclides, including actinides and technetium, from acidic high-level radioactive wastes.

Phosphine oxide bearing different substituents [R¹R²R³P(O), PODS], where R¹, R² and R³ are the C₆H₁₃–C₉H₁₉ alkyl groups, is one of the most efficient MNOPC.

The technological scheme, which has been developed in China^{154, 155} and Germany¹⁵⁶ and tested on real high-level radioactive wastes, provides a way of extracting actinides from high-level radioactive wastes in quantitative yields (99.9%) using solutions of PODS in kerosene. Solutions of high-level radioactive wastes containing nitric acid at concentrations, generally, higher than 2.5 mol litre⁻¹, should be pre-neutralised to a concentration of no higher than 1 mol litre⁻¹. To achieve the complete extraction of neptunium, Np(V) is electrochemically oxidised to Np(IV). Technetium is extracted together with actinides and lanthanides (and also partially, with Zr and Mo), which are selectively washed away from the organic phase. Thus, Am, Cm and lanthanides are washed away with HNO₃ (5.5 mol litre⁻¹), Pu and Np (together with Zr and Mo) are washed away with oxalic acid and U (together with Tc) is washed away with sodium carbonate. The overall purification from α -emitters is $> 10^3$. Different modifications of this process have also been developed in Russia. The advantages of this method are low prices of the reagents and diluent and the possibility of the efficient extraction of Tc along with actinides.

The use of bidentate neutral organophosphorus compounds for the extraction of long-lived radionuclides, *viz.*, actinides and technetium, makes it possible to eliminate the main drawbacks of the above-described processes involving alkylphosphoric acids and monodentate neutral organophosphorus compounds, among which are the necessity of performing neutralisation of high-level radioactive wastes before the extraction of actinides and the use of solutions of nitric acid for reextraction of TPE from the organic phase. Bidentate neutral organophosphorus compounds extract actinides from acidic solutions, and TPE are reextracted with dilute solutions of nitric acid. The so-called TRUEX process developed at the Aragon National Laboratory (USA) is based on one of BNOPC, *viz.*, octylphenyl(*N,N*-diisobutylcarbamoylmethyl)phosphine oxide (C₈H₁₇)PhP(O)CH₂C(O)NBu₂ (OctPhBu₂).¹⁵⁷ Different versions of this process involving the same reagent were also developed in other countries, primarily in Japan and India.^{158, 159} Another BNOPC, *viz.*, diphenyl(*N,N*-di-*n*-butylcarbamoylmethyl)phosphine oxide (Ph₂Bu₂), is also often used in this process.

In the TRUEX process, solutions of OctPhBu₂ (0.2 mol litre⁻¹) in a mixture with TBP (1.0–1.4 mol litre⁻¹) in saturated hydrocarbons are used for the extraction of actinides and lanthanides from high-level radioactive wastes containing nitric acid at a concentration of 0.7–5 mol litre⁻¹ to which a complex-forming compound (most often, oxalic acid) is added to suppress the extraction of zirconium. After washing of the extract with a solution of a mixture of nitric acid with either aluminium nitrate or oxalic acid, transplutonium elements and lanthanides are

reextracted by dilute solutions of nitric acid. Thereafter plutonium and neptunium are extracted with a solution of ammonium carbonate or a mixture of dilute nitric acid with HF or oxalic acid. If high-level radioactive wastes contain uranium, the latter is washed away by a solution of sodium carbonate (together with Tc). The factor of purification of high-level radioactive wastes from actinides is $> 10^3$. Japanese researchers plan to improve this process with the aim of separating lanthanides and transplutonium elements by selective reextraction of the latter by a DTPA– NaNO_3 mixture.¹⁶⁰

In the Russian version of the TRUEX process developed at the Mayak Production Association, the V I Vernadsky Institute of Geochemistry and Analytical Chemistry of the Russian Academy of Sciences and the V G Khlopin Radium Institute, polar diluents are used. This makes it possible to do away with the addition of TBP and to use cheaper diphenyl(*N,N*-di-*n*-butylcarbamoylmethyl)phosphine oxide.¹⁶¹ Investigations demonstrated that Ph_2Bu_2 in polar diluents possesses higher extracting ability with respect to actinides and lanthanides than that in a mixture of hydrocarbons with TBP. The higher distribution coefficients are observed throughout the concentration range of nitric acid from 0.01 to 10 mol litre⁻¹.

The U.S. version of the TRUEX process was used for reprocessing of real wastes of different origin and with different compositions, *viz.*, wastes of analytical laboratories, wastes from reprocessing of zirconium jackets that hold the fuel rods as well as wastes from the PUREX process employed at the plutonium production plants at the Hanford Site (USA).¹⁵⁷ The Russian version of the TRUEX process was tested at the Mayak Production Association under both dynamic and static conditions with the use of simulators and real solutions of raffinates from the PUREX process and high-level radioactive wastes.¹⁶¹

c. Partitioning of high-level radioactive wastes by solutions of diamides

The process of extraction of actinides from high-level radioactive wastes by diamides of the general formula $[\text{R}^1\text{R}^2\text{NHC(O)}]_2\text{CHR}^3$, where R^1 , R^2 and R^3 are alkyl substituents, is called the DIAMEX process. Di-*n*-butyl-*N,N'*-dimethyl-*N,N'*-1,2-tetradecylmalonamide was proposed and used in France.^{162,163} The extraction properties of diamides are similar to those of bidentate neutral organophosphorus compounds, in particular, of OctPhBu_2^1 , used in the TRUEX process.

Actinides(III, IV, VI) together with lanthanides are extracted from solutions of high-level radioactive wastes containing nitric acid at concentrations of 3–5 mol litre⁻¹ to which oxomalonic acid and hydrogen peroxide are added to suppress the extraction of zirconium and molybdenum. After washing of the organic phase, actinides together with lanthanides are reextracted with a solution of nitric acid (0.5 mol litre⁻¹) and a solution of potassium nitrate (0.01 mol litre⁻¹). In addition to the DIAMEX process, a technological scheme was developed for the separation of actinides and lanthanides from dilute HNO_3 solutions by solutions of 2,6-bis(1,2,4-triazin-3-yl)pyridine with saturated hydrocarbons and octanol. This process has advantages over the known TALSPEAK and TRAMEX processes (USA) used for the separation of actinides and lanthanides, because it does not require the strict maintenance of pH and the use of salts, whereas the extraction equilibrium is rapidly reached.

d. Extraction of technetium from high-level radioactive wastes

In the best-developed procedures for the extraction of actinides from high-level radioactive wastes, no provision was made for separating fractions of other hazardous long-lived radionuclides (^{99}Tc , ^{90}Sr , ^{137}Cs and ^{129}I) within the framework of a single technological extraction scheme.

In the course of reprocessing of fuel from early Russian fast-neutron reactors, uranium was regenerated by sublimation followed by separation of fluorinated fission products by sorption with the use of fluorine condensers and columns with NaF.

Technetium was trapped by a lime absorber, thus being separated from virtually all fission products.⁷ Later on, a Russian technology was developed for the extraction of technetium from wastes from nuclear fuel reprocessing based on sorption of technetium on the AV-17 anion-exchange resin from a solution pre-neutralised to pH 7–9. The factor of purification from the fission products was $\sim 2 \times 10^2$. After desorption with concentrated nitric acid and neutralisation of the eluate, technetium was extracted with acetone. Further purification was carried out by precipitation of technetium as poorly soluble Tc_2S_7 and tetraphenylarsonium pertechnetate and their annealing under a stream of hydrogen to reduce these compounds to metal.¹⁶⁴

In recent years, the PUREX process was supplemented by a scheme of the deep recovery of technetium and neptunium in the course of extraction by tributyl phosphate together with uranium and plutonium followed by their separation and combination with the TPE + REM fraction isolated from the raffinate of the first cycle.¹⁶⁵

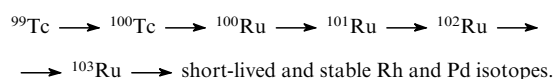
The so-called PARK process (Partitioning Conundrum Key),¹⁶⁶ which is another improved version of the PUREX process, was developed at the Japan Atomic Energy Research Institute. This scheme provides the extraction of neptunium and technetium (together with uranium and plutonium), which are subsequently separated from uranium and plutonium by two successive reextractions by a reducing agent, *viz.*, butyraldehyde, and concentrated nitric acid. In the PARK process, iodine is also removed by distillation and sorption concentration.

3. Methods for utilisation and disposal of technetium

Being a long-lived radionuclide, technetium-99 released from nuclear power stations must be extracted and reliably isolated from the biosphere. For this purpose, either the so-called transmutation of Tc, *i.e.*, the transformation of Tc into stable isotopes, is performed or Tc is incorporated into the corresponding matrices, which provides reliable isolation for thousands of years until Tc completely decays.

a. Transmutation of technetium

In full measure, technetium can be rendered harmless only by transmutation into stable nuclides under neutron irradiation. Since the ^{99}Tc nucleus has high neutron-capture cross-sections in the thermal and, particularly, epithermal energy ranges (main resonance peaks are in the range of 2–20 eV), thermal reactors, which generally have a sufficient spectral hardness ($\gamma = 0.3 \pm 0.1$), hold promise for burning this radionuclide.¹⁶⁷ In the above-mentioned neutron energy range, the process is described by the following scheme:



The contribution of other nuclear reactions is virtually insignificant. The dynamics of transmutation of the ^{99}Tc point target at $\gamma = 0.3$ is shown in Fig. 6.

The ^{100}Ru , ^{101}Ru and ^{102}Ru isotopes are stable. The ^{103}Ru isotope has a half-life of 39.3 days and decays to stable ^{103}Rh . Consequently, after the extraction of non-burned Tc from the irradiated technetium target, the product occurs as stable ruthenium with impurities of rhodium and palladium.¹⁹

It is presently assumed that technetium metal or its carbide TcC , which are rather stable at high temperatures in the absence of oxygen, are the forms of Tc most probable for transmutation. Graphite, potassium hydride, D_2O , *etc.* were proposed as neutron moderators.¹⁶⁷

In most cases, calculations of the transmutation of long-lived nuclides in modern reactors are based on the assumption that these reactors provide the conditions for the formation of an appropriate neutron spectrum and/or for an increase in the neutron flux density. Calculations of the transmutation of ^{99}Tc in light-water, thermal-water and fast reactors demonstrated that

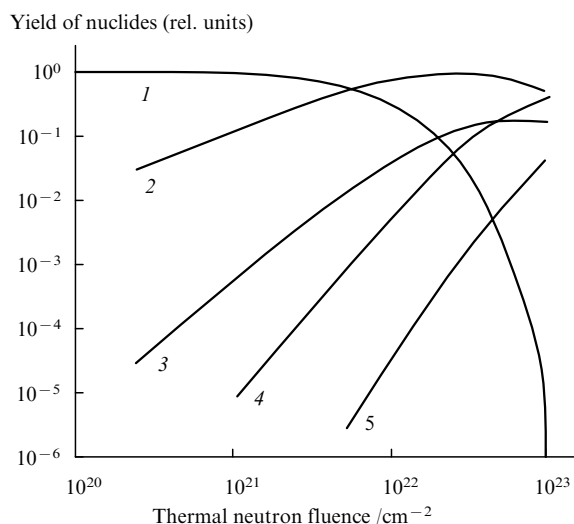


Figure 6. Dynamics of transmutation of ^{99}Tc upon thermal neutron irradiation with the spectrum hardness $\gamma = 0.3$.¹⁶⁷
(1) ^{99}Tc , (2) ^{100}Ru , (3) ^{101}Ru , (4) ^{102}Ru , (5) impurities.

this problem cannot be solved in light-water reactors. In thermal-water and fast reactors (neutron moderation), the half-life of ^{99}Tc burning varies in the range of 15–25 years at loadings of 2.5–4.0 t and the rate of transmutation of technetium of 100–140 kg year⁻¹. Simultaneously, ~20 kg of ruthenium are produced per year.¹⁶⁸ These half-lives of burning are close to half of the service life of the reactor. In addition to technetium, it is also planned to burn a series of other radionuclides, including neptunium, americium and other actinides. Energy reactors are of no use for solving this problem of transmutation. This was confirmed by irradiation of a technetium target for 193 days on the HFR research reactor in the Netherlands under conditions more favourable than those provided in a fast-neutron nuclear reactor without substantial construction changes. Irradiation of a technetium target with the use of the total neutron fluence of $1.5 \times 10^{22} \text{ cm}^{-2}$ and thermal component of $2.5 \times 10^{21} \text{ cm}^{-2}$ led to the burn-up of only ~5% of ^{99}Tc .¹⁶⁹

Hence, it is necessary to design special fast-flux transmutation systems providing a high rate of transmutation of technetium into stable nuclei to burn-up ^{99}Tc . In the experiments carried out at the Scientific Research Institute of Atomic Reactors (Dimitrovgrad, Russia) on an SM-3 experimental reactor, a much higher degree of technetium burning was achieved (under particular conditions, up to 15%).¹⁷⁰

Apparently, the full-scale solution of the problem of ^{99}Tc burning should involve one of the modes of transmutation of early actinides using their irradiation with thermal neutron fluxes with the density of $10^{15} - 10^{16} \text{ cm}^{-2} \text{ s}^{-1}$.¹⁷¹ In the Accelerator-Driven Transmutation of Waste (ATW) Programme (USA) and the ACTINEX Subprogramme of the SPIN Programme of the French National Agency for Radioactive Waste Management,¹⁷² the possibility of the simultaneous burning of minor actinides and ^{99}Tc as well as of some other nuclides was considered.^{173, 174} The transmutation of ^{99}Tc not only makes it possible to convert it into the safe form but also serves as a source of the valuable metal of the platinum group, *viz.*, stable ruthenium, which is used in the electronics and electrotechnical industry (the price of ruthenium is ~\$10 per gramme).¹⁷⁵ The total reserves of ruthenium in ores are estimated at ~3100 t, whereas the world demand for this element is about 7.4 t per year and is close to the rate of accumulation of ^{99}Tc in nuclear power engineering.¹⁷⁶

b. Incorporation of technetium into solid matrices

One of the procedures for isolating technetium from the biosphere is based on its cementation to form matrices stable on storage.

These studies were carried out at the Savannah River Site (USA).¹²⁵ It appeared that technetium-containing cement matrices are unstable upon storage because they include Tc as pertechnetate ions readily soluble in water. Hence, cementation of technetium-containing high-level radioactive wastes requires the transformation of technetium into a water-insoluble form, for example, into TcO_2 . Either an ash or additives of FeS or Na_2S can be used as reducing agents. These reagents reduce pertechnetate to a stable form with equal ease. However, it was believed¹²⁵ that only partial reduction of Tc(VII) to Tc(IV) could be achieved with the use of these reagents. Hence, this process is not sufficiently efficient.

Incorporation of technetium into a cement-like matrix, such as bentonite, also does not lead to stabilisation of Tc. For example, up to 40% of technetium is leached when the matrix is exposed to water during 20 days. Thereafter, the rate of leaching decreases due, apparently, to the formation of a new mineral phase involving technetium.^{173, 177} It is believed that cement based on Al oxides without bentonite is more stable than a mixed cement.¹⁷³ The best results were obtained with the use of cement annealed in a furnace. However, all the above-mentioned materials appeared to be unstable, as a result of which cementation methods were rejected. Hence, the examination of new ceramic, mineral-like or other matrices for reliable disposal of technetium remains an urgent problem.

VI. Behaviour of technetium in environmental objects

1. Main sources of the release of technetium into the environment

Problems associated with the control of the behaviour of technetium in the environment are becoming increasingly important.^{178, 179} The ^{99}Tc isotope has accumulated in the geosphere since the 1950s. This isotope is one of the long-lived radionuclides released into the environment (along with ^{14}C and ^{129}I).

The main sources of the release of Tc into the environment are nuclear weapons testing (180 TBq), wastes from nuclear power stations (4 GBq), atmospheric fallout after the Chernobyl accident (0.75 TBq) and wastes from nuclear fuel processing plants.^{180–182} One more source of the release of technetium into the environment to the use of $^{99\text{m}}\text{Tc}$ in medicine, the scale of which will increase.¹⁸³

The world annual accumulation of Tc from nuclear power station operation is about 6 t, and ~60 t of Tc have already been produced.¹ An increase in the degree of burn-out of nuclear fuel will lead to further accumulation of technetium. Hence, one would expect that the contribution of technetium to the population radiation dose will be substantially increased with the development of nuclear power engineering. For example, the level of ^{99}Tc contamination of forest soil in the 30-km zone around the Chernobyl reactor is ~1.1–14.1 Bq kg⁻¹.^{184–187}

2. Forms of the existence of technetium in environmental objects

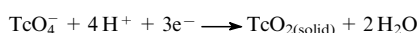
Forms of the existence of technetium in a multicomponent system of the geological medium depend primarily on the following factors: the redox potential (E_h) and pH of the system, interactions with inorganic compounds, the influence of organic complex-forming agents and microorganism action.

The redox conditions in the geological medium are responsible for stabilisation of technetium in particular oxidation states and forms of its occurrence. The $\text{Fe}^{2+} - \text{e}^- = \text{Fe}^{3+}$ ($E^\circ = 0.77 \text{ V}$) and $\text{O}_2 + 4\text{e}^- + 2\text{H}_2\text{O} = 4\text{OH}^-$ ($E^\circ = 0.401 \text{ V}$) pairs are the main potential-forming pairs having influence on the redox behaviour of technetium in environmental objects.

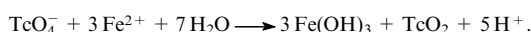
Iron is involved in many rock-forming minerals. In the areas with a low water exchange or under anaerobic conditions, iron is stabilised as Fe(II) . The reduced form of iron loses stability when exposed to atmospheric oxygen (aerobic conditions) dissolved in

groundwaters in the zone of active water exchange and stabilises in the Fe(III) state.

The formal oxidation potential of the pair



is higher than 0.8 V.^{101, 188} In the zone of a low water exchange and in its absence, TcO_4^- can be reduced to Tc(IV) in groundwaters according to the reaction



Electrophoresis measurements and atomic absorption spectroscopy revealed the presence of the following forms of Tc(IV) under reducing conditions and at alkaline pH: TcO^{2+} , $\text{TcO}(\text{OH})^+$, $\text{TcO}(\text{OH})_2$, $\text{TcO}_2 \cdot 2\text{H}_2\text{O}$ and $\text{TcO}_2 \cdot n\text{H}_2\text{O}$ (Fig. 7). These forms of technetium would be expected to undergo hydrolytic adsorption or co-precipitation on Fe(III) hydroxide to give complexes with Fe—O—Tc bonds.^{189, 190}

Under aerobic conditions, Tc(IV), occurring in the form of TcO_2 in aqueous solutions, is oxidised by atmospheric oxygen to Tc(VII) with a rate of ~ 1 mass % during two months followed by

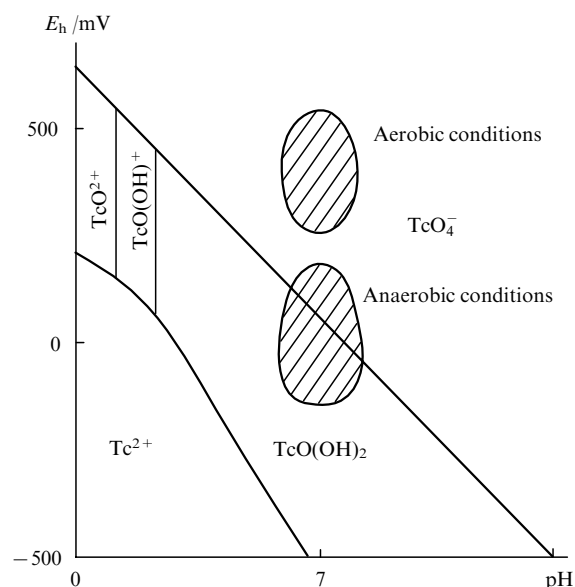


Figure 7. Forms of the existence of technetium in an aqueous solution depending on E_h and pH.⁶⁵

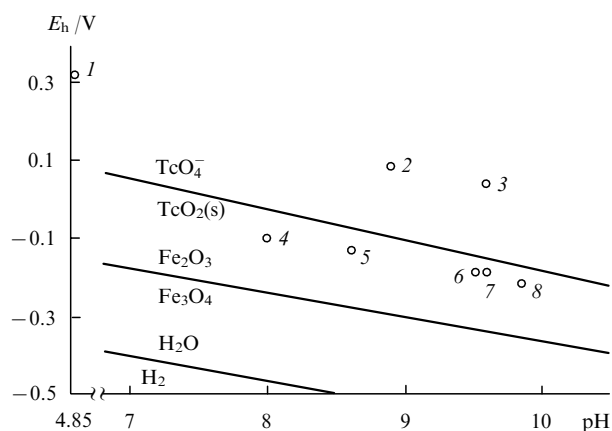


Figure 8. Effect of E_h and pH on the redox equilibrium $\text{Tc(VII)} \rightleftharpoons \text{Tc(IV)}$ in a rock–water system. Samples of argillaceous slates or clays (Conasauga, USA) (1–3); granites: Westerly granite, USA (4, 7); Climax Stock granite, USA (6); Sentinel Gap basalts, USA (5, 8).¹⁹¹

dissolution of the precipitate.⁶⁵ The resulting pertechnetate ions are quite stable under aerobic acidic, neutral or alkaline conditions.

The data from the E_h –pH diagram are widely used for the prediction of the sorption behaviour of Tc in environmental objects. By way of example, let us consider the results of the determination of the Tc(VII)–Tc(IV) redox equilibrium, which depends on E_h and pH and was calculated taking into account the maximum allowable (in USA) concentration of technetium in drinking water ($0.3 \mu\text{Ci litre}^{-1}$)^{191, 192} (Fig. 8). Under real geological conditions, Tc in groundwaters is stabilised in the tetravalent state and is sorbed onto different granites (New Hampshire, USA) and basalts (Mattawan, USA). By contrast, technetium in argillaceous slates or clays (Catasauqua, USA) occurs as pertechnetate ions and is not sorbed onto soils.

Data on the complex formation of technetium with inorganic and organic ligands are of great interest.

a. Sulfide ions

In addition to $\text{TcO}_2 \cdot n\text{H}_2\text{O}$, other stable technetium compounds, for example, Tc sulfides, can also be sorbed onto soil (Fig. 9). Technetium(IV) sulfide TcS_2 is precipitated by hydrogen sulfide generated upon plant degradation. Natural sulfur-containing organic compounds serve as another source of sulfide ions in water-saturated soil.^{183, 193}

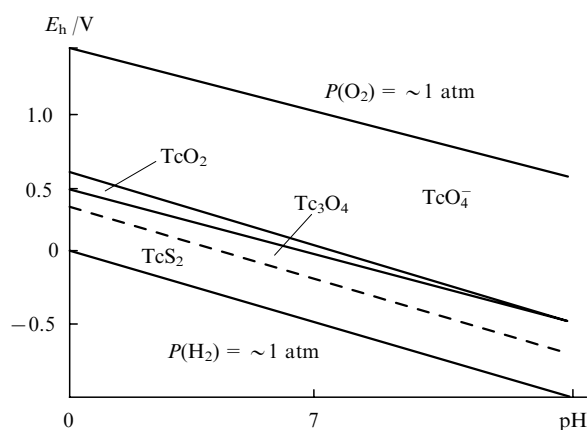


Figure 9. Behaviour of Tc in the Tc–S–OH system, 25 °C, ~ 1 atm (thermodynamic data).¹⁹³

Technetium(IV) sulfide is also formed upon reductive precipitation of the TcO_4^- ions onto the FeS surface in a rock layer. The structures of the mixed FeS–Tc(VII) and FeS–Tc(IV) compounds were studied by EXAFS spectroscopy and it was found that technetium is present as an individual phase structurally similar to TcS_2 rather than being incorporated into the FeS phase.^{191, 194}

The reaction of the TcO_4^- and S^{2-} ions in a solution of Na_2S afforded technetium(VII) sulfide Tc_2S_7 , the type of the precipitate being dependent on the concentration of sodium sulfide. If the concentration of $\text{Na}_2\text{S} > 0.33 \text{ mol litre}^{-1}$, large precipitate particles form spontaneously. At lower concentrations of sodium sulfide, a suspension of colloidal Tc_2S_7 is produced, the formation of the suspension being completed within ~ 3 days.¹⁹⁵ The solubility of Tc_2S_7 in water is $0.257 \text{ g litre}^{-1}$.⁹⁰

b. Carbonate ions

Only in carbonates (unlike many other aqueous media), internal γ -irradiation of Tc(VII) samples does not lead to its self-reduction to Tc(IV). The possible reoxidation of Tc(IV) to Tc(VII) is accounted for by the fact that radiolysis in solution affords $\text{CO}_3^\cdot$ radicals, which can transform technetium into the heptavalent state.^{23, 121}

c. Humic acids

It is assumed that technetium in deep beds of groundwater occurs primarily in complexes with humic acids (Tc–HA). Their percentage was estimated at ~50–70% (Fig. 10).^{196–199}

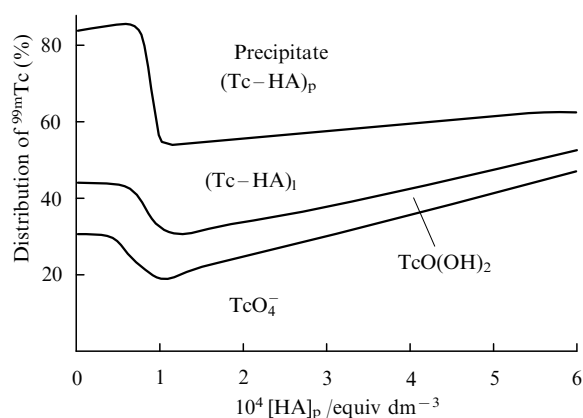


Figure 10. Different forms of the existence of ^{95m}Tc depending on the initial concentration of humic acids $[\text{HA}]_0$ at $[\text{Sn}^{2+}] = 10^{-5}$ mol litre $^{-1}$.¹⁹⁶

The indices 'p' and 'l' correspond to the precipitate and mother liquor, respectively.

The compositions of the complexes depend on the pH of the solution, concentration of humic acids, salt background and the presence of reducing agents. Under aerobic conditions, the Tc–HA complexes in solutions of pH 9–11 occur as poorly soluble precipitates. An increase in the salt background leads to suppression of Tc sorption on minerals. The presence of reducing agents [hydrazine and Fe(II)] gives rise to readily sorbable forms and a precipitate of hydrated TcO_2 .¹⁹⁶

Finally, microorganisms also have an effect on the forms of the existence of Tc in environmental objects. Microorganisms absorb oxygen dissolved in water and shift the redox equilibrium in the system to small E_h .^{200, 201}

3. Sorption of technetium on natural materials

In studies of the sorption of technetium by natural systems, the following three types of processes should be taken into account: sorption on the outer surface of solid particles, sorption on porous particles and irreversible precipitation or coprecipitation.²⁰²

Under aerobic conditions, sorption of technetium by natural minerals is low. At pH 6, the distribution coefficients $K_d^{\text{Tc(VII)}}$ were determined for sandstone ($2.57 \text{ cm}^3 \text{ g}^{-1}$), peat ($1.89 \text{ cm}^3 \text{ g}^{-1}$), feldspar ($1.66 \text{ cm}^3 \text{ g}^{-1}$), phosphorite ($1.05 \text{ cm}^3 \text{ g}^{-1}$), bauxite, basalt ($0.98\text{--}1.01 \text{ cm}^3 \text{ g}^{-1}$) and pyrite ($0.32 \text{ cm}^3 \text{ g}^{-1}$).⁹⁰ At pH 5.8–7.4, the coefficients of sorption of Tc on minerals decrease by a factor of $\sim 10^4$ as E_h in solution increases from 180 to 220 mV (Fig. 11).^{65, 203–205}

It is assumed that technetium occurs as the TcO_4^- anions, which are poorly adsorbed on different rocks, in aerated solutions with high E_h . This assumption was supported by studies of the extraction of technetium by tetraphenylarsonium chloride. It was also demonstrated that colloidal particles of Tc do not occur in solution, which was confirmed by ultrafiltration of solutions.^{65, 189, 204}

It is known that $K_d^{\text{Tc(VII)}}$ is proportional to the initial concentration of TcO_4^- and depends only slightly on the specific surface of the sample. Hence, it was hypothesised^{65, 130, 189, 205} that technetium in deep layers is stabilised as $\text{TcO}(\text{OH})_2$ or TcO_2 under anaerobic conditions at reduction potentials E_h and its sorption by minerals is, apparently, associated with irreversible precipitation of poorly soluble forms of Tc(IV).^{89, 205} To test this assumption, experiments were carried out on sorption of technetium(VII) from flowing groundwater (pH 9; $E_h = 158 \text{ mV}$; conductivity $1340 \mu\text{S cm}^{-1}$) by finely dispersed (180–850 μm) strongly metamorphosed rocks taken from the fracturing zone at a depth of 250 m without contact with the atmosphere.²⁰³ The material filling the column consisted of quartz, alkaline feldspar, plagioclase, biotite, chlorite and trace amounts of magnetite. It was found that about 40% of technetium was sorbed on fractions of ferrous minerals, which are composed primarily of biotite and other so-called mafic minerals, such as hematite, magnetite and iron hydroxides (7% of the overall weight). It was demonstrated that sorption on mafic minerals occurs through chemisorption rather than being due to precipitation in the bulk of groundwater.²⁰³ It can be assumed that sorption of technetium proceeds in two steps, *i.e.*, through reduction of Tc(VII) to Tc(IV) by divalent iron present in rocks and chemisorption on their surfaces. This assumption was confirmed by the results of the studies,^{101, 189, 194, 199, 206, 207} in which it was found that technetium(VII) was not sorbed by Fe(III)-containing minerals, whereas sorption of TcO_4^- increased on Fe(II)-containing minerals.

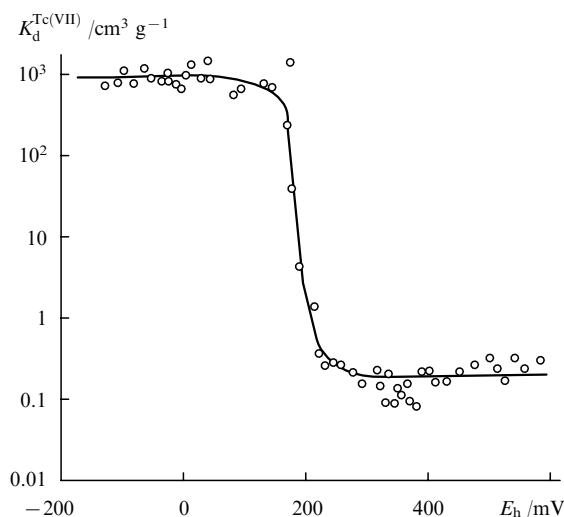


Figure 11. Plot of the coefficient of sorption of technetium by minerals from solutions of groundwaters (pH 5.8–7.4) vs. E_h . $[\text{TcO}_4^-] = 10^{-6}$ mol litre $^{-1}$. The ratio of the volume of the solution to the weight of the sample is $2.5 \text{ cm}^3 \text{ g}^{-1}$.⁶⁵

tium(VII) from flowing groundwater (pH 9; $E_h = 158 \text{ mV}$; conductivity $1340 \mu\text{S cm}^{-1}$) by finely dispersed (180–850 μm) strongly metamorphosed rocks taken from the fracturing zone at a depth of 250 m without contact with the atmosphere.²⁰³ The material filling the column consisted of quartz, alkaline feldspar, plagioclase, biotite, chlorite and trace amounts of magnetite. It was found that about 40% of technetium was sorbed on fractions of ferrous minerals, which are composed primarily of biotite and other so-called mafic minerals, such as hematite, magnetite and iron hydroxides (7% of the overall weight). It was demonstrated that sorption on mafic minerals occurs through chemisorption rather than being due to precipitation in the bulk of groundwater.²⁰³ It can be assumed that sorption of technetium proceeds in two steps, *i.e.*, through reduction of Tc(VII) to Tc(IV) by divalent iron present in rocks and chemisorption on their surfaces. This assumption was confirmed by the results of the studies,^{101, 189, 194, 199, 206, 207} in which it was found that technetium(VII) was not sorbed by Fe(III)-containing minerals, whereas sorption of TcO_4^- increased on Fe(II)-containing minerals.

Sorption of Tc on samples of soils taken in the region of the production site of the Mayak Production Association was studied (Table 5).¹⁹⁹ It was demonstrated that the distribution coefficients of technetium in water–soil sample systems $[K_d^{\text{Tc(VII)}}]$ depend on the content of organic components in the soil. Thus, the distribution coefficients $K_d^{\text{Tc(VII)}}$, which are in the range of $\sim 6\text{--}$

Table 5. Coefficients of sorption of Tc in soil–water systems.¹⁹⁹

Sample	Organic component (%)	pH after sorption	$K_d^{\text{Tc(VII)}}$ / $\text{cm}^3 \text{ g}^{-1}$
Sand	0	7.1	10
Kaolin clay	0	7.5	12
Loam	2	7.3	14
Grey soil	5	7.3	18
Humus	35	6.9	25
Bottomset bed (Uvildy lake)	43	7.4	30
Deciduous foliage (birch)	52	7.2	140
Mushroom chitin	—	6.5	39

Note. The starting concentration of technetium was 45 mg litre^{-1} , $V/m = 50 \text{ cm}^3 \text{ g}^{-1}$, 20°C , the duration of the contact was 8 weeks.

$12 \text{ cm}^3 \text{ g}^{-1}$ for samples of sand and kaolin clay devoid of organic compounds, slowly increase as the percentage of the organic component increases. High distribution coefficients of Tc in soil samples were observed for humus ($25 \text{ cm}^3 \text{ g}^{-1}$) and bottomset beds ($30 \text{ cm}^3 \text{ g}^{-1}$) containing organic components (algae, fungi, etc.). Biosorption by bacterial cell walls and fungal melanins makes the major contribution to bioaccumulation of Tc. Thus, the anomalously high coefficient $K_d^{\text{Tc(VII)}} = 140 \text{ cm}^3 \text{ g}^{-1}$ was found for deciduous foliage.

Hence, the available experimental data indicate that, occurring in the anionic form at high reduction potentials E_h , technetium is very poorly sorbed by minerals. Apparently, the fixation of technetium by soils and rocks under reductive conditions results, primarily, from chemical precipitation.²⁰⁸ An increase in $K_d^{\text{Tc(VII)}}$ for samples containing organic compounds is proportional to their percentage. Taking into account that organic components of soil are, primarily, humus and various cell organisms and that humus, in turn, consists of humine and humic acids, it was hypothesised¹⁹⁹ that it is these components that are favourable for active fixation of Tc by soil samples.

4. Diffusion properties of technetium

It is commonly assumed that ^{99}Tc possesses high mobility in environmental waters. As mentioned above, oxidised technetium occurs in the water-soluble anionic form and is sorbed by neither minerals nor clay–sand soils to a noticeable degree. According to in-field observations,²⁰³ technetium can be transferred by ground-water through the water-bearing sand bed in the form of TcO_4^- ions.²⁰⁹ In the case of crystalline rocks, water-filled cracks serve primarily as migration channels. Generally, walls of these cracks are covered with a layer of metamorphised minerals. It was demonstrated that the coefficient of diffusion of $^{99}\text{TcO}_4^-$ in samples of metamorphised granite and bentonite taken from the fractured zone of Precambrian batonite at a depth of about 250 m is $1.4 \times 10^{-12} \text{ m}^2 \text{ s}^{-1}$.^{117,210}

5. Distribution of technetium in the World Ocean

The World Ocean serves as an indicator of the ecological state of the main Earth shells. Hence, data on the presence of particular pollutants, including radionuclides released into the hydrosphere, in the World Ocean are of great importance.

The specific activities of ^{99}Tc in coastal sea waters of the World Ocean are presented in Fig. 12. In seas and the Pacific Ocean, the specific activities are in the ranges of 1.0–7.4 and 0.49–3.33 $\mu\text{Bq litre}^{-1}$, respectively. The ^{99}Tc concentrations in the Irish Sea and the North Sea are higher than the average level due to their pollution with industrial wastes from the Sellafield plant, where spent nuclear fuel is reprocessed. The authors of the

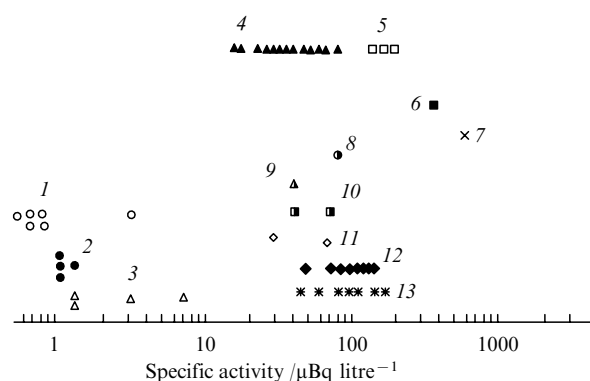


Figure 12. Specific activity of ^{99}Tc in waters from different seas.¹¹³ (1–3) Pacific Ocean (1, 1992; 2 and 3, 1993); (4) and (5) Baltic Sea [4, 1986, 5, 1988]; (6), Norwegian Sea (1980); (7) Barents Sea (1980); (8) Greenland Sea (1988); (9) Davis Strait (1984); (10) Baltic Sea (1983, 1986); (11) Mediterranean Sea (1985–1987); (12) and (13) Japan Sea (1987).

study¹¹³ believed that the occurrence of Tc in other regions of the World Ocean is associated primarily with the global fallout.

Being constant in different regions of the World Ocean, the activity ratio $^{99}\text{Tc}/^{137}\text{Cs} = (2.7 \pm 0.6) \times 10^{-4}$ depends on the release of fission products from nuclear explosions, mechanical dispersion of nuclear explosion products and chemical and physical fractionation of radionuclides.

6. Behaviour of technetium in biosystems

The behaviour of technetium in biosystems has been studied in detail. Most of the available data indicate that Tc is readily transferred from soils (or waters) into plants or organisms under anaerobic conditions, which is, apparently, associated with high solubility of pertechnetates and their mobility in soils.^{88, 210–212} It was demonstrated^{106, 211, 213, 214} that the mechanism of transfer of Tc into biosystems involves the transport of TcO_4^- through a plant cell membrane⁸⁹ (energy consumption is $\sim 9.4 \text{ kJ mol}^{-1}$) as the first step²¹¹ followed by photoreduction of Tc(VII) to Tc(IV) in chloroplasts by plant gelatin serving as the complex-forming reducing agent present in plants.¹⁰⁶

The equilibrium concentration of Tc in a biomass, for example, in duckweed *Lemna minor*, is established very rapidly (already within 2 h). The kinetics of bioaccumulation of Tc in plants depends on the intensity of their illumination, the concentrations of technetium and nitrate ions in solution and temperature. At 25°C , the rate of Tc reduction under solar illumination is close to $200 \mu\text{mol m}^{-2} \text{ s}^{-1}$.²¹¹

Generally, the absorption of radionuclides from soil by vegetables is characterised by the transport factor (TF)^{126, 215, 216} or concentration factor (CF), which are determined as the ratio of the radionuclide concentration in a fresh plant to its concentration in dry soil (Bq kg^{-1}). The transport factor is among the most important parameters used for the estimation of the intake of radionuclides into the human body. The transport factors depend on the nature of the plant. For example, the transport factors for foliar vegetables are much higher than those for root vegetables. The transport factors for old leaves are much higher than those for young leaves. Since root and stalk tissues cannot retain technetium that enters into plants, it is transferred to leaves and accumulated there when water is evaporated. Apparently, the transfer of technetium together with photosynthesis products, for example, with carbohydrates, from leaves to tubers, fruits and follicles is insignificant.

As can be seen from Table 6, the transport factor of technetium calculated for the weight of dry samples of the plants under

Table 6. Transport factors of ^{99}Tc (Bq kg^{-1}) from soil to different organs of vegetables (radionuclide label was introduced into soil when cropping).²¹⁵

Plant	Non-edible part/ edible part	TF / Bq kg^{-1}	
		wet plant	dry plant
Lettuce (<i>Lactuca sativa</i> L.)	lower/upper leaves	16/2	340/26
Sweet pepper (<i>Capsicum annuum</i> L.)	old leaves/fruits	30/0.03	184/0.03
Aubergine (<i>Solanum melongena</i> L.)	old leaves/fruits	5/0.01	22/0.1
Kidney bean (<i>Phaseolus vulgaris</i>)	old leaves/follicles	16/0.02	127/0.2
Cauliflower (<i>Brassica oleracea</i> L. var. botrytis)	lower leaves/flowers	135/0.1	456/0.9
Yam (<i>Dioscorea japonica</i> Thunb)	leaves/tubers	—/1	218/4
Soya (<i>Glycine max</i> L.)	leaves/legumes	—/—	1416/0.8

examination changes from 5 to 1416 Bq kg⁻¹ (dry soya leaves)²¹⁵ and even to 2600 Bq kg⁻¹ (dry spinach leaves).¹²⁶

It is reasonable to compare the above-mentioned transport factors of Tc into edible parts of plants with the safe level of technetium recommended by the International Atomic Energy Agency (5 Bq kg⁻¹).

Of sea organisms, annelida (*Fucus serratus*, **I**), crustacea (*Perinereis cultrifera*, **II**) and brown algae (kelps) (*Homarus gammarus*, **III**) intensively accumulate Tc. The corresponding concentration factors are 1500 (**I**), 1200 (**II**) and 1000 Bq kg⁻¹ (**III**). The concentration factors for other sea plants and animals (fish, shellfish, phytoplankton, etc.) are much lower (1–10 Bq kg⁻¹). In studies of the concentrations of Tc in sea organisms taken in the region of the La Hague Strait (European Continent), the following concentration factors were found: 44.4, 155.4 and 125.8 Bq kg⁻¹ for **I**, **II** and **III**, respectively. The concentrations of technetium in fish, for example, in *Blenius pholis* or *Labrus bergultra*, varied from 0.92 to 1.48 Bq kg⁻¹, respectively.²¹⁷

Microorganisms readily adsorb technetium through interactions with the sulfur atoms of amino acids and proteins. From this viewpoint, Tc is similar to iodine, which also readily interacts with microorganisms. For example, the data on bioaccumulation of Tc and other long-lived radionuclides by bottom sediments from different basins under the action of microorganisms were analysed in the studies.^{200, 202, 217–223}

7. Influence of radiolysis on the behaviour of Tc in environmental objects

It is known that the migration properties of Tc and other radionuclides in the biosphere can depend on self-irradiation of the samples, which has an effect on the stability of their oxidation state and diffusion in geological formations.^{23, 121} For example, γ -irradiation of solutions of Tc(VII) leads to its reduction to Tc(IV) depending on the composition of the medium. It was demonstrated that a neutral solution of TcO₄⁻ turned brown and TcO₂ or TcO₂ · nH₂O colloidal particles with the grain size of 30–130 nm formed at the irradiation dose of 2 kGy. In deaerated solutions, TcO₄⁻ is reduced at lower doses. It was found that the yield decreased in the course of reduction with increasing concentration of carbonate ions in solution.²²⁴

VII. Use of technetium in technological processes and medicine

1. Catalytic properties

The catalytic activity of technetium metal has been predicted by Balandin²²⁵ on the basis of a sextet model of dehydrogenation of cyclohexane. Since technetium metal has a hexagonal crystal structure and the smallest distance between the atoms (~2.74 Å) is in the range of distances for known catalysts (2.49 Å for Ni or 2.77 Å for Pt), it should serve as a catalyst for the transformations of six-membered cyclic hydrocarbons.

It was demonstrated that a catalyst containing 1 mass % of Tc on SiO₂ or Al₂O₃ support, like a rhenium catalyst, accelerates hydrogenation of benzene to form cyclohexane and hydrogenolysis of benzene at 100–350 °C, the best results being achieved with the use of γ -Al₂O₃ as the support.²²⁶ In the above-mentioned processes, the specific catalytic activity of metals changes in the series Ru > Pt > Tc > Pd > Re and Ru > Tc > Re.^{227, 228}

The promotion action of technetium was studied in hydrogenation and dehydrogenation of hydrocarbons on applied catalysts based on platinum metals (Pt, Pd, Rh, Ru).^{229–231} It was found that the catalytic activity was substantially increased upon the addition of technetium (synergistic effect). The physicochemical properties of technetium-metal catalysts were examined.

Technetium serves as a catalyst for hydrogenation of anhydrides (for example, the transformation of succinaldehyde into tetrahydrofuran²³²), conversion of aliphatic hydrocarbons (for

example, dehydrocyclisation of heptane to form toluene²³³) and decomposition of aliphatic alcohols to hydrogen and the corresponding aldehyde.²²⁶

The Standard Oil Corp. (USA) developed catalysts involving technetium and its dioxide as the activator for petroleum reforming, and these catalysts were covered by patents. The concentration of technetium on an Al₂O₃ support was 0.01%–0.2%. The noble metal served as the major component.²³⁴

Catalysts based on complex Tc compounds are of particular interest from both the theoretical and practical standpoints. In many cases, these compounds proved to be more efficient than catalysts based on metals or their oxides.²³⁵ One of the most promising applications of complex catalysts is the activation of molecular nitrogen, which opens up possibilities for the direct synthesis of ammonia under mild conditions. For example, the complex technetium compound with composition TcCl₄(PPh₃)₂ catalyses reduction of molecular nitrogen to ammonia under the action of lithium naphthalide.²³⁶

2. Superconducting properties of technetium and its compounds

The superconductivity of technetium was discovered in 1953 when studying the magnetic susceptibility of powdered metal with purity of no lower than 99.9%.²³⁷ The superconducting transition begins at 11.2 K and is completed at 7.7–7.8 K. Hence, technetium is the second best superconductor, exceeded only by niobium ($T_c = 9.25 \pm 0.02$ K). Technetium differs from other metals in the degree of anisotropy of the superconducting properties. Technetium is the only representative of type II superconductors belonging to the hexagonal system.²³⁸ It should be noted that although Tc in the bulk state is somewhat inferior to niobium as a superconductor, its films exhibit better superconducting properties. Superconducting Tc films have obvious advantages over niobium films. That was the reason why technetium was chosen as a material for superconducting RF cavities for an accelerator in the USA.²³⁹

Technetium is of interest because its alloys combine phases typical of rhenium and manganese. Since technetium alloys can simultaneously possess physical properties exhibited by rhenium and manganese alloys, they can be considered as materials with special properties.²⁴⁰ The so-called 'rhenium effect' is of obvious interest for superconducting technetium-based materials. This effect lies in the fact that both the strength and plasticity of the metal increase simultaneously upon the addition of Tc or Re.²⁴¹

An alloy containing 5%–75% of Mo is the first commercial Tc-containing alloy (Western Electric Company, USA; covered by a UK patent), which can be used for the construction of electromagnets.²⁴²

3. Technetium as an inhibitor of corrosion

High inhibiting ability of the pertechnetate ion was first established by Cartledge as early as 1955^{243–245} and then confirmed by investigations of Russian researchers.^{246–248} It was demonstrated that the pertechnetate ion (like other known inhibitors of the MO₄ⁿ⁻ type, where M = Cr, Mo or W) is among the most efficient inhibitors of corrosion of carbon and stainless steels, the action of TcO₄⁻ being observed even at a concentration of ~10⁻⁵ mol litre⁻¹ at 250 °C.²⁴³ It was established that the mechanism of action of TcO₄⁻ is identical to that of CrO₄²⁻ and WO₄²⁻.²⁴⁹ However, the required protective concentration of the pertechnetate ions is ~10 times lower.²⁵⁰ Besides, the TcO₄⁻ ion is more resistant to radiation than the CrO₄²⁻ and WO₄²⁻ ions. These results opened up possibilities for the use of Tc as an inhibitor of corrosion of water-cooled nuclear reactors. Thus, K₂TcO₄ (0.5 kg) was introduced into the bulk of a D₂O core coolant (47 m³) to prevent corrosion of the CANDU energy reactor with an output of 200 MW.²⁵¹

Technetium coatings were also proposed for the protection of the underside of oceangoing ship hulls from microorganisms.²⁵² The commercial Technetium Corp. (USA) established in 1976 was

aimed at extending business activity in the design, use, sale and licensing of technetium coatings for their application in marine and industrial media.

4. Use of technetium compounds in medicine

Radionuclide methods of examination and treatment are widely used in different fields of scientific and practical medicine. Radionuclides used in these fields and the corresponding radiopharmaceuticals based on them are classified as diagnostic therapeutic according to the areas of their application. Diagnostic radiopharmaceuticals, in turn, are divided into groups of radionuclides for single photon emission computed tomography (SPECT, γ -emitters with energies in the range of 100–200 keV and half-lives from several minutes to several days) and positron emission tomography (β^+ -emitters with half-lives from several seconds to several hours). In the last two decades, the overwhelming majority of diagnostic procedures (up to 80%) employing the SPECT technique were carried out with the use of radiopharmaceuticals containing ^{99m}Tc (see Refs 253, 254), which is called the 'work horse' of nuclear medicine.²⁵⁵

The ^{99m}Tc isotope belongs to the category of short-lived isotopes, whose application allows one to study the same object repeatedly at short intervals without overirradiation.

Numerous studies demonstrated that ^{99m}Tc can be used for the diagnosis of diseases of the liver, thyroid,²⁵⁶ kidneys and adrenals,²⁵⁷ spleen,²⁵⁶ respiratory system,²⁵⁸ cerebrum,²⁵⁶ spinal cord,²⁵⁹ bone marrow,²⁶⁰ salivary glands, digestive system,²⁵⁶ bones and joints of the skeleton²⁶¹ and also for studies of the physiological functions of the cardiovascular system,²⁵⁶ lymphatic system²⁶² and urological system,²⁶³ investigations of the glomerular filtration rate and plasma volume.^{264,265} In addition, ^{99m}Tc can be used for examining internal cavities,²⁶⁶ infectious heart diseases,²⁶⁷ infectious brain diseases,²⁶⁸ infectious eye diseases,²⁶⁹ infectious dermal diseases²⁷⁰ and skin transplantation.²⁷¹

The synthesis of efficient ^{99m}Tc radiopharmaceuticals is of considerable importance for using technetium in medicine. In Russia, a methodology was developed for the design of generators for ^{99m}Tc and technological schedules were applied to the production of various radiopharmaceuticals, among which are $^{99m}\text{TcO}_4^-$, ^{99m}Tc citrate, groups of colloidal ^{99m}Tc pharmaceuticals, etc.^{272,273}

Pharmaceuticals containing ^{99m}Tc are prepared in different forms specific for particular organs, groups of organs or systems. The possibility of the use of a drug for the diagnosis of diseases of a particular organ depends substantially on both the oxidation state of the radioactive label and the properties of the drug into which it is incorporated.

Radiopharmaceuticals containing ^{99m}Tc can be divided into three groups according to their biological specificity: Na or K pertechnetates, technetium(VII) complexes with various ligands and technetium(IV) complexes with various ligands. Sodium pertechnetate is accumulated primarily in glandular organs of the human body, viz., in the thyroid gland, gonads, parotid gland and kidneys.²⁷⁴ Since the pertechnetate ion is biologically non-specific, radiopharmaceuticals of the first group can be used for the diagnosis of almost all organs and systems. These pharmaceuticals are removed from the organism during one day.²⁵⁵ In the radiopharmaceuticals of the second group, which are more biologically specific than pertechnetate, Tc is involved in micelles in the hepta- or tetravalent state.^{275,276} The third group containing  the largest number of representatives includes complex compounds, which are prepared by reduction of the pertechnetate ion to lower oxidation states. The biological specificity of Tc complexes is most pronounced. Many of these complexes involve organic compounds of different classes, viz., alcohols, sugars, nucleic acids, nucleoproteins, amino sugars, polysaccharides, drugs containing phytin, penicillamine acetazolamide, bleomycin, dihydrothioctic, glucoheptonic, gluconic and other acids^{94,276} as well as Tc chelate complexes.¹⁶⁶

In Russia, the problem of the production of a standard list of reagent sets has already been solved. These reagents are produced by virtually all corporations. Thus, the Medradiopreparat Plant of the Ministry of Health of the Russian Federation produces reagent sets for the preparation of the drugs Pentatech (^{99m}Tc complex with diethylenetriaminepentaacetic acid used for the determination of glomerular filtration rate in kidney disease or visualisation of brain tumours), Pyrphotech (^{99m}Tc complex with pyrophosphate used for scintigraphy of the skeleton or acute myocardial infarction), Coren (^{99m}Tc complex based on rhenium sulfide used for scintigraphy of the liver, spleen or bone marrow). The Diamed Plant produces the above-mentioned pharmaceuticals along with Technephor (^{99m}Tc complex with oxabiphor used for scintigraphy of the skeleton), etc.²⁵³

Extensive studies are being conducted on the design of new pharmaceuticals based on ^{99m}Tc complexes with the $\text{N}_2\text{S}_2-\text{NS}_3$, S_3N ligands, carbonyl ligands and peptides.²⁵³

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Single-layer dispersions of transition metal dichalcogenides in the synthesis of intercalation compounds

A S Golub, Ya V Zubavichus, Yu L Slovokhotov, Yu N Novikov

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Abstract. Chemical methods for the exfoliation of transition metal dichalcogenides in a liquid medium to give single-layer dispersions containing quasi-two-dimensional layers of these compounds are surveyed. Data on the structure of dispersions and their use in the synthesis of various types of heterolayered intercalation compounds are discussed and described systematically. Structural features, the electronic structure and the physicochemical properties of the resulting intercalation compounds are considered. The potential of this method of synthesis is compared with that of traditional solid-state methods for the intercalation of layered crystals. The bibliography includes 192 references.

I. Introduction

A crystal structure of layered transition metal dichalcogenides TX_2 consists of the alternating infinite triatomic layers $\text{X}-\text{T}-\text{X}$ (where T is a transition metal atom, X is a chalcogen atom — S, Se or Te).¹ The neighbouring metal and chalcogen atoms are strongly bound by covalent bonds within the layers, while the layers are weakly bonded to each other due to van der Waals interactions. These compounds have found practical applications as materials used in electronics (e.g., in power sources), in different fields of technology (e.g., as lubricants) and in petrochemistry (as catalysts). They also attract attention in the fundamental research of physical and chemical properties of the low-dimensional compounds.

Approaches common to dichalcogenides of different metals can be used in studies (and for the modification) of their properties, because of their structural similarity. One of the approaches makes use of the ability of these substances to form intercalation compounds due to the existence of the interlayer space between

the adjacent TX_2 layers. This allows one to obtain systems with alternating TX_2 monolayers and layers of different (inorganic or organic) nature. In such heterolayered structures both the electronic structures and the properties of the TX_2 layers can be modified due to charge transfer between the components and changes in the nature and concentrations of intercalated substances (which consequently changes interlayer distances).

An unusual chemical property of transition metal dichalcogenides discovered recently is their ability to form rather stable systems containing quasi-two-dimensional monomolecular layers separated by the solvent molecules (single-layer dispersions). To some extent, this property is analogous to the ability of layered aluminosilicates and zirconium hydrogen phosphates² to exfoliate in aqueous media. A general character of this phenomenon for the layered systems can be supposed, and based on this a versatile method can be developed for the preparation of intercalation compounds and nanocomposite materials including films.

This method is of particular importance for the synthesis of heterolayered systems that cannot be obtained by traditional procedures of solid-state chemistry. In this respect, formulation of the basic principles of the synthesis of intercalation compounds with the use of TX_2 single-layer dispersions is the subject of current interest, and the present review is expected to provide additional insights into the problem.

In this review, the data on the nature of TX_2 single-layer dispersions and their use in the synthesis of new heterolayered materials as well as the data on the types, properties and structural features of these materials published in the few last years are considered. To reveal the reactivity of the single-layer dispersions, it was appropriate to compare it with that of the solid-state intercalation reactions of crystalline layered metal dichalcogenides. It should be mentioned that different aspects of solid-phase intercalation were discussed in several reviews published in the 1980–1990's (see, e.g., Refs 3–9), while the studies of single-layer dispersions have up to now been surveyed in only one review¹⁰ dealing with molybdenum disulfide chemistry.

II. Characteristic features of the layered metal chalcogenide structures

Many transition metals characterised by the oxidation state +4 [Group IVB, VB and VIB metals and some Group VIIB (Tc, Re) and VIIIB (Pt) metals] form dichalcogenides of the layered

A S Golub, Ya V Zubavichus, Yu L Slovokhotov, Yu N Novikov
A N Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, 119991 Moscow, Russian Federation. Fax (7-095) 135 50 85.
Tel. (7-095) 135 93 26. E-mail: golub@ineos.ac.ru (A S Golub).
Tel. (7-095) 135 93 04. E-mail: Yan.Zubavichus@urz.uni-heidelberg.de (Ya V Zubavichus), slov@ineos.ac.ru (Yu L Slovokhotov).
Tel. (7-095) 135 92 13. E-mail: novik@ineos.ac.ru (Yu N Novikov)

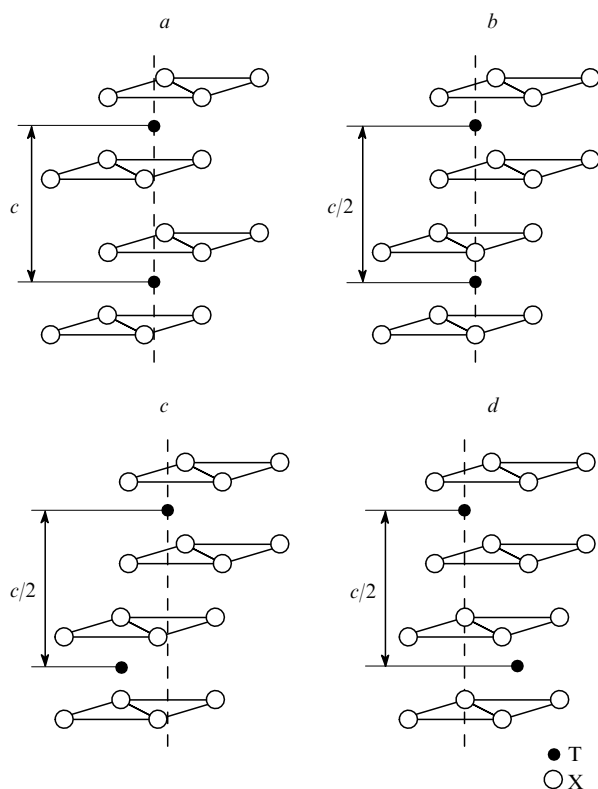


Figure 1. The main types of crystal structures of transition metal dichalcogenides.

Polytypes: (a) 1T, (b) 2H_a, (c) 2H_b, (d) 2H_c.

structure.¹ Their crystal structure can be described as stacking of closely packed hexagonal sheets of chalcogenide anions with each second interlayer space occupied by metal atoms (Fig. 1). With the close packing, the stacking of the anions accords with the principle ‘an atom is placed over the centre of the triangle formed by the atoms of the adjacent layer’, and this principle is held in all cases where the adjacent chalcogen sheets with no metal atoms in between are stacked and bound to each other only by the van der Waals forces (to form a van der Waals gap). This arrangement causes the existence of octahedral and tetrahedral vacant sites in the ratio of 1 : 2 in the interlayer space between the neighbouring triatomic X–T–X...X–T–X layers. The electron configuration of the metal atom T determines the intralayer mutual arrangement of the chalcogen sheets and specifies its octahedral (which corresponds to the close packing of the anions) or trigonal prismatic (where the packing of the anions is not close) nearest-neighbour surrounding the chalcogen atoms. According to quantum-chemical calculations,^{11–13} a trigonal prismatic coordination is favoured by a d² metal atom electron configuration (the Group VIB metals, Mo and W) while the octahedral coordination is characteristic of a d⁰ metal atom configuration (Group IVB metals, Ti and Zr). For the Group VB metals (Nb and Ta) with d¹ electron configuration, both coordination surroundings are energetically close to each other. For this reason, both trigonal prismatic and octahedral coordinations are usually present in real structures.

In addition to the type of coordination polyhedron (octahedron or trigonal prism), the motives of the X–T–X layer packing can vary as well as the relative positions of the metal cations in the adjacent layers with respect to each other in the structures of metal dichalcogenides.¹⁴ These three factors taken together determine the syngony [hexagonal (H), trigonal (T) or rhombohedral (R)] and the space group of the crystalline compound. Thus in the case of an octahedrally surrounded metal atom, the sole one-layered packing, which corresponds to the

trigonal space group *P3m* (1T polymorph), is realised. In the case of trigonal prismatic coordination, much more variation in the packing exist. For two-layered packing, three structural types differing in the relative positions of the metal cations in the adjacent filled layers are possible (2H polymorph, 2H_a, 2H_b and 2H_c polytypes).³ Three-, four- and six-layered sequences in packing as well as more exotic long-period structures are also known. Some compounds exhibit structures with a mixed coordination environment. They contain alternating layers with octahedral and trigonal prismatic nearest-neighbour surrounding of a metal atom.^{1,3} The main polymorph modifications and polytypes of layered dichalcogenides are listed in Table 1 and schematically depicted in Fig. 1.

Table 1. Structural types of transition metal dichalcogenides.³

Poly-morph	Poly-type	Coordination type	Layer stacking motif ^a	Space group	Examples
1T	1T	O	AbC	<i>P3m</i>	TiS ₂ , VS ₂ , TaS ₂
2H	2H _a	TP	AbACbC	<i>P6₃/mmc</i>	NbS ₂ , TaS ₂
	2H _b	TP	AbABcB	<i>P6m2</i>	NbSe ₂ , TaSe ₂
	2H _c	TP	AbABaB	<i>P6₃/mmc</i>	MoS ₂ , WS ₂
3R	3R	TP	AbACaCBcB	<i>R3m</i>	MoS ₂ , WS ₂
4H	4H _a	TP	BcBAcABcBCaC	<i>P6m2</i>	NbSe ₂ , TaSe ₂
	4H _b	O + TP	BcBCaBCaCBaC	<i>P6₃/mmc</i>	TaS ₂ , TaSe ₂
	4H _c	TP	BcBAcABaBCaC	<i>P6₃mc</i>	TaSe ₂
6R	6R	O + TP	BcBCaBCaCABcABcA	<i>R3m</i>	TaS ₂ , TaSe ₂

Note. The following notations are used: O, octahedral coordination; TP, trigonal prismatic coordination; O + TP, mixed coordination.

^a Upper- and lower-case letters designate the location of the chalcogen and metal atoms, respectively. Coincidence of the letters corresponds to the situation where the atoms in the adjacent layers are disposed exactly one below the other.

The electronic structures of layered dichalcogenides TX₂ are also determined by the nature of the metal T. The TX₂ valence band structure was found to consist of two sub-bands, where the lower sub-band is composed mainly by *ns*- and the upper sub-band by *np*-states of the chalcogen atom (*n* = 3 for X = S and *n* = 4 for X = Se) (Fig. 2). The lower free states of the vacant band (conduction band) consist mainly of d-orbitals of the transition metal. Due to the splitting of d-orbitals of the metal T by a crystal field of the chalcogen, the d_{z²}-orbital becomes the lowest in energy and forms a separate sub-band. In the case of Group IVB metal chalcogenides (d⁰ configuration), this orbital is situated entirely in the vacant band, whereas for Group VB metal chalcogenides (d¹ configuration) this orbital is half-filled, and for Group VIB metal dichalcogenides (d² configuration), the d_{z²}-orbital is completely occupied and lies in the valence band.^{11, 15–17} Thus, according to the calculations and experimental data [measurements of conductivity, magnetic properties,^{18, 19} photoelectronic spectra,^{17, 20} X-ray absorption near-edge structure (XANES),²¹ and optical reflection spectra²²], the occupied and vacant levels are separated by a very narrow energy gap (0.1–0.2 eV) in 1T-TiS₂, while they overlap in 2H-TaS₂. In 2H-MoS₂ and 2H-WS₂, the energy gap reaches ~ 1.5 eV.

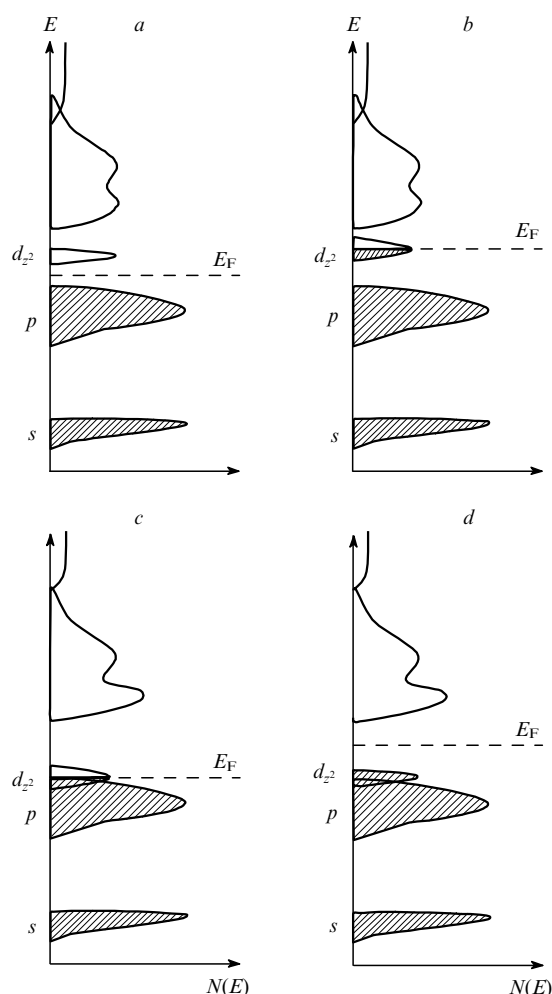


Figure 2. Band structures for dichalcogenides of Group IVB (a), VB (b, c) and VIB (d) transition metals with octahedral (a, b) and trigonal prismatic (c, d) coordination of the central atom.¹¹

Let us consider the structure of MoS₂ in more detail, because this compound is inert in solid-state intercalation reactions, and it is the most common subject of studies on single-layer dispersion phenomenon. Molybdenum disulfide is a unique naturally occurring layered metal dichalcogenide. The mineral molybdenite contains its most stable 2H-modification (2H_c polytype, see Table 1), which has two-layered packing AbABaB with a trigonal prismatic coordination of molybdenum atoms [the space group *P6₃/mmc*, *a* = 3.16 Å, *c* = 12.30 Å, *Z* = 2 (see Ref. 23)]. Another thermodynamically stable modification of MoS₂ is 3R, which is characterised by three-layered packing and also has a trigonal prismatic coordination of molybdenum atoms [space group *R3m*, *a* = 3.16 Å, *c* = 18.37 Å, *Z* = 3 (see Ref. 24)]. Virtually amorphous molybdenum disulfide consisting of strongly disordered fragments of the 2H structure can be obtained by ion-exchange reactions of molybdenum chloride with alkali metal sulfides in non-aqueous solvents.²⁵ Recently, the preparation of molybdenum disulfide in the form of multi-layered polyhedral structures, resembling carbon ‘onions’ and nanotubes, by sulfidation of ultra-dispersed molybdenum oxide^{26,27} or by reduction of MoS₃ with hydrogen has been reported.²⁸ Though today the atomic structures of these systems are not known in detail, they are presumably close to the 2H-modification and have a certain number of defects needed for deformation of the flat S—Mo—S layer to the given curvature. The minimum diameter of such MoS₂ particles (containing 2–3 layers) is approximately 30–50 Å.²⁹ Flat one-layered nanosized MoS₂ clusters of approximately the same diameter have

been obtained by the reaction of MoCl₄ with H₂S in a micellar solution.³⁰

Synthesis of a metastable molybdenum disulfide modification, in which the octahedral coordination of molybdenum atoms and one-layered packing are assumed, has been reported.³¹ This modification can be assigned to the 1T polymorph (see Table 1). For the synthesis of this compound, the intercalation compound K_{0.7}MoS₂ was subjected to controlled hydrolysis up to the composition of K_{0.33}(H₂O)_{0.6}MoS₂ followed by its electrochemical or chemical oxidation (using potassium dichromate in dilute sulfuric acid or iodine in acetonitrile). According to the powder X-ray diffraction analysis, the structure of the obtained compound belongs to a hexagonal syngony and has the unit cell dimensions *a* = 5.597 Å, *c* = 5.994 Å.³¹ The structure is characterised by a shorter interlayer distance (by ~0.16 Å) than 2H-MoS₂, and by the existence of a superstructure $\sqrt{3}a \times \sqrt{3}a$ in the *ab* plane of the layer. This compound possesses a negative temperature coefficient of electronic conductivity and exhibits the Pauli paramagnetism, *i.e.*, displays metallic properties. Thermal analysis showed that decomposition of the compound proceeds at ~100 °C with a small exothermic effect resulting in the formation of strongly disordered 2H-MoS₂. The structural study of 1T-MoS₂ by electronography³² confirmed the retention of a hexagonal symmetry of the MoS₂ layer and the formation of the superstructure $\sqrt{3}a \times \sqrt{3}a$ due to the displacement of the molybdenum atoms from their ideal positions in the layer. This structural model is consistent with the data from scanning tunneling microscopy³³ and with the results of quantum-chemical calculations.³⁴ Nevertheless, since the atomic structure of the MoS₂ modification under consideration has not been determined up to now, the notation ‘1T-modification’ has to be used with care. In particular, ‘1T-MoS₂’ was suggested³⁵ to be a product of proton insertion into molybdenum disulfide — H_x⁺(MoS₂)^{x-}. (Similar intercalation compounds with hydrogen are known for some chalcogenides of the Group VB metals.^{36,37})

III. Solid-phase intercalation of metal dichalcogenides and the types of their intercalation compounds

In the literature, TX₂ intercalation compounds with various electron donors such as alkali metals and their complexes with solvating molecules, transition and post-transition metals, organic molecules (Lewis bases) and metal complexes of low ionisation potentials are described. The main traditional methods applied for the intercalation of powdered crystalline dichalcogenides, TX₂, are as follows: thermally activated insertion of the guest (metal atoms, molecules of electron-donating substances) into the TX₂ interlayer space, intercalation under electrolysis conditions where TX₂ is used as a cathode, and, in the case of alkali metals, the action of reducing agents (for instance, *n*-butyllithium or NaBH₄) on TX₂. The early publications concerning the methods of synthesis and the structures of certain classes of intercalation compounds are summarised in several reviews (see, for example, Ref. 3–6, 38).

It has been repeatedly noticed that the crystals of Group IVB and VB metal dichalcogenides can be intercalated by each of the above-mentioned types of the compounds using classical methods of solid-state chemistry, while molybdenum and tungsten dichalcogenides can only be intercalated with alkali metals under the same conditions. The different reactivities of the matrices can be explained by the distinctions in their electronic structures. Actually, taking into account the TX₂ valence band model considered above and in the framework of the rigid band model (RBM) (which is obeyed fairly well for the majority of dichalcogenides), the filling of the vacant matrix levels by the electrons of the guest is expected to proceed most easily in the cases of matrices based on the Group IVB and VB metals and should be most hindered in the case of Group VIB metal dichalcogenides where

d_{z^2} -orbitals are occupied and the electrons have to fill higher non-bonding levels.

According to this model, a new molybdenum disulfide 1T-modification, which exhibits a metal-type conductivity, should be more reactive in the intercalation than 2H-MoS₂. This is consistent with the fact that 1T-MoS₂ undergoes intercalation with metallic mercury³⁹ as well as with Ag⁺ and Cu⁺ cations (see Ref. 40).

However, even with TX₂ the electronic structures of which favour the acceptance of electrons, the key step of intercalation that limits the rate of the process, is apparently a transfer of the electrons to the matrix layers. The data on the kinetics of the gas-phase intercalation of hydrazine into NbSe₂⁴¹ as well as of the solution intercalation of cobaltocene into TaSe₂⁴² shows that the filling of the interlayer space is preceded by an induction period, which is needed for the 'activation' of the matrix due to its interaction with the absorbed molecules. The limiting influence of this step also follows from the effect of the acceleration of TiS₂ intercalation with various amines upon introduction, in the reaction system, of lithium amides or butyllithium, which can easily reduce the matrix layers. Probably, activation occurs due to weakening of the layer attraction because of the transfer of a certain number of electrons into the layers, which results in Coulombic repulsion. This facilitates the entering of the cations into the interlayer space.⁴³

It is important for the next steps of the process that cations should easily diffuse into the interlayer space, liberating the edge positions for the entering of new atoms or molecules (Fig. 3). The mobilities of compounds intercalated evidently diminish with the increase in their radii and with the augmentation of covalence of the guest–matrix bonding. This causes rather severe conditions for the insertion of many of the guest compounds into the interlayer space, thus limiting the range of compounds that can be intercalated in the crystalline dichalcogenides TX₂.

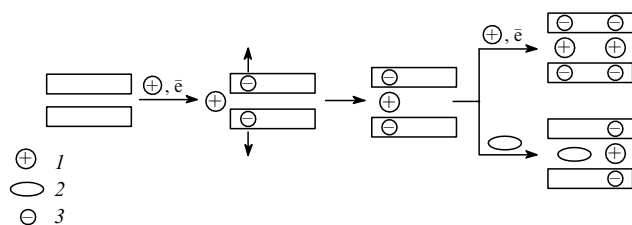


Figure 3. Schematic representation of the activation of a crystalline layered matrix in intercalation reactions;
(1) a cation; (2) a neutral molecule; (3) negative charge on the layer.

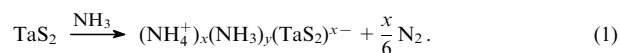
1. Compounds with molecular electron donors

In most cases, the intercalation of molecular compounds in the dichalcogenide matrices demands long (often, for many days) heating of a TX₂ powder in contact with a liquid or vaporous intercalant.³ Steric factors play an important role in this process. For this reason, two-stage synthetic methods are often used. For instance, TaS₂ was intercalated with ammonia, which was then replaced by bulkier molecules of pyridine⁴⁴ or *n*-alkylamines.⁴⁵

Entering of guests in the van der Waals gap leads to a significant increase in the interlayer spacing (Δc), which can vary from 3 Å (in the case of NH₃) to 50 Å (in the case of stearamide),⁴⁴ and to the essential lowering of the overall structural ordering of the materials. In the compounds obtained, the interlayer arrangement of the matrix layers is determined by the van der Waals guest–matrix interactions and by the orientation of the guest molecules. Therefore, there are no correlations in the stacking of adjacent matrix layers in these compounds, *i.e.*, the layers are packed turbostratically. In most cases, the guest molecules are almost closely packed in the interlayer space of the matrix, which

implies van der Waals guest–guest interaction. As a rule, the periodicity in the guest layer appears quite weakly or not at all in the diffraction pattern.

Intercalation compounds of this type were initially believed to contain only neutral molecules which interact with the matrix due to the overlap of the heteroatom lone pair of the electrons with vacant orbitals of the matrix.^{44,46,47} Such a viewpoint can sometimes be found in the current literature (see, for instance, Ref. 48) though it contradicts the known data on the substantial electron transfer from an intercalant to the vacant band of the matrix (in particular, up to 0.3 $\bar{e}$ per atom of Ta in a compound of TaS₂ with pyridine⁴⁹). Further studies revealed the presence of ions along with neutral particles in the interlayer space. The former are produced in various reactions accompanying the intercalation. For instance, in the case of ammonia intercalation into TaS₂ at 25 °C in the absence of oxygen and water, the formation of molecular nitrogen has been found by mass spectrometry. This suggests the occurrence of a redox reaction between the matrix and the intercalant resulting in the formation of ammonium cations, which are intercalated into TaS₂ together with neutral NH₃ molecules (see Ref. 6).



The composition of a compound of TiS₂ with ammonia where the cationic species amount to 20% (Ref. 50) can be formulated as (NH₄⁺)_{0.2}(NH₃)_{0.8}(TiS₂)^{0.2-}. On heating at 147 °C, all the neutral ammonia molecules can be removed and the compound becomes an ammonium analogue of the entirely ionic TX₂ intercalation compounds with alkali metals.

2. Compounds with alkali metals

Alkali metals (A) can be introduced into the interlayer space of crystalline dichalcogenides TX₂ by several methods:

- (1) from vapour phases of alkali metals;⁴
- (2) from the alkali metal solutions in liquid ammonia;^{38,51,52}
- (3) from the alkali halide melts;⁵³
- (4) by electrochemical intercalation using non-aqueous solutions of alkali metal salts;³⁸
- (5) by the reaction of TX₂ with some alkali metal compounds (BuⁿLi/hexane, ABH₄);^{54,55}
- (6) by other methods that do not imply direct intercalation.

It should be mentioned that in the cases of heavy alkali metals the vapour-phase synthesis (1) is carried out at elevated temperatures, which is accompanied by a side reaction, *viz.*, the reduction of TX₂ to a lower chalcogenide with the formation of the corresponding A₂X.⁴ In most cases, the method (2) allows the preparation of TX₂ intercalation compounds with alkali metals solvated by ammonia.³⁸ The reduction of alkali metal thiomolybdates, A₂MoS₂, by hydrogen provides example of the synthesis of intercalation compounds according to the method (6).³²

Intercalation compounds A_xTX₂ obtained in these reactions undergo spontaneous hydration in the presence of traces of moisture and self-ignite upon exposure to air. This makes the investigation of their structure and properties very difficult. The available structural data were obtained with polycrystalline samples. The attempts to synthesise single crystals of A_xTX₂ failed. It was noted⁵⁶ that single crystals of titanium disulfide were destroyed during intercalation due to strong local stresses and deformations of its layers.

The content of alkali metals in A_xTX₂ varies from 0.3 to 1 atom per T atom depending on the nature of A and the method of preparation. The maximum content of alkali metal ($x \geq 1$) has been achieved for A = Li.⁵⁷ For all the A_xTX₂ compounds, interlayer spacing augments as the ionic radius of A⁺ increases.

Solid-state NMR studies of Li_xTiS₂ showed that the guest atoms are virtually fully ionised in the compounds with alkali metals.^{58,59} Thus, taking into account the maximum stoichiometry of these compounds, charge transfer to the vacant orbitals of the matrix can reach 1 $\bar{e}$ per titanium atom. In spite of the fact

that the sulfur atoms are involved in the acceptance of the electron density (XAFS data²¹), this comes mainly to d-orbitals of titanium since they form a lower-energy vacant band. According to X-ray spectroscopic data, this leads to a formal reduction of titanium. Thus, using X-ray emission Ti $K_{\alpha 1}$ spectra it was established⁶⁰ that the charge states of titanium in LiTiS_2 and in $\text{TiS}_{1.5}$ are identical.

Electrophysical properties of the materials are changed in the expected way due to a charge transfer. In particular, the intercalation of Group IVB metal dichalcogenides results in a change in the conductivity character from semi-conducting to metallic. On the contrary, the properties of dichalcogenide phases containing Group VB metals change from metallic to semi-conducting with an increase in the guest metal concentration.⁶¹ Many compounds of this type were found to be superconductors. To our knowledge, the maximum transition temperature (~ 6.9 K) was found for MoS_2 compounds with rubidium and caesium.⁴

Intercalation with alkali metals cannot always be reduced to mere filling of the vacant tetrahedral or octahedral sites in the initial TX_2 structure since this often triggers structural transformations. For instance, the shift of the S—Ti—S layers one with respect to another occurs upon intercalation of 1T- TiS_2 , so that the environment of the guest atoms becomes trigonal prismatic for certain guest: host ratios. A similar structural transition has been described for Na_xTiS_2 and K_xTiS_2 .⁵¹

Yet another type of transformation changing the geometry of the TX_2 layer itself occurs in the intercalation of lithium into 1T- TaS_2 . In this case, the transition octahedron—trigonal prism was found to occur in the local environment of tantalum.⁶² It seems likely that the reverse change in the T metal coordination is induced by the intercalation of Group VIB metal dichalcogenides with alkali metals. As was found in the study of electrochemical insertion of lithium into 2H- MoS_2 , the structural phase transition appeared as a plateau in the voltammogram for the composition $\text{Li}_{0.1}\text{MoS}_2$.⁵⁷ An X-ray diffraction study of the resulting polycrystalline phase with the composition LiMoS_2 showed that intercalation of lithium not only leads to an increase in the lattice parameters ($a = 3.36$ Å, $c = 6.30$ Å) with respect to those of 2H- MoS_2 ($a = 3.16$ Å and $c = 2 \times 6.15$ Å), but also changes the layer stacking from the two-layered sequence to one-layered and, consequently, the coordination surrounding the molybdenum atoms from trigonal prismatic to octahedral. For the intercalates with high lithium content (Li_xMoS_2 , $x > 1$), electronography revealed the formation of a $2a \times 2a$ superstructure which disappears irreversibly on heating of the sample.⁶³ This effect was construed to be a consequence of lithium ion ordering within octahedral vacant sites. However, the reason for the appearance of the superstructure reflections is most likely the ordering not only in the intercalated layer, but also in the matrix layers. This viewpoint is supported by the Mo K -edge EXAFS data,^{39, 64} which demonstrated significant redistribution of the Mo—Mo bond lengths in LiMoS_2 , and by the analysis of atomic pair distribution function (PDF)⁶⁵ for this compound as well.

Probably, charge transfer from the other guest alkali metals to the MoS_2 matrix layers results in similar changes in these layers. For instance, electron microdiffraction and X-ray powder diffraction studies of the intercalation compound $\text{K}_{0.7}\text{MoS}_2$ obtained by reduction of potassium thiomolybdate with hydrogen, revealed the existence of a $2a \times 2a$ superstructure in the MoS_2 layer.³² Taking into consideration the stacking of neighbouring layers, the crystal structure of $\text{K}_{0.7}\text{MoS}_2$ [also as in the case of LiMoS_2 (Ref. 65)] does not have hexagonal symmetry and was described using a triclinic unit cell with the following parameters: $a = b = 6.6$ Å, $c = 8.0$ Å, $\alpha = 76.2^\circ$, $\beta = 88.3^\circ$, $\gamma = 60.3^\circ$ (the space group $P1$).³²

3. Layered solvates

Layered solvates of the TX_2 intercalation compounds with alkali metals, $\text{A}_x(\text{solv})_y\text{TX}_2$, can be obtained in the reaction of solvating reagents (water, liquid ammonia, dimethyl sulfoxide, dimethoxy-

ethane, dimethylformamide) with A_xTX_2 or in the direct intercalation reaction, if it is carried out in the required solvent.^{66–70} These compounds are of much interest as the direct precursors of single-layer dispersions.

Normally, the content of alkali metals in solvated phases is lower than in the intercalation compounds with the same non-solvated metals. Typical x values lie in the range 0.1–0.33. For this type of compound, the guest and host charges remain separated, *i.e.* the atoms of the alkali metals remain virtually fully ionised. For these compounds, the expansion of interlayer spacing with respect to the interlayer spacing in the initial TX_2 structure depends weakly on the ionic radius of the alkali metal and is mainly determined by the van der Waals thickness of solvating molecules. For this reason, the distance between the adjacent layers may change in a stepwise manner depending on whether the solvating molecules form a monolayer, bilayer *etc.* In the case of water as a solvent, it was found that Li^+ and Na^+ ions, which have a high energy of hydration (the ions characterised by the ratio $n/r \geq 1$, where n is the cation charge, r is the ionic radius/Å), tend to form intercalation compounds containing two water layers, whereas all the other cations stabilise only one-layered packing of water in the interlayer space (Fig. 4).^{66, 71}

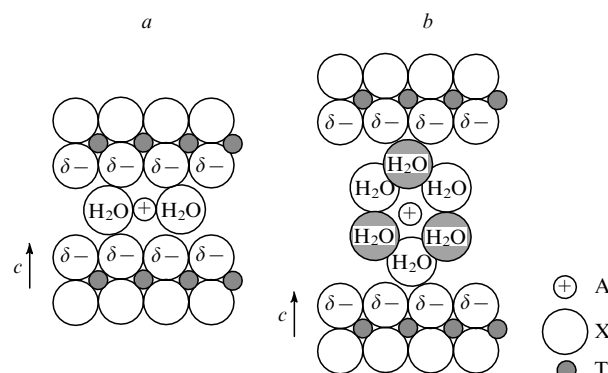


Figure 4. Coordination of the intercalated alkali metal cation with water molecules arranged in one-layer (a) or bilayer (b) packing in compounds $\text{A}_x(\text{H}_2\text{O})_y\text{TX}_2$.⁷¹

For the majority of layered solvates, only a periodicity in the direction normal to the layers was determined by structural methods. Structural data are known in greater detail only for the isolated examples. One of them represents the intercalation compound $\text{K}_{0.33}(\text{H}_2\text{O})_{0.66}\text{MoS}_2$, which has a monoclinic unit cell with the parameters $a = 5.70$ Å, $b = 3.24$ Å, $c = 9.46$ Å, $\beta = 100.5^\circ$ as was found by XRPD and electron microdiffraction methods.^{31, 32} Thus, the interlayer spacing in this compound is larger than in 2H- MoS_2 by 3.15 Å, which is close to the van der Waals thickness of the monolayer of water molecules.

For the series of intercalation compounds $\text{A}_x(\text{H}_2\text{O})_y\text{MoS}_2$ ($\text{A} = \text{Li}, \text{Na}, \text{K}, \text{Cs}$), the ordering and dynamic behaviour of water molecules and alkali metal cations have been investigated by magic-angle-spinning NMR (^1H , ^7Li , ^{23}Na , ^{133}Cs).⁷¹ It was found that alkali metal cations have a strongly distorted octahedral environment and that water molecules possess high mobility in the intercalated layer where their chaotic motion can be observed even at 20 °C.

In these compounds, the cations of alkali metals can be involved in ion-exchange reactions (for instance, with alkylammonium cations) giving rise to new intercalation compounds.⁶⁷

4. Compounds with transition and post-transition metals

Compounds with the composition M_xTX_2 (M is a 3d-metal, Cu, Ag *etc.*) are usually obtained by thermal synthesis at 600–1100 °C in tubes containing a mixture of TX_2 and M or a mixture of three elements T, M and X in the appropriate stoichiometry. Note that

this reaction, in particular, in the latter combination, can hardly be considered as the intercalation of a layered matrix. However, the compositions of these ternary metal chalcogenides can be considered as intercalation compounds from the structural point of view, because the host matrix and the guest layers can be distinguished in their structure. Due to strong covalence of the M–X bond, the accommodation of M atoms in the interstitial sites of these compounds results in a small increase or, for some 3d-metals (Co, Ni), even in a decrease in the interlayer distance.⁷² The crystallinity of M_xTX_2 compounds is usually high. Using gas-transport reactions (for instance, in the presence of iodine or chlorine), single crystals of $Co_{0.25}TiS_2$,⁷³ $Fe_{0.34}TiSe_2$,⁷⁴ $Ag_{0.6}NbS_2$ (Ref. 75) and $In_{0.67}TaS_2$ (Ref. 76) could be grown.

In most M_xTX_2 compounds described, the guest M atoms are localised in the octahedral sites formed by chalcogen atoms of the adjacent layers, though filling of the tetrahedral sites is also known [Cu, Ag (see Ref. 77)]. Ultimate concentration of the guest atoms in M_xTX_2 is limited not only by the number of available sites, but also by the ‘capacity’ of the d_{z^2} -sub-band part, which is vacant in the non-intercalated matrix. According to RBM, this sub-band can adopt 2 and 1 e per T atom in cases of Group IVB and VB metal dichalcogenides, respectively. Actually, the maximum x values found experimentally for M_xTX_2 are close to the expected values. For instance, the x values are equal to 0.75 and 0.5 for TiS_2 and NbS_2 , respectively,^{78,79} when they are intercalated with 3d-metals (Mn, Fe, Co, Ni), having a formal charge $2+$ over the whole x range. The approach of the d_{z^2} -sub-band to its full occupancy may induce structural transformations as was observed, for instance, for Ga_xNbSe_2 and Ga_xTaSe_2 systems the structures of which transformed to the spinel structure at $x = 0.12$ (Ref. 80). Depending on the M_xTX_2 phase composition, various modes of guest metals ordering are realised or the structures without long-range order in the guest layer are formed. The ordering occurs where the guest atoms’ concentration exceeds a certain value, that is, where guest–guest interactions become significant. For instance, for intercalation compounds with the compositions of $M_{0.25}TX_2$ and $M_{0.33}TX_2$, the superstructures $2a \times 2a$ and $\sqrt{3} \times \sqrt{3}a$, formed due to the occupation by the guest atom of each fourth or third octahedral vacant site, respectively, are often observed (see, e.g., Refs 78 and 79). In the series of related compounds $(Cr,Ni)_{0.33}TX_2$ (where T = Nb, Ta and X = S, Se) containing the atoms of two different metals in the TX_2 interlayer space, a number of structural transitions were found⁸¹ by X-ray and neutron diffraction upon change of the Cr:Ni ratio. According to XAFS data,⁸² these transitions are accompanied by a change in the ordering of the local environment of T atoms.

Layered ternary molybdenum sulfides with 3d-metals having the stoichiometry $M_{0.5}MoS_2$ were obtained by high-temperature synthesis.^{83–89} Complete X-ray single-crystal investigations were performed for some of these compounds.^{85,87,88} The data obtained, for instance, for $Co_{0.5}MoS_2$ (as well as for structurally similar $Fe_{0.5}MoS_2$)^{85,87} demonstrate that molybdenum atoms inside the layer have a distorted octahedral environment composed of the sulfur atoms and that the closest Mo–Mo interatomic distances are not equivalent (as in 2H- MoS_2), but are broadly scattered over the range from 2.75 Å to 3.8 Å. The interlayer spacing in this compound is somewhat smaller than in 2H- MoS_2 . Syntheses of other layered molybdenum sulfides were reported^{90,91} (in particular, with indium and tin) with interlayer spacings virtually coinciding with that of 2H- MoS_2 , although no detailed structural data for these compounds were given. It is noteworthy that interaction of a $TaReSe_4$ matrix isoelectronic to 2H- MoS_2 with indium or tin results in its intercalation, whereas interaction with 3d-metals or with gallium leads initially to disproportionation into $TaSe_2$ and $Ta_{1-y}ReSe_{4-2y}$ and then to intercalation of the phases formed.⁹¹

Since intercalated metals donate electrons to TX_2 , systems with various types of magnetic orderings [see, for instance,

Refs 61, 89, 92] as well as spin glasses^{93,94} are formed with 3d-metals.

Intercalation compounds Hg_xTS_2 (T = Ti, Ta; $x = 1–1.3$) containing mercury atoms in the interlayer space^{95–97} can formally be assigned to the class considered owing to their compositions. In contrast to other chalcogenides with the composition M_xTX_2 , these compounds are formed even at 20 °C. In the interlayer space, mercury atoms form chains or closely packed hexagonal sheets⁹⁷ with a ‘thickness’ close to the atomic radius of Hg(0). Guest-to-host charge transfer is small in these compounds and amounts to 0.2 e per Hg atom in $HgTiS_2$.⁹⁶ It is of note that 2H- MoS_2 does not react with mercury, whereas a metastable phase of molybdenum disulfide obtained from $LiMoS_2$ by lithium deintercalation (presumably, 1T modification) does react. The formation of the chains and closely packed hexagonal sheets stabilised by partial charge transfer is probably the characteristic property of mercury. This feature is inherent in related layered compounds of graphite $KHgC_4$ (Ref. 98) and in crystalline complexes of low-valent mercury with a hexafluorometallate anion Hg_3MF_6 , (M = Nb, Ta).⁹⁹

IV. Single-layer dispersions of metal dichalcogenides

The exfoliation of crystalline TX_2 intercalation compounds in a solvent under certain conditions, which gives highly dispersed systems containing X–T–X single layers, was first observed for the case of TaS_2 intercalated with hydrogen. The H_xTaS_2 phase was prepared by electrolysis of a sulfuric acid solution using tantalum disulfide as a cathode.³⁶ Hydration of the compound obtained with a large excess of water led to the formation of opalescent dark-brown solutions stable for ~ 1 h.⁶⁹ X-Ray studies of these solutions and of solutions of NbS_2 formed under similar conditions have shown that the interlayer ordering is absent in these systems.⁶⁹

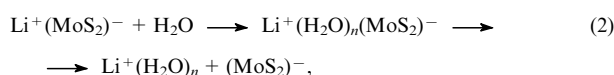
The formation of dark-blue colloid solutions was also observed upon solvation of the intercalation compound Na_xTiS_2 by *N*-methylformamide.⁶⁶ It was noticed that these solutions remained stable in an inert atmosphere for a long time and that the constituent single-layer species carried negative charges, which was deduced from their movement to the positive electrode in the electrophoresis.⁶⁶

Yet another popular method of layer separation consists of the ultrasound promoted hydration of TX_2 -lithium intercalation compounds. Frindt *et al.*¹⁰⁰ pioneered the use of this method for dispersion of $LiMoS_2$. An analogous procedure was later used to prepare dispersions from lithium intercalation compounds of TiS_2 ,¹⁰¹ $NbSe_2$,¹⁰² TaS_2 ,¹⁰³ WS_2 (Refs 104, 105) and $MoSe_2$.¹⁰⁶

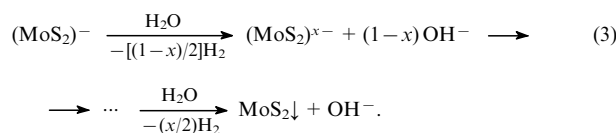
The structure of MoS_2 single layers in an aqueous solution has been studied in detail by various methods.^{107–111} Total decomposition of a three-dimensional structure has been reliably confirmed by powder diffraction.^{106–109} Such typical features of the two-dimensional diffraction as the absence of the reflections corresponding to translational periodicity along the c axis (00/ lines series) as well as broadening and asymmetry of $hk0$ lines (the Warren effect¹¹²) were found to be characteristic of a single-layer dispersion. Based on the shape analysis of $hk0$ reflections, it was suggested¹¹⁰ that T atoms in MoS_2 , $MoSe_2$ and WS_2 dispersions have octahedral coordination (which was additionally confirmed in the case of molybdenum disulfide by Raman spectroscopy) instead of a trigonal prismatic coordination of the initial TX_2 . Moreover, diffraction patterns of these dispersions were found to contain additional $hk0$ lines which can be assigned to a superstructure in the TX_2 layers.^{106,107,109} For dispersions of the same metal dichalcogenides, significant distortions of the local environment of molybdenum and tungsten atoms, in particular, the appearance of short T–T contacts (~ 2.8–2.9 Å) corresponding to metal–metal bonds were revealed by the EXAFS technique.^{106,109} Rearrangement of the energy band structure of the $(MoS_2)^{x-}$ layers in single-layer dispersions is indicated by optical

absorption spectra where no absorption maximum corresponding to a transition between valence and conduction band at 700 nm typical of the initial matrix was present.¹⁰⁹

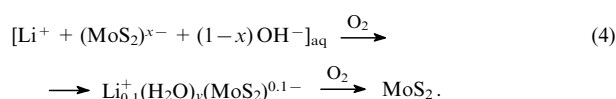
The presence of a negative charge on the layers of disulfide TS₂ dispersed in aprotic media (for instance, in the above-mentioned system Na_xTiS₂–*N*-methylformamide) appears to be evident. As for dispersions obtained by hydration of lithium-intercalated compounds, they were originally considered as containing only neutral TX₂ layers.^{100, 113, 114} However, experimental facts support the idea that dispersions prepared by the latter procedure are also ionic systems which contain macroanions (TX₂)^{x–}, retaining partial negative charge, solvated lithium cations and hydroxide anions.^{115, 116} Actually, the interaction between water and the initial ionic compound, for instance, Li⁺(MoS₂)[–], in which valence electrons are present on the molybdenum disulfide layers, should include two processes, *viz.*, hydration of lithium cations leading to separation of the matrix layers,



and redox interactions between the negatively charged (MoS₂)^{x–} layers and water molecules leading to precipitation of MoS₂.



Slowing down of the redox interaction (3) as the number of electrons on the layers decreases leads to retention of a partial negative charge on these layers for a long time. This appears to be the reason for the prolonged (up to 24 h) aggregative stability of aqueous dispersed systems [Li⁺ + (MoS₂)^{x–} + (1–*x*) OH[–]]_{aq}. This suggestion is supported by the fact that acceleration of crystalline MoS₂ precipitation occurs on removing the layer negative charge under the action of acid or air on the single-layer dispersion.^{115, 117} In the case of acid, the process goes rapidly to completion and results in immediate precipitation of neutral molybdenum disulfide at low pH values. In the case of air, the process occurs much more slowly and includes initial precipitation of the layered compound Li_{0.1}(H₂O)_y(MoS₂)^{0.1–} (see Ref. 115).



The composition of this compound shows directly the number of electrons remaining on the layers of the matrix at the moment of coagulation. Thus, the minimum negative charge needed to maintain stability of this dispersed system in water is close to 1 *e* per 10 molybdenum atoms.

V. Layered compounds obtained from single-layer dispersions

As was noted above, the intercalation of TX₂ crystals using traditional solid-state chemistry methods implies activation of the matrix by electron transfer to its vacant band. Because of a rather broad band gap for the Group VIB metal dichalcogenides, their activation can only be achieved in reactions with strong reducing agents. Therefore, many types of heterolayered compounds based on these matrices cannot be obtained by traditional methods. In addition, such methods are of limited utility also for other dichalcogenide matrices if potential guests are not sufficiently thermally stable or their diffusion in the interlayer space of the matrix is substantially hindered, as, for instance, in the case of polymers. The use of single-layer dispersions as precursors for the preparation of intercalation compounds allows one to eliminate

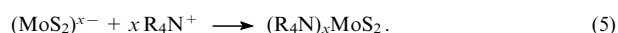
activation and diffusion restrictions, since the single-layers in dispersions bear negative charge and their entire ‘surface’ is available for absorption and chemical binding with an intercalant. That is why single-layer dispersion is most often used for both the preparation of the layered compounds based on molybdenum or tungsten disulfides and the synthesis of the nanocomposites containing polymeric molecules.

1. Compounds with organic and metal complex molecules

The formation of intercalation compounds with organic guest molecules was observed on adding water-immiscible organic solvents to aqueous single-layer dispersions of molybdenum disulfide.¹¹⁸ In this case, thin films of layered compounds containing molecules of the solvent or dissolved organic compounds are formed on the interface. This method has been employed to prepare large series of intercalation compounds with benzene, styrene, hexane,¹¹⁸ tetrachloroethylene,^{119, 120} ferrocene¹¹⁸ and its derivatives,¹²¹ and clusters Co₆X₈(PR₃)₆ (X = S, Se, Te, R = Alk)¹¹⁴ as the guest molecules. Unfortunately, experimental data reported in the cited publications do not allow one to make conclusions concerning the formation mechanism of the compounds obtained and, in particular, to answer the question whether the negative charge is retained on the matrix layers. Actually, according to the ionic model of the single-layer dispersion structure, the layers of metal dichalcogenides are negatively charged. If this charge rests, at least partially, in the intercalation compounds with neutral molecules listed above (what is more, most of them are not electron donors) on the matrix layers, the cations, as, for instance, Li⁺ or H⁺, have to be present along with these molecules. Thus the lithium cations are very likely to balance a residual negative charge of the matrix layers in the compounds Li_{0.1}(HNR₂)_yMoS₂,¹²² which was found to be formed in the reaction of neutral dialkylamines with dispersed MoS₂.

It cannot also be excluded that macroanions (MoS₂)^{x–} are completely discharged during the formation of the layered compounds. The driving force of the occlusion of neutral molecules between the non-charged matrix layers may lie in lowering the surface energy of quasi-two-dimensional layers due to the sorption of the guest molecules. The possibility of this mechanism is deduced, for instance, from the precipitation of a layered compound with naphthalene from aqueous lithium-containing MoS₂ dispersion and a solution of naphthalene in CH₂Cl₂. It was reported¹²³ that storage of the dispersion–organic phase system for a long time (up to 14 days) did not result in precipitate formation, but a precipitate of compound (C₁₀H₈)_x(H₂O)_yMoS₂ containing only traces of lithium was obtained upon acidification to pH 2. As the time of stirring increased, the *x*-value in the compounds obtained increased from 0.07 to 0.20.

Unambiguous proof of the ionic structures of aqueous MoS₂ and WS₂ dispersions was obtained in the studies of their interactions with cationic compounds. It was reported¹¹⁵ that the replacement of lithium cations in the dispersions by cations less prone to hydration (*e.g.*, tetraalkylammonium cations) results in virtually immediate precipitation of the layered compounds containing monolayers of the corresponding cations. These compounds contain neither water molecules as the hydration shell of the cations between the layers nor noticeable amounts of the halogen, which is consistent with the ionic mechanism of their formation.



An analogous conclusion concerning the ionic mechanism of the reaction was made from the study¹²⁴ of the intercalation of a cationic cluster [Al₁₃O₄(OH)₂₄(H₂O)₁₂]⁷⁺ (AL13) into MoS₂ and WS₂ matrices using their aqueous dispersions obtained by hydration of lithium-containing intercalation compounds and washed with water up to neutral pH. The same mechanism is supported by the results of intercalation of AL13, Fe₆S₈(PEt₃)₆²⁺ and Cp₂Co⁺ into TaS₂ using single-layer dispersions obtained by exfoliation of Na_xTaS₂ in a water–*N*-methylformamide medium.^{125, 126}

As might be expected from the ionic mechanism of the reaction (5), the content of the intercalated cations in precipitated products depends on the negative charge retained on the layers at the moment of formation of a given compound as well as on the geometrical sizes of the cations (more precisely, on the minimum matrix layer area occupied by the corresponding cation). As was shown for the series of compounds $(R_4N)_xMoS_2$,^{115,127} this charge can reach $\sim 0.3 \bar{e}$ per Mo atom for the intercalation of Me_4N^+ or RMe_3N^+ cations, which form closely packed monolayers between the neighbouring MoS_2 layers. In this case, the long-chain *n*-alkyl substituents *R* in RMe_3N^+ are oriented perpendicular to the MoS_2 layers (Fig. 5). For the cations occupying a greater layer matrix area (*e.g.*, for *R* = Et, Pr, *etc.*), the content of the cation $x = 0.3$ cannot be achieved in a closely packed monolayer for steric reasons. Therefore, even with the excess of R_4NX salt, the charge on the MoS_2 single layers decreases in the course of formation of the compounds up to the sterically permitted value (Table 2). It can also be noted that the packing of organic cations between the layers of molybdenum disulfide depends on the content of cations in the compound and that in all cases the packing giving minimum interlayer spacing

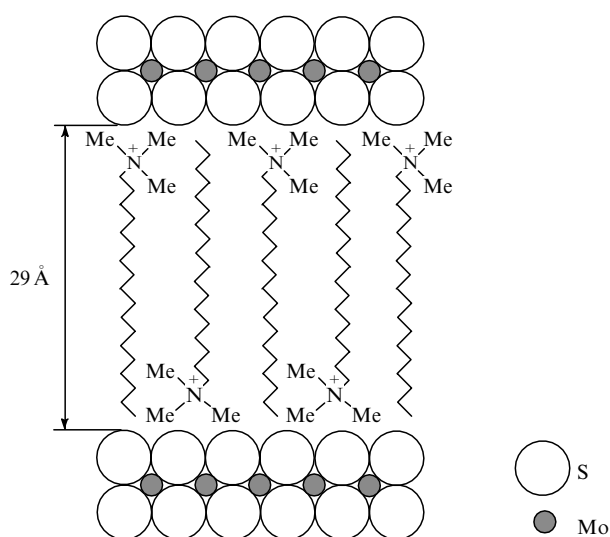


Figure 5. Orientation of intercalated tetraalkylammonium cations in the layered compound $(C_{18}H_{37}Me_3N)_{0.25}MoS_2$.¹²⁷

Table 2. Composition and structural parameters for intercalation compounds $(R_4N)_xMoS_2$ obtained from aqueous single-layer dispersions.¹²⁷

Guest	Guest : host /mol mol ⁻¹	$\Delta c / \text{\AA}$
$(CH_3)_4N^+$	0.29	4.9
$(C_2H_5)_4N^+$	0.17	4.8
$(n-C_3H_7)_4N^+$	0.14	5.4
$(n-C_4H_9)_4N^+$	0.15	7.9
	0.12	5.2
$(n-C_6H_{13})_4N^+$	0.12	8.3
	0.05	5.0
$n-C_{12}H_{25}(CH_3)_3N^+$	0.16	8.2
	0.15	8.2
	0.08	4.8
$n-C_{14}H_{29}(CH_3)_3N^+$	0.19	12.2
	0.05	5.0
$n-C_{16}H_{33}(CH_3)_3N^+$	0.27	27.1
	0.05	4.9
$n-C_{18}H_{37}(CH_3)_3N^+$	0.25	29.2
	0.05	4.9

with the given guest content is realised. Thus, varying the nature and the concentration of intercalated cations, the thickness of organic layer in the compound may be changed from its minimum value of $\sim 5 \text{ \AA}$ which is characteristic of all tetrasubstituted ammonium cations (and corresponds to the NC_4 tetrahedra orientation shown in Fig. 6) to $\sim 29 \text{ \AA}$ for the case of $n-C_{18}H_{37}Me_3N^+$ (see Ref. 127).

Nitrogen-containing bases may also serve as sources of cations that initiate the formation of intercalation compounds from MoS_2 single-layer dispersions. Upon protonation in aqueous solution, these bases are intercalated as mixtures of cationic species and neutral molecules. For instance, the synthesis of two types of MoS_2 intercalation compounds with 1,10-phenanthroline (phen) has been described.¹²⁸ Their structures depended on the acidity of the reaction medium. In $(phen)_{0.1}MoS_2$, the flat phenanthroline molecules are parallel to molybdenum disulfide layers ($\Delta c = 3.5 \text{ \AA}$), whereas, in $(phen)_{0.35}MoS_2$ ($\Delta c = 8.8\text{--}9.4 \text{ \AA}$), they are inclined and probably form piles (Fig. 7). Structural models proposed for compounds with phenanthroline were confirmed by EELS data obtained on the oriented particles. Calculations of the volumes occupied by the guest showed that in both cases phenanthroline molecules are closely packed in the interlayer space of MoS_2 . Close packing was also observed upon MoS_2 intercalation with another compound, *viz.*, hexamethyltetraazacyclotetradecaneacetic acid. In this case, guest molecules were oriented parallel to the matrix layers.¹²⁹

However, the examples where the space between the guest molecules is occupied by solvent molecules are also known for the intercalation compounds obtained from single-layer dispersions. In particular, this was observed for the above-mentioned co-

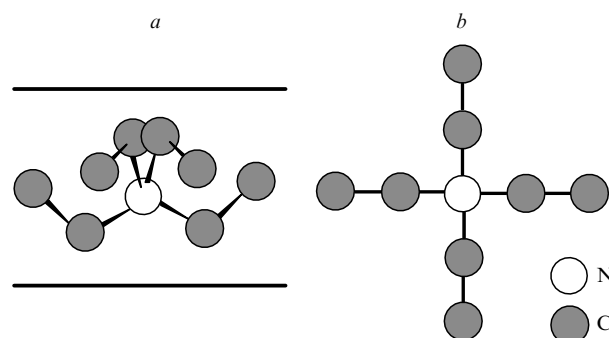


Figure 6. Orientation of Et_4N^+ cations with respect to the matrix layer corresponding to the minimum guest layer thickness.¹²⁷ Projections onto the *ac* (a) and *ab* (b) planes.

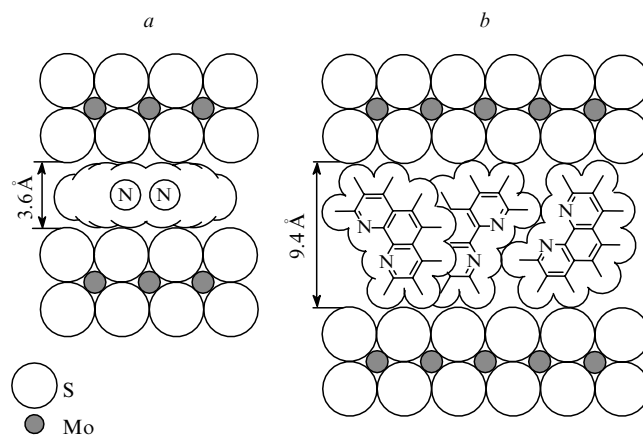


Figure 7. Schematic representation of the structures of two types of MoS_2 intercalation compounds with phenanthroline.¹²⁸ (a) $(phen)_{0.1}MoS_2$, (b) $(phen)_{0.35}MoS_2$.

intercalation of naphthalene and water into MoS₂.¹²³ In the case of MoS₂ intercalation with polyoxoanions AL13, their content (0.04 mol per mol MoS₂) was lower than the maximum allowed for a closely packed monolayer (0.06 mol per mol MoS₂) and up to 20 water molecules per cluster was contained in the interlayer space.¹²⁴ In the compound [Fe₆S₈(PEt₃)₃]_{0.05}TaS₂, there are up to 40 molecules of H₂O or *N*-methylformamide for each intercalated cation (according to the elemental and thermogravimetric analysis data).¹²⁶

It is worth noting that single-layer dispersions were found to be a rather convenient 'tool' for the intercalation of cationic complexes. In addition to the above-mentioned examples, preparation of the MoS₂ intercalation compounds with cationic tris(phenanthroline)- and tris(bipyridine)-3d-metal complexes,¹³⁰ the Fe(III) complex with porphyrin¹³¹ as well as with the ruthenium-arene aqua complexes¹³² may also be noted.

In a number of examples, intercalation of complexes at room temperature is accompanied by their chemical transformations. For instance, the elimination of three phosphine ligands occurred in the formation of the layered compounds from cobalt phosphine chalcogenide clusters Co₆X₈(PR₃)₆²⁺ (Refs 114, 133) and their iron-containing analogue Fe₆S₈(PEt₃)₆²⁺ (Ref. 125). The intercalated layer thickness in the layered systems formed varied from 9.5 to 15.3 Å depending on the structural features of the ligands. It is thought that the liberated coordination sites around the metal atom were initially occupied by solvent molecules and not by the sulfur of the TX₂ layers. This follows from the orientation of the complexes in the interlayer space [with the C₃ axis of the Fe₆ octahedron perpendicular to the layers (Fig. 8a)] proposed on the basis of the X-ray diffraction study of the electron density distribution along the *c* axis in compound [Fe₆S₈(PEt₃)₃]_{0.05}TaS₂ ($\Delta c = 11.5$ Å).^{125, 126} Heating at 200 °C (Refs 114, 126) as well as the action of the electron beam in the electron microscope¹³³ results in the removal of residual phosphine ligands and in the decrease in the intercalated layer thickness up to 6–8 Å. Based on these facts, it was suggested that the species with composition Co₆X₈ or Fe₆S₈ remain in the interlayer space. Note that such clusters are most likely chemically bound to the sulfur atoms of the matrix layers.

Interaction of an MoS₂ single-layer dispersion with ruthenium-arene aqua complexes [(arene)Ru(H₂O)₃]²⁺ may also be accompanied by their chemical transformations. It was shown¹³² that, depending on the pH of the reaction media, the complexes are intercalated in a monomeric form (weakly acidic

medium) or in the form of dimeric complexes [(arene)Ru(μ-OH)₃Ru(arene)]⁺ produced *in situ* due to condensation if the reaction is carried out in a weakly basic medium. Interatomic Ru–C, Ru–O and Ru...Ru distances in the intercalated complexes found by EXAFS for the benzene derivative corresponded to the distances in the known dimeric complex [(C₆H₆)Ru(μ-OH)₃Ru(C₆H₆)]⁺. Interlayer spacings and compositions observed for intercalation compounds with binuclear complexes [(arene)Ru(μ-OH)₃Ru(arene)]⁺ depended on the substituents in the ligands and were found to be 6.0 Å (*x* = 0.12), 10.6 Å (*x* = 0.11), and 5.8 Å (*x* = 0.06) for benzene, 1,2,4,5-tetramethylbenzene and 1-methyl-4-isopropylbenzene derivatives. These data agree well with the structural model in which arene ligands are oriented perpendicular to the matrix layers (Fig. 8b) and the complexes completely fill the interlayer space.¹³²

Filling of the interlayer space of molybdenum disulfide by tris-phenanthroline- and tris(bipyridine)-metal complexes M(chel)₃²⁺ (M = Fe, Co, Ni, chel = 2,2'-bipyridine, 1,10-phenanthroline) in their reactions with an aqueous MoS₂ single-layer dispersion is accompanied by partial dissociation of these complexes.¹³⁰ It is evidenced by the presence of metal oxides (hydroxides) in the reaction products found by Mössbauer spectroscopy for iron complexes as examples. The oxide compounds present as an admixture are removed by treatment with acid. Mössbauer parameters of the complexes remaining in the interlayer space conform to those of their low-spin crystalline analogues and suggest somewhat greater distortions in ligand surrounding of the metal in the intercalated cationic complexes.¹³⁰ Interlayer spacings in [M(chel)₃]_{*x*}MoS₂ (*x* = 0.02–0.03) with phenanthroline (8 Å) and bipyridine (8.5 Å) ligands are consistent with the orientation of the C₃ axis of the corresponding complexes perpendicular to the layers (Fig 8c).

It was also reported¹³⁴ that MoS₂ is intercalated with alkali metal complexes of crown ethers (12-crown-4, 15-crown-5 and 18-crown-6). However, the obtained layered compounds were unstable and washing with water resulted in the extraction of the intercalant.

2. Nanocomposites with polymers

A wide range of compounds in which the interlayer space of TX₂ is filled with polymeric molecules are currently known.^{101–103, 134–148} Such compounds, which consist of two extended structures differing in chemical nature, belong to nanocomposite materials. Experimental data for nanocomposite materials based on TX₂ and polymers are given in Table 3. It should be mentioned that synthesis of polymer-inorganic matrix hybrid composite materials is now taking features of the whole line of inquiry which continues to grow in popularity (*e.g.*, see Ref. 149). Such nanocomposites based on metal dichalcogenides are mostly obtained by adding aqueous solutions of a polymer to aqueous TX₂ single-layer dispersions. Sometimes, other solvents are also used as, for instance, *N*-methylpyrrolidinone for PANI,¹³⁵ CF₃CH₂OH for Nylon-6 and decalin for polyethylene.¹³⁸ In this case, the formation of nanocomposites can proceed in a water-organic solvent biphasic system. For pyrrole¹⁴⁷ and styrene,¹⁴⁸ *in situ* polymerisation was carried out. Pyrrole was introduced in an aqueous dispersion as a monomer along with FeCl₃, and macromolecules formed upon its oxidative polymerisation filled the space between the molybdenum disulfide layers. Polymerisation of styrene is believed to occur in the interlayer space.¹⁴⁸ An interesting modification of a procedure for the preparation of these materials is a layer-by-layer deposition of the MoS₂ layers from dispersions and the layers of a polymer from its solution in poly(allylamine hydrochloride).¹⁴³ It was noted¹⁴³ that, independent of the absorption time, the increase in the film thickness in each cycle corresponded to one monolayer in agreement with a growth mechanism based on the mutual compensation of the charges of polyanions of single-layer (MoS₂)^{x-} and the polycationic polymer.

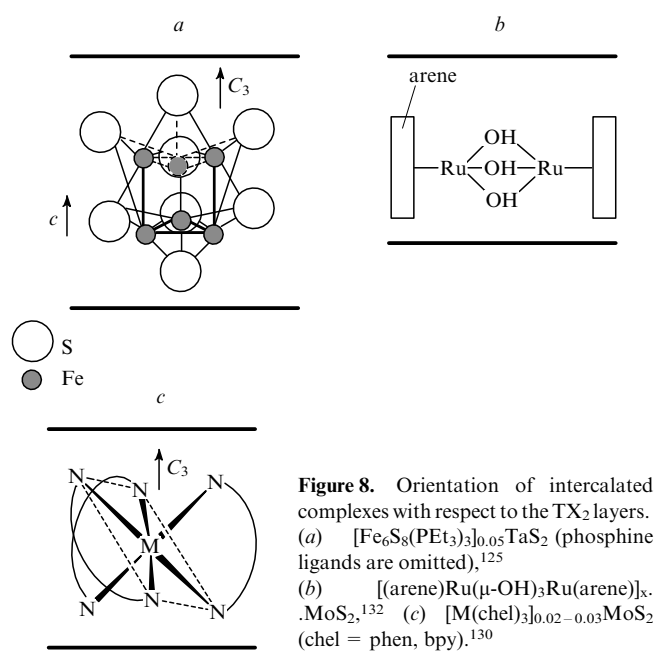


Figure 8. Orientation of intercalated complexes with respect to the TX₂ layers. (a) [Fe₆S₈(PEt₃)₃]_{0.05}TaS₂ (phosphine ligands are omitted).¹²⁵ (b) [(arene)Ru(μ-OH)₃Ru(arene)]_{*x*}.MoS₂.¹³² (c) [M(chel)₃]_{0.02–0.03}MoS₂ (chel = phen, bpy).¹³⁰

Table 3. Nanocomposite materials based on TX₂ and polymers.

Composition ^a	$\Delta c / \text{\AA}$	$\sigma / \Omega^{-1} \text{ cm}^{-1}$	Ref.	Composition ^a	$\Delta c / \text{\AA}$	$\sigma / \Omega^{-1} \text{ cm}^{-1}$	Ref.
Poly(ethylene oxide) as the polymer				Poly(propylene glycol) as the polymer			
(PEO) _{1.0} MoS ₂	8.35	0.02	136, 138	(PPG) _{0.5} MoS ₂	8.25	0.20	136, 138
(PEO) _{0.92} MoS ₂ (see ^b)	10.1	0.10	136, 138	Poly(vinylpyrrolidone) as the polymer			
Li _{0.12} (PEO) _{1.34} MoS ₂	8.4	—	139	(PVP) _{0.76} MoS ₂	14.95	0.003	136, 138
Li _{0.1} (PEO) _{1.0-1.3} MoS ₂	8.0	—	101	(PVP) _{0.14} NbSe ₂	17.7	140	102
Li _{0.1} (PEO) _{0.5} MoS ₂	5.4	0.0005	145	Li _{0.2} (PVP) _{0.95} TaS ₂	25.1	31	103
Li _{0.1} (PEO) _{1.0} MoS ₂	10.2	0.0066	145	Li _{0.2} (PVP) _{1.28} (H ₂ O) _{0.35} TaS ₂	24.7	0.5	103
Li _{0.09} (PEO) _{1.28} MoS ₂	8.2	—	144	Methylcellulose as the polymer			
Li _{0.21} (PEO) _{1.6} MoS ₂	10.0	0.061	134	(MCell) _{0.26} MoS ₂	14.25	0.0004	136, 138
Na _{0.13} (PEO) _{0.8} MoS ₂	6.4	0.0011	134	Poly(ethylene imine) as the polymer			
K _{0.22} (PEO) _{0.3} MoS ₂	3.3	0.047	134	(PEI) _{0.83} MoS ₂	4.05	0.005	136, 138
Rb _{0.17} (PEO) _{0.6} MoS ₂	3.5	0.084	134	Li _x (PEI) _{0.82} TaS ₂	4.0	125	103
Cs _{0.45} (PEO) _{1.0} MoS ₂	10.0	0.0004	134	Li _x (PEI) _{3.2} (H ₂ O) _{0.56} TaS ₂	30.8	0.18	103
K _{0.1} (PEO) _{0.5} MoS ₂	4.8	—	140	Nylon-6 as the polymer			
K _{0.1} (PEO) _{1.2} MoS ₂	9.0	—	140	(Nylon-6) _{3.6} MoS ₂	11.35	<10 ⁻⁶	136, 138
M _{0.3} (PEO) _{0.8} TiS ₂ (M = Li, Na)	8.2	—	101	Polyethylene as the polymer			
Li _{0.15} (PEO) _{1.14} (H ₂ O) _{0.56} (PbS) _{1.18} (TiS ₂) ₂	8.5	—	146	[(CH ₂) _n] ₃ MoS ₂	4.15	<10 ⁻⁶	136, 138
Li _{0.25} (PEO) _{1.79} (H ₂ O) _{0.88} (PbS) _{1.18} (TiS ₂) ₂	8.4	—	146	Polyaniline as the polymer			
Li _x (PEO) _y MoSe ₂	7.9	—	101	(PANI) _{0.35} MoS ₂	10.4	0.4	135, 136
(PEO) _{0.94} NbSe ₂	13.3	250	102	Polypyrrole as the polymer			
(PEO) _{0.80} NbSe ₂ ^b	12.5	240	102	(PPY) _{0.24} MoS ₂	4.5	—	147
Li _{0.2} (PEO) _{1.36} TaS ₂	9.6	19	103	Poly(allylamine) as the polymer			
Li _{0.2} (PEO) _{1.68} TaS ₂	9.5	3.0	103	see ^c	8.65	—	143
Li _{0.2} (PEO) _{1.51} (H ₂ O) _{0.23} TaS ₂	9.2	2.2	103				
Li _{0.2} (PEO) _{0.75} (H ₂ O) _{0.06} TaS ₂	9.1	17	103				

Note. The following notations are used: PEO, poly(ethylene oxide); PPG, poly(propylene glycol); PVP, poly(vinylpyrrolidone); MCell, methylcellulose; PEI, poly(ethylene imine); PANI, polyaniline, PPY, polypyrrole.

^a The composition displays the content of monomer units per TX₂ formula unit. ^b Low-molecular polymer with $M_w < 10\,000$ is used. ^c Film obtained by layer-by-layer deposition of polymer and MoS₂.

Most polymer-containing nanocomposites were obtained with the use of molybdenum disulfide single-layer dispersions (see Table 3). The same approach was also used for other dichalcogenide matrices which can form dispersions, such as, NbSe₂,¹⁰² TaS₂,¹⁰³ TiS₂ (Ref. 101) and MoSe₂.¹⁰¹ A misfit compound (PbS)_{1.18}(TiS₂)₂ has also been used as a matrix in the synthesis of nanocomposites with polymers.¹⁴⁶ In the structure of this compound, uncommensurate layers¹⁵⁰ alternate in the sequence S—Ti—S...S—Ti—S...PbS. Synthesis of the nanocomposite was carried out by intercalation of lithium followed by the exfoliation performed directly in an aqueous PEO solution. The data from X-ray and electron diffraction analysis¹⁴⁶ are consistent with the viewpoint that the polymer molecules fill the van der Waals gaps only between the adjacent TiS₂ layers.

It was noted for many examples, that alkali metal cations enter into the interlayer space (0.1–0.2 atom per T atom) along with a polymer.^{101, 103, 139, 140, 144, 145} This agrees with the retention of the charge separation between the guest and the host in these intercalation compounds as in the case of compounds with molecular guests.

The cations situated in the interlayer space of metal dichalcogenides may form complexes with polymers. This is particularly characteristic of PEO. Based on the analysis of ²³Na NMR spectra, it has previously been noted that strong cation–polymer interactions take place in related systems with aluminosilicates.¹⁵¹ Similar conclusion has been made from the study of ⁷Li NMR spectra and electron density distribution in Li_x(PEO)_yMoS₂ phases¹⁰³ as well as from the data from IR spectroscopy obtained for Li_x(PEO)_y(PbS)_{1.18}(TiS₂)₂.¹⁴⁶ Complexing properties of poly(ethylene oxide) with respect to alkali metals have been specially

used for the preparation of the nanocomposites with MoS₂.¹³⁴ Precipitation was carried out from aqueous solutions of PEO and ACl (A is an alkali metal). The nanocomposites obtained contained no chlorine and relative amounts of A and PEO depended on the nature of the alkali metal. Thicknesses of the polymer-containing layers also depend on the nature of the metal and vary in the reaction products from 3.3 to ~10 Å (see Table 3). This is apparently due to the difference in geometry of the complexes formed by the metal with the polymer units.

¹³C NMR studies of the conformation of poly(ethylene oxide) in the nanocomposite Li_{0.09}(PEO)_{1.28}MoS₂ do not give an unambiguous answer to the question about the polymer packing. It was found that ~90% of the O—C—O fragments of the polymer chain are in the *gauche* conformation, whereas, according to the calculations, the content of such fragments in stretched polymer molecules inscribed into the tunnels of 8 Å diameter should be 50% and 100% upon chaotic and spiral packings, respectively (in the latter case, all the *gauche* conformers are of the same sign).¹⁴⁴ It should be mentioned that spiral packing is characteristic of PEO–ACl complexes.¹⁵² Yet another model accounting for possible solvation of lithium cations by oxygen atoms of the polymer is that polymer units form flat rings resembling crown ethers, with the oxygen atoms being directed inward. In this case, the content of O—C—C—O fragments in *gauche* conformations (with the alternating signs) may amount to 75%. This percentage may be exceeded which requires that the conformational equilibrium of C—O—C—C chain fragments are shifted from *trans* to *gauche* conformers.

As was pointed out in many publications dealing with nanocomposites of molybdenum disulfide and polymers, the electrical

conductivity (σ) of the nanocomposites markedly increases with respect to that of MoS_2 ; σ values were found to be $\sim 6 \times 10^{-6}$ (Ref. 134) or $2 \times 10^{-7} \Omega^{-1} \text{cm}^{-1}$ (Ref. 145). Despite the differences in the σ values (*cf.* Table 3, compounds with PEO), this increase has been well established for the nanocomposites with both conducting (*e.g.*, PANI) and non-conducting (*e.g.*, PEO) polymers. The exception is provided by the compounds with nylon and polyethylene for which no increase in conductivity was observed. The fact that electrical conductivity of nanocomposites slightly increases with temperature and that these materials exhibit Pauli paramagnetism at 50–300 K^{136,138} allow one to attribute them to semimetals. The increase in electronic conductivity in the nanocomposites based on MoS_2 is usually associated with a structural rearrangement of the layers of the initial MoS_2 (and a corresponding change in the type of its electronic structure) from 2H (semiconductor) to 1T (semimetal) modification during the dispersion process. In some cases, the conductivity of the compounds was found to decrease gradually on ageing or on heating at 100–200 °C. This is interpreted as a gradual structural reverse transition 1T $\rightarrow$ 2H which has earlier been observed³¹ for pure 1T- MoS_2 . However, it should be noted that the 1T modification is apparently stabilised in the presence of a polymeric guest or/and the charge on the matrix layers. This is deduced from the fact that the transition to the 2H-structure manifested as an exothermic effect in the curves of differential thermal analysis occurs at higher temperatures (up to 177 °C) for the nanocomposites than for pure 1T- MoS_2 (94 °C).¹³⁸

Conductivity is noticeably higher for polymer-containing nanocomposites based on the Group VB metal dichalcogenides than for their analogues based on MoS_2 . However, conductivity of the former is lower than that of the corresponding non-intercalated TX_2 , as could be expected from band structure considerations.

The nanocomposites considered also possess ionic conductivity (σ_i) along with electronic conductivity (σ_e). It was shown¹⁴⁵ that the ionic conductivity of $\text{Li}_{0.1}(\text{PEO})_1\text{MoS}_2$ is $\sim 10^{-6} \Omega^{-1} \text{cm}^{-1}$, while σ_e/σ_i is 10^3 . The ionic conductivity of this compound is obviously caused by the mobility of lithium ions which is significantly higher in the nanocomposites than in Li_xMoS_2 . For instance, at 25 °C the diffusion coefficient of lithium in $\text{Li}_{0.1}\text{MoS}_2$ equals $4 \times 10^{-13} \text{cm}^2 \text{s}^{-1}$, whereas it reaches 5×10^{-12} and $10^{-10} \text{cm}^2 \text{s}^{-1}$ in $\text{Li}_{0.1}(\text{PEO})_1\text{MoS}_2$ and $\text{Li}_{0.1}(\text{PEO})_{0.5}\text{MoS}_2$, respectively.¹⁴⁵

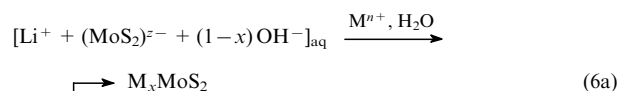
At a temperature of 14–15 K, a metal–insulator transition is observed for MoS_2 -based nanocomposites,¹³⁸ while NbSe_2 - and TaS_2 -based compounds exhibit superconductivity at cryogenic temperatures.^{102,103} The highest temperature of the transition to the superconducting state, $T_c = 7.1$ K, which is virtually equal to T_c for a non-intercalated matrix [7.2 K (see Ref. 3)] was found for $(\text{PVP})_{0.14}\text{NbSe}_2$.¹⁰² In the cases of TaS_2 nanocomposites with PEO, PVP and PEI, an increase in T_c (up to 2.5–2.9 K) as compared with T_c of the initial 2H- TaS_2 (0.8 K) was observed.¹⁰³

3. Compounds with metals and metal hydroxides

The formation of precipitates upon addition of metal salts to single-layer dispersions has been observed in the earliest publications describing the behaviour of dispersed TX_2 . Thus Lerf and Schöllhorn⁶⁶ pointed to the precipitation of compounds with non-established structures upon action of lanthanum salts on TiS_2 dispersion in *N*-methylformamide. The precipitation of powdered compounds upon action of salts of various metals (Al, In, Ni, Co, Ce, Sr, Cd, Zr, Zn, Pb) on single-layer dispersions was observed by Gee *et al.*¹⁵³ In the authors' opinion, these were the 'inclusion compounds' containing metal hydroxides distributed throughout the MoS_2 matrix.

However, more recent studies on the reactivity of molybdenum disulfide dispersed in water showed that the compounds formed may differ in their nature, the latter being determined by both the nature of metal cations involved in the interaction and the reaction conditions. If the alkali metal cations are present in

solution, the corresponding layered solvates $\text{A}_x(\text{H}_2\text{O})_y\text{MoS}_2$ ($\text{A} = \text{Li}$, $x = 0.12$; $\text{A} = \text{K}$, $x = 0.2$) are precipitated from single-layer dispersions, the same solvates are also formed in the exchange of intercalated organic cations with cations A^+ (see Ref. 115). In the presence of metal (M) cations able to form coordination bonds with sulfur atoms of the MoS_2 layers, two reaction pathways are possible. One of them leads to the formation of compounds similar to the above-described ternary molybdenum sulfides M_xMoS_2 , the other leads to the filling of the interlayer space with metal hydroxo compounds (Eqns 6a, 6b).



Obviously, the type of the compound formed is determined by the tendency of metal cations to form sulfide derivatives with MoS_2 or oxo(hydroxo) compounds in an aqueous medium. Thermodynamic characteristics of sulfide macroanions $(\text{MoS}_2)^{x-}$, in particular the stability constants of their complexes are not known, while the characteristics of binary sulfides are well known. Therefore, for a large series of metals, the compositions of intercalation compounds formed were correlated with the difference in solubility products (pK_{sp}) of the corresponding metal sulfides MS_y and hydroxides $\text{M}(\text{OH})_n$.¹⁵⁴ It was noted that, if $K_{\text{sp}}[\text{MS}]$ and $K_{\text{sp}}[\text{M}(\text{OH})_2]$ differ by 2–4 orders of magnitude (Mn^{2+} , Fe^{2+} , Co^{2+} , Ni^{2+}), compounds with alternating S–Mo–S and hydroxide-like $\text{M}(\text{OH})_{2-x}(\text{H}_2\text{O})_x$ layers are formed [see Eqn (6b)]. The cations characterised by $K_{\text{sp}}[\text{MS}] - K_{\text{sp}}[\text{M}(\text{OH})_2] \approx 10^{11} - 10^{14}$ (Pb^{2+} , Cd^{2+}) exhibit a strong tendency to form coordination bonds with sulfur atoms of MoS_2 , but can yet be intercalated in the form of hydroxo compounds upon increase in pH. It is only in the case where the difference mentioned exceeds 16 orders of magnitude that the formation of ternary sulfides (6a) dominates in single-layer dispersions.

a. Phases intercalated with hydroxo compounds

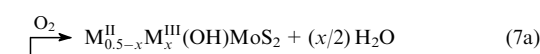
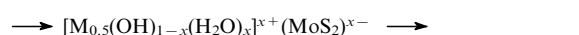
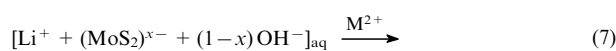
Upon precipitation of aqueous MoS_2 single-layer dispersions in the presence of hydrated rare-earth $[\text{La}^{3+}$, Er^{3+} , Th^{4+} (see Ref. 155)] or 3d-metal cations, aqua(hydroxo) compounds fill the interlayer space.^{153,155} Freshly precipitated compounds with rare-earth elements possess distinct layered structures and are characterised by a large increase in the interlayer distance (for instance, in the case of Er^{3+} , Δc value reaches 9.8 Å). However, amorphisation of these compounds occurs in a few hours. This may be explained by the tendency of intercalated cations to form compounds with a high (up to 8–12) and variable content of water molecules in the hydration shell and it is the loss of these molecules on ageing that causes amorphisation.

The parameters of layered MoS_2 compounds with 3d-metals remain invariable at room temperature for a long time. For the substances formed in the interlayer spaces of these compounds, both the composition (atomic M:O ratio determined by EELS¹¹⁶) and the local structure [interatomic M–O and M...M distances determined by EXAFS for the compounds with Mn, Co, Ni (see Refs 64, 156–158)] are close to those of the corresponding metal hydroxides $\text{M}(\text{OH})_2$. These hydroxides themselves are known to have a layered hexagonal structure in which the metal atoms occupy the octahedral sites between two closely packed layers of the hydroxide ions (which corresponds to the polytype 1T in the classification of transition metal dichalcogenides).¹⁵⁹ For some crystalline 3d-metal (Mn, Fe, Co, Ni) hydroxides, the parameters *a* of their hexagonal lattices, defining the M...M and anion–anion distances inside the layer, are close to those of MoS_2 , the deviation being in the range of a few percents (Table 4). Commensurability of the lattices of two substances

Table 4. Structural parameters (Å) of intercalation compounds $[M(OH)_2]_{1/2}MoS_2$ and the corresponding metal dihydroxides $M(OH)_2$ determined by powder diffraction and EXAFS.¹⁵⁸

M	$[M(OH)_2]_{1/2}MoS_2$				$M(OH)_2$		
	<i>c</i>	Δc	r_{M-O}	$r_{M...M}$	<i>c</i>	r_{M-O}	$r_{M...M}$
Mn	11.3	5.1	2.20	3.29	4.68	2.23	3.33
Co	11.3	5.1	2.08	3.15	4.64	2.10	3.18
Ni	11.5	5.3	2.06	3.11	4.60	2.07	3.14

different in nature obviously favours the formation of the structure with alternating metal sulfide and metal hydroxide layers (Fig. 9) in a single-layer dispersion.



Presumably, in the formation of compounds with 3d-metals, the extended two-dimensional aqua-hydroxo-clusters $[Mo_{0.5}(OH)_{1-x}(H_2O)_x]^{x+}(MoS_2)^{x-}$, which compensate the negative charge of the disulfide monolayer, are initially produced on the surface of $(MoS_2)^{x-}$ single layers [Eqn (7)]. During precipitation and ageing, the structure of these intercalated clusters is transformed into a thermodynamically more stable structure of pure metal hydroxide through replacement of water molecules by OH^- anions. Such a transformation can occur upon oxidation of part of the ions $M(II)$ in the guest layer by oxygen leading to a mixed hydroxide $M(II,III)(OH)_2$ [reaction (7a)] and also upon reduction of water molecules with evolution of molecular hydrogen [reaction (7b)].¹³⁰

It is obvious that the reaction (7a) is favoured by the ability of metal ions to adopt a higher oxidation state. It has been shown by means of ⁵⁷Fe Mössbauer spectroscopy and electron microscopy that the reaction of single-layer dispersion with $Fe(II)_{aq}$ follows this pathway and that the product contains $Fe(II)$ and $Fe(III)$ in the oxygen environment.¹¹⁶ Temperature dependence of the Mössbauer spectra of the iron-containing compound indicates that magnetic ordering occurs simultaneously for both iron forms

in a narrow temperature range (~ 10 K). This suggests the presence of both these forms in a single structure. The character of the transition points to a small size of magnetic domains and their narrow size distribution. The formation of a joint structure by both forms of iron is also deduced from the occurrence of a thermally activated fast electronic exchange between them, which results in the appearance of an iron state with intermediate Mössbauer parameters at 300–380 K.^{160, 161}

The reaction pathway (7b) is realised in the case of compounds with $Co(II)$ and $Ni(II)$. Measurements of magnetic characteristics of the precipitated products point to the occurrence of both the Co^{2+} ($\mu = 5.2 \mu_B$) and Ni^{2+} ($\mu = 3.2 \mu_B$) ions in the octahedral environment characteristic of the corresponding metal hydroxides,¹⁶² while the interatomic distances in the intercalated layer are consistent with those in $M(OH)_2$ as was mentioned above. Complete substitution of OH^- for H_2O probably takes a long time, so the MoS_2 layer in the intercalation compounds continues to bear partial negative charge. This agrees with the prolonged conservation of characteristic distortions in the matrix layer (the set of non-equivalent $Mo-Mo$ distances^{64, 157, 158} and a superstructure in the plane of the layers¹⁶³) in these compounds.

b. Phases intercalated with metals

Compounds with the composition M_xMoS_2 ($M = Cu, Ag, Cd, Hg, Pd, Pb$) formed where the $(MoS_2)^{x-}$ layers act as polysulfide macroligands were obtained by precipitation of single-layer dispersions in the presence of the cations noted.^{154, 164–166} Judging from the $M-S$ distances, the intercalated metal atoms form direct covalent or ionic-covalent bonds with sulfur atoms of the matrix layers (EXAFS data^{154, 165, 166}). It is of note that there are no direct analogues to the above-mentioned compounds among the known ternary molybdenum sulfides obtained by high-temperature synthesis where the $S-Mo-S$ layers are only present in the structures of compounds with 3d-metals [V, Cr, Fe, Co (see Refs 83–89)]; the other metals [*e.g.*, Ga and Al (see Ref. 167)] form compounds with a spinel structure.

In the dispersions, the charged molybdenum disulfide single-layers exhibit reducing properties with respect to the cations characterised by the positive redox potentials.¹⁵⁴ For instance, for Ag^{2+} , Pd^{2+} and Hg^{2+} , their reduction products $[Ag(0), Pd(0), Hg_2^{2+}]$ were obtained along with the M_xMoS_2 phases.^{154, 165, 166} In the case of Cu^{2+} , the reduced Cu^+ cations were incorporated into the layered compound formed. Hence, all the copper atoms in the prepared $Cu_{0.35}MoS_2$ had the oxidation state $+1$.¹⁶⁵ Experimental data show that the single-layers $(MoS_2)^{x-}$ reduce metal cations if the layer charge x exceeds some threshold value. The maximum layer charge equal to $1\bar{e}$ per Mo atom in $LiMoS_2$ decreases during the dispersion (which is accompanied by hydrogen evolution) and subsequent ageing, thus lowering the reducing ability of the $(MoS_2)^{x-}$ layers. The composition of compound $Cu_{0.35}MoS_2$ formed upon the action of Cu^{2+} ions on the MoS_2 single-layer dispersion indicates that this charge can reach $\sim 0.7\bar{e}$ per Mo atom in the freshly prepared dispersions and that the single-layer no longer reduces Cu^{2+} when the charge decreases to $\sim 0.35\bar{e}$ per Mo atom (see Ref. 165).

Structural parameters for the M_xMoS_2 phases are given in Table 5. It is clear from the Table that the increase in the interlayer spacing is small for various metal atoms introduced into the MoS_2 matrix, but it increases with the increase in the sizes of the guest cations. It is of note that a comparison of either Δc for this compound or the radii of the intercalated cations with the sizes of the interstitial vacant sites between the sulfur atoms (octahedral of ~ 0.7 Å radius and tetrahedral of ~ 0.4 Å radius) does not allow unambiguous determination of the type of occupied vacancies since the MoS_2 matrix itself may be essentially distorted and 'the thickness' of its layers may change. For instance, in the crystalline $Co_{0.5}MoS_2$ (prepared by high-temperature synthesis), the coordination environment of molybdenum is octahedral and the interlayer distance is 5.72 Å,⁸⁷ *i.e.*, the thickness of the $S-Mo-S$ layers is smaller by ~ 0.5 Å in this compound than in non-

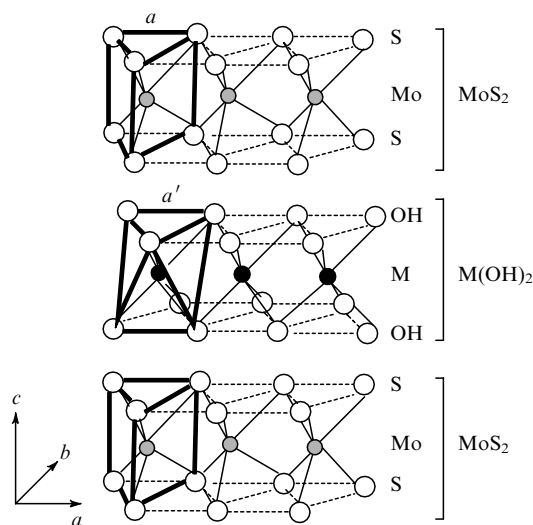


Figure 9. Alternating monolayers of MoS_2 and $M(OH)_2$ in the layered compound.

Table 5. Interlayer spacings (c), interlayer spacing expansions with respect to MoS_2 (Δc) and parameters of the local environment of the guest atoms for ternary sulfides M_xMoS_2 obtained from single-layer dispersions.

Compound	$c/\text{\AA}$	$\Delta c/\text{\AA}$	Radius of the M^{n+} cation according to Shannon for the indicated coordination number (C.N.)			$N_{\text{M-S}}$	$r_{\text{M-S}}/\text{\AA}$	Coordination polyhedron for M	Ref.
			$r/\text{\AA}$	$n+$	C.N.				
$\text{Cu}_{0.35}\text{MoS}_2$	6.25	0.1	0.60	1+	4	3.1	2.29	tetrahedron	165
$\text{Pd}_{0.45}\text{MoS}_2$ (60% $\text{Pd}_{0.25}\text{MoS}_2$ + 40% Pd)	6.2	0.05	0.64	2+	4	2.6 ^a	2.33	"	154
$\text{Hg}_{0.20}\text{MoS}_2$	6.3	0.15	0.69	2+	2	1.1	2.37	strongly distorted octahedron	154
$\text{Hg}_{0.02}\text{MoS}_2$	—	—	—	—	—	1.9	2.38	the same	166
$\text{Hg}_{0.32}\text{MoS}_2$	—	—	—	—	—	1.5	2.37	"	166
$\text{Cd}_{0.20}\text{MoS}_2$	6.55	0.4	0.78	2+	4	4.0	2.55	tetrahedron	154
$\text{Ag}_{0.86}\text{MoS}_2$ (95% $\text{Ag}_{0.82}\text{MoS}_2$ + 5% Ag)	7.0	0.85	1.00	1+	4	1.0 ^a	2.40	strongly distorted tetrahedron	154
$\text{Ag}_{0.61}\text{MoS}_2$	—	—	—	—	—	1.6	2.43	the same	166
$\text{Pb}_{0.18}\text{MoS}_2$	7.1	0.95	1.19	2+	6	5.7	2.87	octahedron	154

^a The $N_{\text{M-S}}$ value as calculated for a pure phase of ternary sulfide.

intercalated 2H- MoS_2 in which the environment of molybdenum is trigonal prismatic.

EXAFS data has been used to estimate the type of coordination environment of intercalated metals.^{154, 165, 166} The type of coordination of the guest atoms M with sulfur atoms is primarily determined by the preferable coordination polyhedra of M, both in TX_2 compounds with metals prepared by high-temperature synthesis and in M_xMoS_2 compounds obtained from single-layer dispersions. Thus Pb^{2+} ions occupy the octahedral vacancies while Cd^{2+} , Pd^{2+} , Cu^+ and Ag^+ ions have tetrahedral surroundings, non-distorted for cadmium and distorted to a variable degree for palladium, copper and silver. For the two last-mentioned metals, the displacement of their atoms to one of the vertices inside a tetrahedral vacancy is assumed based on both the experimental results and comparison with the structures of related sulfide compounds. The strongest distortion of coordination polyhedron in the interlayer space of M_xMoS_2 is probably characteristic of mercury compounds because the basic site occupied by mercury is strongly deformed to realise the most suitable near-linear coordination for Hg(II) with S atoms.

The Mo K -edge EXAFS^{154, 165, 166} and, in some cases, X-ray and electron diffraction¹⁶⁵ data showed that the layer matrix in M_xMoS_2 sulfides obtained from single-layer dispersions is distorted owing to the formation of Mo–Mo bonds. At the same time, due to covalent guest–matrix bonding, these compounds are distinguished among the intercalation compounds prepared from single-layer dispersions by their most structural ordering. In particular, X-ray diffraction data¹⁶⁸ indicate that three-dimensional correlations in the layer stacking (rather than turbostratic packing) for the distances of 50–70 Å is characteristic of copper and silver compounds.

VI. Structural transformations of the chalcogenide matrices in the formation of single-layer dispersions

A study of the atomic structure of the TX_2 layers in both the dispersions and the layered materials precipitated from them is a non-trivial task because the subjects of investigation are layered nanostructured species, in many cases thermodynamically metastable, characterised by the absence of a long-range order and by a strong anisotropy of the interatomic interactions. Only scarce information can be obtained by XRPD for such compounds (even for those precipitated) since the diffraction is essentially two-

dimensional in character owing to turbostratic packing and does not allow the unit cell structure to be completely determined. For this reason, structural studies of these materials require the application of a combination of instrumental and calculation methods. These were mainly carried out for materials based on molybdenum and tungsten disulfides because of their potential practical use and also owing to unusual structural transitions found in their quasi-two-dimensional layers.

The distinctions between the atomic structures of the MoS_2 (WS_2) layers present in single-layer dispersions or in the precipitated products and those of the most stable 2H-modifications have repeatedly been observed using physical methods, first of all, EXAFS,^{64, 109, 154, 157, 158} and X-ray and electron diffraction.^{109, 163, 165, 169} The main feature of the local order in the layered compounds formed is the redistribution of T...T distances. For MoS_2 compounds, three non-equivalent Mo...Mo distances (~ 2.8 , ~ 3.2 and ~ 3.8 Å) were observed in the EXAFS spectra instead of one (3.16 Å) distance in 2H- MoS_2 . The shortest Mo–Mo contact in the modified layer corresponds to the formation of a metal–metal chemical bond.

Currently, it is agreed that the Mo(W) atoms in the layered compounds prepared from the single-layer dispersions have an octahedral rather than a trigonal prismatic (as in 2H- MoS_2 and 2H- WS_2) coordination environment. Though this supposition is not experimentally verified to date, it appears to be quite probable taking into account the partial retention of the negative charge on the TS_2 layer in all the following consecutive transformations: $\text{LiTS}_2 \rightarrow \text{dispersions} \rightarrow \text{precipitated layered compound}$. Even the first calculations of the band structure carried out in the early 1970's showed that the octahedral coordination becomes more energetically advantageous for the molybdenum atoms upon adding of 1 $\bar{e}$ per Mo atom to the conduction band formed mainly by the 4d-orbitals of molybdenum. Thus, at least part of the atoms in the charged $(\text{TS}_2)^{x-}$ layer should be in the octahedral environment. Indirect evidence for the octahedral coordination has been reported.⁵⁷ In addition, this coordination is well established by X-ray diffraction analysis for single crystals of ternary sulfides $\text{M}_{0.5}\text{MoS}_2$ prepared by high-temperature synthesis.^{83–88} As in LiMoS_2 , the formal oxidation state of molybdenum in these layered derivatives of molybdenum disulfide remains +3. For LiMoS_2 and materials prepared from dispersions, all the structural models are based on the octahedral coordination of molybdenum postulated for the metastable modification 1T- MoS_2 .³¹

Calculations by the extended Hückel method in the rigid band approximation showed¹⁷⁰ that the Fermi surface is characterised

by nesting[†] in the case of the layered systems with an octahedrally coordinated central atom with d^2 or d^3 electron configuration. In such systems, the metal atom sublattices are unstable, they undergo distortions to form charge density waves (CDW) unrigging this symmetry. In same sense, CDW formation is analogous to the Jahn–Teller distortions in molecular systems,¹⁷¹ while the splitting of the partially filled degenerate orbitals leading to lowering of the overall energy of the system may serve as an analogue of the splitting of partially filled d-sub-band of the metal atom causing the appearance of an energy gap between the filled valence band and the conduction band in the case of infinite quasi-two-dimensional layers. The most probable result of the distortions is the formation of triangular clusters or infinite zigzag chains built of metal atoms.^{13, 170, 171}

The calculations of the LiMoS_2 structure with optimisation of the geometry by DFT FLAPW (Density Functional Theory, Full-Potential Linearised Augmented Plane Wave) method showed¹⁷² that the formation of a $2a \times 2a$ superstructure (zigzag chains formed by rhombus-shaped clusters of molybdenum atoms) lowers the energy of the system. The results obtained, namely, the lengths of the contracted and elongated (with respect to the lengths in the initial 2H-MoS_2) Mo–Mo bonds in the optimised LiMoS_2 structure are consistent with the EXAFS results obtained at the Mo K -edge.³⁹ The same type of ordering is present in the structure of LiMoS_2 , which was simulated based on the analysis of PDF obtained from X-ray diffraction data (Fig. 10 *a*).⁶⁵ According to this model, the structure as a whole is characterised by a triclinic symmetry ($a = 6.963 \text{ \AA}$, $b = 6.386 \text{ \AA}$, $c = 6.25 \text{ \AA}$, $\alpha = 88.60^\circ$, $\beta = 89.07^\circ$, $\gamma = 120.06^\circ$; the space group $P\bar{1}$).

According to the data from X-ray single crystal analysis, the clusters consisting of molybdenum atoms are also present in the molybdenum ternary sulfides obtained by high-temperature synthesis.⁸⁷ For instance, the zigzag chains with direct Mo–Mo bonds exist in the $\text{Co}_{0.5}\text{MoS}_2$ structure, which contains four symmetrically independent molybdenum atoms in the unit cell (Fig. 10 *b*). Taking into account the layer stacking, the crystal lattice of $\text{Co}_{0.5}\text{MoS}_2$ belongs to a face-centered monoclinic syngony (the space group Cc , $Z = 4$, $a = 11.793$, $b = 6.548$, $c = 12.680 \text{ \AA}$; $\beta = 115.5^\circ$) and the relationships between its parameters and the parameters of 2H-MoS_2 (a_0 , c_0) are as follows: $a \approx 2\sqrt{3}a_0$ and $b \approx 2a_0$, $c \sin \beta \approx c_0$. Thus, the displacements of the molybdenum atoms in $\text{Co}_{0.5}\text{MoS}_2$ with respect to their

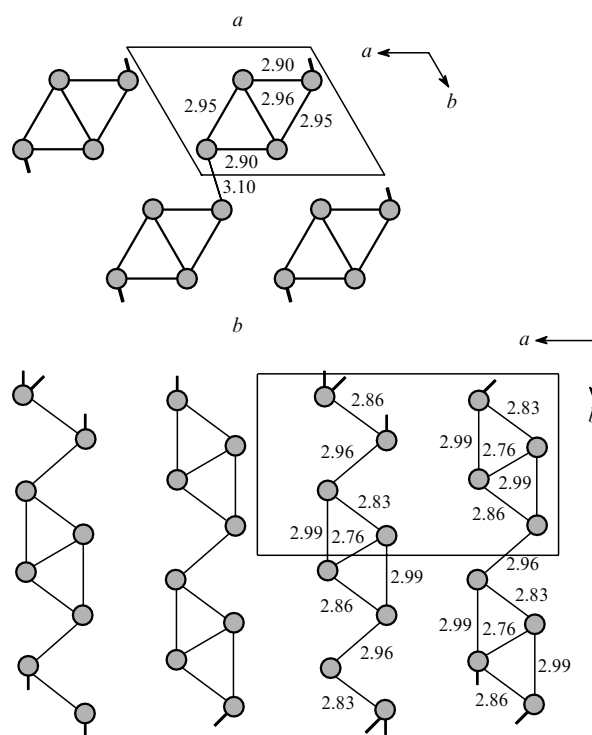


Figure 10. Schematic representation of the chains formed by molybdenum atoms in the ab plane in LiMoS_2 (*a*)⁶⁵ and $\text{Co}_{0.5}\text{MoS}_2$ (*b*).⁸⁷ Figures indicate (in $\text{\AA}$) the values of interatomic distances contracted as compared with 2H-MoS_2 .

positions in the 2H-MoS_2 layer can also be approximated with a $2a \times 2a$ superstructure.

From EXAFS and X-ray diffraction studies carried out on the single-layer dispersions themselves, it was suggested that the molybdenum atoms in the single layers are displaced from their positions in the hexagonal $a \times a$ structure and form rhombuses (Fig. 11 *a, b*). This should result in two Mo–Mo distances (2.8 and $3.8 \text{ \AA}$) and multiplication of the in-layer parameters of the unit cell to $2a \times 2a$.^{107, 109} Such a model fits the experimental data best of all provided the molybdenum atoms are displaced by $0.45 \text{ \AA}$ along the a -axis of the unit cell ($a = 3.27 \text{ \AA}$). Redistrib-

[†] The regions of the Fermi surface coinciding with each other upon parallel transfer of the electron quasi-pulses in space.

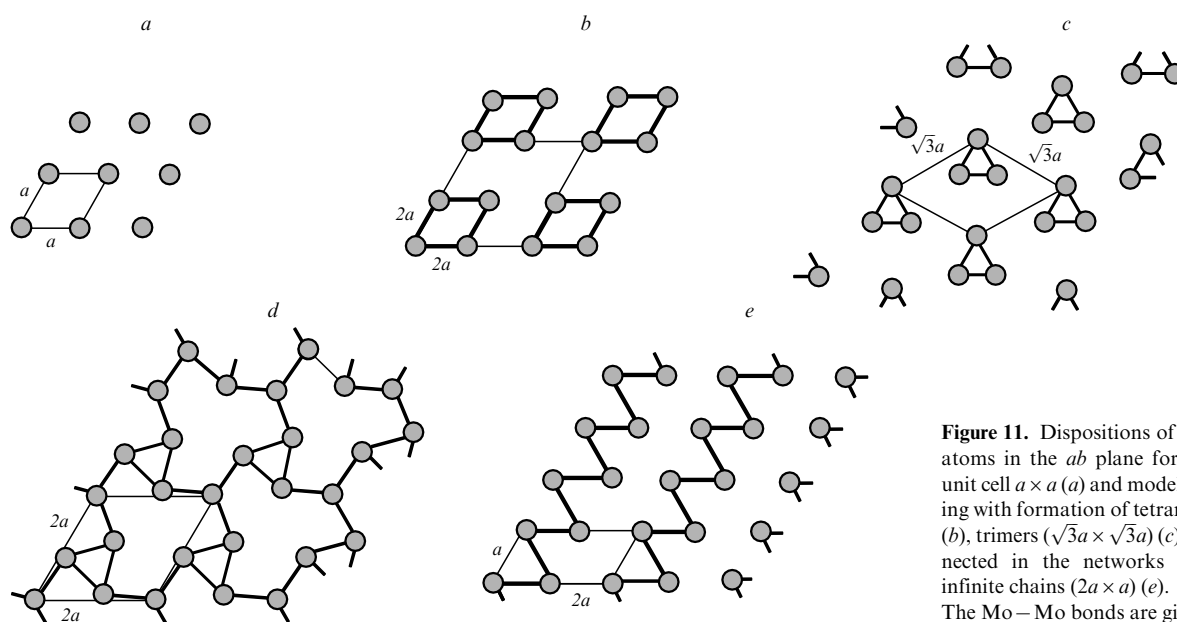


Figure 11. Dispositions of molybdenum atoms in the ab plane for a hexagonal unit cell $a \times a$ (*a*) and models of its ordering with formation of tetramers ($2a \times 2a$) (*b*), trimers ($\sqrt{3}a \times \sqrt{3}a$) (*c*), trimers connected in the networks ($2a \times 2a$) (*d*), infinite chains ($2a \times a$) (*e*). The Mo–Mo bonds are given in bold.

ution of the Mo–Mo distances and the superstructure $2a \times 2a$ were also observed in the MoS₂ layered compounds with intercalated metal hydroxides^{157, 158} and metals (Cu, Ag)¹⁶⁵ obtained from dispersions. For the latter compounds, the comparison of X-ray diffraction and electron diffraction data showed that the $2a \times 2a$ superstructure was characteristic of most particles of the sample, however, yet another type of a superstructure, namely, $\sqrt{3}a \times \sqrt{3}a$ was present. The latter type of ordering, also found by scanning tunneling microscopy and electron diffraction in 1T-MoS₂ [the oxidation product of the layered solvates $K_x(H_2O)_yMoS_2$ (see Ref. 32 and 33)], can be described as a result of trimerisation of the molybdenum atoms giving triangular clusters (Fig. 11 c).

Based on the data obtained by EXAFS and electron diffraction for the precipitated MoS₂ dispersion, another variant of the cluster-like ordering of molybdenum atoms was proposed (Fig. 11 d).⁶⁴ This model assumes the displacement of molybdenum atoms in the *ab* plane of the 2H-MoS₂ layer by ~ 0.5 Å to form a trigonal unit cell (space group *P3*, $a = 6.5$ Å) containing 2 and 4 independent molybdenum and sulfur atoms, respectively. Thus, this type of ordering can be considered as being derived from a $2a \times a$ superstructure in the hexagonal cell. It is worth noting that the above-considered models imply an existence of only two M–M distances in the matrix layer, the short and the long (2.8 and 3.8 Å for MoS₂ derivatives), and do not imply the intermediate distance (~ 3.2 Å) which is usually detected by EXAFS in the products precipitated from dispersions. This contradiction can be caused by the inhomogeneity of the nano-materials in which both distorted and non-distorted fragments of the layers are present⁶⁴ or by the inadequacy of the models.

Based on the data from scanning tunnelling microscopy for the MoS₂ films precipitated from the dispersions,^{111, 173} a less symmetrical model of the atom ordering which includes the formation of infinite chains (Fig. 11 e) was proposed. This type of ordering can be described by using $2a$ and a as the periods of translation along the *a*- and *b*-axis of the initial hexagonal structure or by taking an orthorhombic unit cell with the parameters $\sqrt{3}a \times a$ in the *ab* plane (where a is a parameter of the initial hexagonal cell). It should be mentioned that this type of superstructure was found by scanning tunnelling microscopy and electron microdiffraction also in the layered solvates with potassium $K_x(H_2O)_yMoS_2$ at $0 < x < 0.3$.^{32, 33} Based on the analysis of electronograms, a similar type of ordering was proposed for precipitated MoS₂ and WS₂.¹⁶⁹ In this case, the symmetry of the layer was described using a two-dimensional group *pg* and the following parameters for the unit cell (for MoS₂): $a = 5.47$ Å, $b = 3.16$ Å, $\gamma = 90^\circ$. This corresponds to the shortest Mo–Mo distance of 2.92 Å, which is larger by ~ 0.1 Å than the distance inferred from the EXAFS spectra. In the electronograms of the multi-layered particles of the materials studied, the same authors¹⁶⁹ often observed a hexagonal $2a \times 2a$ superstructure which can appear due to stacking of three orthorhombic $\sqrt{3}a \times a$ structures rotated by 120° with respect to each other.

It is of note that only displacements of the molybdenum atoms in the *ab* plane are allowed for in the above-considered models. Meantime, the well established metal dichalcogenide structures are known, where the CDW modulations lead to puckering of the TX₂ layers. An example is given by the rhenium diselenide structure¹⁷⁴ representing a strongly distorted 1T polymorph with puckered layers (space group *P1*, $a = 6.72$ Å, $b = 6.60$ Å, $c = 6.73$ Å, $\alpha = 104.9^\circ$, $\beta = 91.8^\circ$, $\gamma = 118.9^\circ$). The mean deviation of the rhenium atoms from the layer plane is ~ 0.1 Å. The rhenium atoms have a strongly distorted octahedral environment consisting of selenium atoms (interatomic Re–Se distances are in the range of 2.35–2.66 Å), and form zigzag chains of irregular Re₄ rhombuses with Re–Re bonds along the *b*-axis. The motif of ‘clustering’ in ReSe₂ is close to that proposed for LiMoS₂ based on the calculations and PDF data, though the MoS₂ layer is flat in the latter case.

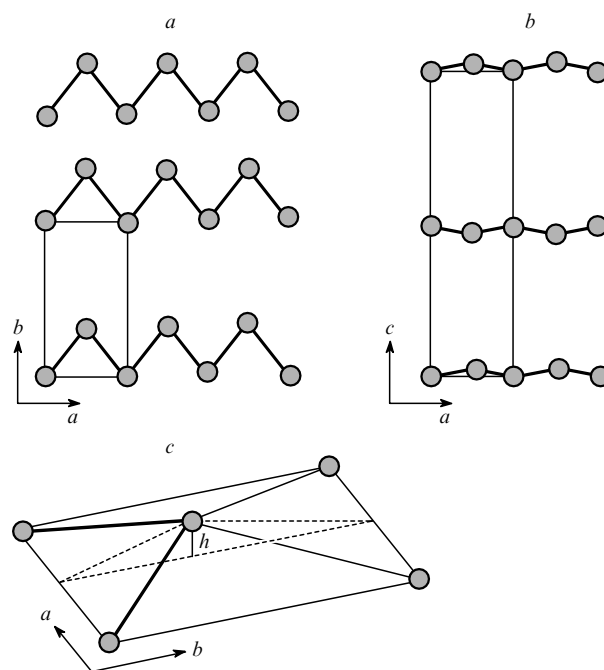


Figure 12. Projections onto the *ab* (a) and *ac* (b) planes and determination of the parameter of puckering for the T atom layer with puckering of WT_{e2} type.

Another type of structure ordering with puckered layers was found for WT_{e2} (Ref. 175) in which the tungsten atoms are also in strongly distorted octahedral environment and form infinite chains (Fig. 12 a, b). Using the model with such puckered layers and considering the diffraction and EXAFS data altogether, the parameters of layer puckering (h , in Fig. 12 c) were found¹⁰⁶ to be 0.46, 0.45 and 0.09 Å for single-layer dispersions of MoS₂, MoSe₂, and WS₂, respectively. It is of note that, upon precipitation of MoSe₂ from dispersion, the chains of the atoms are retained in the layer, while the puckering disappears.

In fact, the same type of chain (a structural motif of WT_{e2}) but a flat variant was earlier used to describe the structure of the precipitated WS₂ on the basis of PDF data analysis.¹⁷⁶ The structure was characterised as monoclinic (space group *P112*₁, $a = 3.27$ Å, $b = 5.71$ Å, $c = 12.31$ Å, $\gamma = 88.48^\circ$). It is important that the existence of all the three metal–metal distances in the distorted layer can be explained employing this model.

Thus, the in-layer structure of the molybdenum- and tungsten-based dichalcogenide matrices dispersed to single layers is modulated by regular distortions with formation of direct metal–metal bonds and these modulations extend for at least tens of Ångströms. It is noteworthy that the electronic interactions of the initial MoS₂ and MoSe₂ matrices with dopant atoms on their surfaces also result in the modulation of their structures, but in this case the modulations are of local character and do not extend for more than one Mo–Mo distance.¹⁷⁷ Note that the variations of superstructure proposed by various researchers may display real dissimilarity in the geometry of the layer in different compounds or even in different particles of the same material. Modification of the layer structure depending on the charge retained on the layer after the formation of the intercalation compound (or, on the time of ageing for precipitation of non-intercalated dichalcogenides TX₂) appears to be quite probable. This follows, for instance, from the difference in the layer geometry between the dispersed and precipitated MoSe₂,¹⁰⁶ as well as from the dependence of the relation between three Mo–Mo distances on the guest content, which has been found in the study of a large series of MoS₂ compounds with various guests.¹⁷⁸

VII. Possible applications of the materials obtained with the use of single-layer dispersions

Layered nanostructured TS_2 -based materials prepared through single-layer dispersions have considerable potential in heterogeneous catalysis,^{179–185} as lubricants,¹⁸⁶ reagents for the extraction of heavy metals,¹⁶⁴ chemical sensors,¹⁸⁷ novel magnetic materials,^{188, 189} and superconductors.¹⁰²

Currently, highly-dispersed molybdenum disulfide doped with 3d-metals (Co, Ni) is the most efficient commercial catalyst for oil hydrotreating. That is why the attempts to use the materials based on the re-precipitated MoS_2 in the hydrodesulfurisation processes appears to be justified.^{180, 190} Moreover, these materials were proposed as highly active and selective catalysts for hydrogenation of carbon monoxide to methane^{181, 184} and for coal liquefaction.¹⁸³ The increase in activity of the $\text{Pt}/\text{Al}_2\text{O}_3$ supported catalysts of methane oxidation are also achieved with the MoS_2 monolayer deposited onto the Al_2O_3 particles.¹⁸⁵

In industry, pure molybdenum disulfide has a large-tonnage application as the base for antifriction composites and solid lubricants exploited in wide temperature and pressure ranges as well as in chemically corrosive media and vacuum. Intercalation of MoS_2 with organic compounds, which has become possible with the advent of the single-layer dispersion technique, allows preparation of tribomaterials with enhanced properties as compared with those of materials obtained by mixing the components in the same composition.¹⁸⁶ An approach to produce magnetic lubricants for ferromagnetic surfaces based on the precipitated molybdenum disulfide doped with 3d-metals appears to be of interest.¹⁹¹

The single-layer dispersions of MoS_2 are able to bind the heavy-metal cations (first of all, Hg^{2+}) and thus can be considered as potential extractants, for instance, in waste-water purification.¹⁶⁴ In this case, the original MoS_2 and metallic mercury can easily be regenerated on heating the Hg_xMoS_2 formed at relatively low temperature ($\sim 400^\circ\text{C}$) under vacuum, and molybdenum disulfide can be repeatedly used in, at least, 3–5 working cycles with retention of its binding capacity.

It was proposed¹⁸⁷ to use thin partially crystalline, oriented MoS_2 films supported on Al_2O_3 and doped with platinum metals in sensitive and selective detectors of molecular hydrogen. Electroconductivity of such films depends linearly on the concentration of H_2 in the environment. Unlike the traditional sensors based on semiconducting transition-metal oxides, the systems mentioned can operate in the temperature range of $25\text{--}150^\circ\text{C}$. They are stable in many oxidising and reducing gaseous media.

Upon thermolysis of metal-containing intercalation compounds of metal dichalcogenides, nanosized metal clusters distributed within the layered TX_2 matrix are formed. Such materials may exhibit unique magnetic properties and are thus candidates for various applications in microelectronics.^{188, 189} In addition, the oriented films in which the interlayer distance can be widely varied are of potential interest for optics, *e.g.*, for developing novel X-ray mirrors and monochromators.¹⁹²

The currently available heterolayered compounds based on TX_2 and polymers have attracted the attention of many researchers as nanostructured conductors and ionic conductors. It has been mentioned that NbSe_2 -based nanocomposites can be used for designing plastic superconductors.¹⁰²

VIII. Conclusion

At present, the method for intercalation of metal chalcogenides based on their dispersion to single layers has gained acceptance among the techniques of solid-state chemistry. With this method, it is quite easy to construct layered compounds at room temperature using extended TX_2 structural units and the reagents introduced into solution.

It should be mentioned that the studies performed to date have mainly been focused on the synthetic aspects. Their prospects have

been showed and the advantages of a single-layer dispersion technique for the synthesis of novel intercalation compounds have been revealed. As shown above, this method permits one to introduce a rather wide variety of the guests in the materials, *viz.*, cations and neutral molecules of organic substances, polymers, polynuclear organometallic complexes, metal cations and metal hydroxide clusters. The method allowed one to extend essentially the range of TX_2 -based layered compounds, first of all, the intercalation compounds of molybdenum and tungsten disulfides as well as nanocomposite materials based on different TX_2 and polymers.

Coincident with manifestation of the advantages, the directions of method perfection have been revealed. It appears that they include, in particular, the use of new non-aqueous solvents providing stability to dispersed systems and possibilities of carrying out further operations for ‘assembling’ layered compounds. In most studies, aqueous (or aqueous-organic) media were used, which imposes special requirements on the nature of the guest. This problem can partly be overcome by performing the reaction in two-phase systems using aqueous media for dispersion and water-immiscible solvents for dissolving the guest. However, the guests sensitive to hydrolytic decomposition cannot be used even in this combination. Besides, such a procedure, which implies the formation of layered compounds on the interface, makes its isolation difficult and was used until now only for the preparation of materials in the form of films.

Yet another direction of method perfection is the enhancement of structural ordering of the compounds obtained. Usually, this is not high because the ‘assembling’ of layered compounds proceeds under non-equilibrium conditions. This may have the following consequences:

- non-uniformity in filling of the interlayer spaces by the guest and difficulties in the regulation of the chemical composition, especially with a low guest content (typically, the minimum content is limited by the composition for which the system does not yet contain the macroscopic phase of non-intercalated TX_2 under the given conditions of synthesis; besides, the solvent molecules or alkali metal cations can enter into the interlayer space along with the guest molecules);

- turbostratic stacking of the layers;

- in most cases, the impossibility of raising structural ordering of the materials obtained by annealing, because heating even at moderate temperatures ($100\text{--}200^\circ\text{C}$) often initiates structural transformations and deintercalation processes.

It is obvious that further optimisation of the characteristics of the compounds should be conducted taking into account the specific fields of application (*e.g.*, electronics, catalysis, coating production) of each type of material, since the specialists working in these fields make different demands to the degree of ordering of the nanostructures obtained.

It should be noted that information on the structure of novel intercalation compounds is fragmentary. Often, new compounds are characterised by the only structural parameter, *viz.*, by the interlayer spacing expansion obtained from the XRPD data. More detailed studies of the atomic structures of both the intercalated layer and matrix layers are not numerous yet. The investigations of the material morphology are almost absent. Nevertheless, a comprehensive approach applied in some cases allowed one to establish the chemical nature and local structure of the guest layer, to reveal and to analyse distortions of the host matrix induced by intercalation and to propose the structural models for the studied classes of intercalation compounds not contradicting the body of experimental data.

In our opinion, yet another prospective direction of research exists which has not been sufficiently developed yet. This is the study of the reactivities of two-dimensional structures of TX_2 and the guest in the layered compounds precipitated from dispersions. The ability of such ultra-dispersed systems to undergo chemical transformations may differ essentially from the reactivity of the corresponding components in a bulk sample and this can also be

used for producing novel materials with various practically valuable characteristics.

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Vinyltetrazoles: synthesis and properties

V N Kizhnyaev, L I Vereshchagin

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Abstract. The published data on the synthesis of *C*- and *N*-vinyltetrazoles and their chemical transformations (homo- and copolymerisation) involving the heterocycle and the vinyl group are systematised and generalised. The areas of possible application of these compounds are considered. The bibliography includes 194 references.

I. Introduction

The first representatives of vinyltetrazoles were obtained 40 years ago by Finnegan and Henry^{1,2} who proposed to use tetrazole-containing polymers as binding agents in the production of gunpowders and matches. A number of comprehensive reviews on the chemistry of tetrazoles have been published since then,^{3–13} but the preparative procedures and properties of tetrazoles containing unsaturated substituents have not been detailed. At the same time, these compounds, particularly vinyl-substituted tetrazoles, can serve as a basis for new in principle polymeric materials possessing unusual and valuable properties. Thus one of the reasons for increased interest in vinyltetrazoles is the possibility of obtaining polymers with high energy characteristics as can be evidenced from numerous patents devoted to the construction of polymeric binding agents for jet engine fuels, gunpowders, explosives, *etc.*^{2, 14–20}

This paper is an overview of the published data and the first attempt to generalise the results of investigations into the synthesis, structures, physicochemical properties and polymerisability of vinyltetrazole derivatives.

V N Kizhnyaev, L I Vereshchagin Department of Chemistry, Irkutsk State University, 664003 Irkutsk, ul. K Marksa 1, Russian Federation. Fax (7-395) 224 22 38; Institute of Petroleum and Coal-Chemical Synthesis, Irkutsk State University, 664003 Irkutsk, ul. Lermontova 126, Russian Federation. Fax (7-395) 295 48 81. Tel. (7-395) 242 67 11. E-mail: kizhnyaev@chem.isu.ru (V N Kizhnyaev). Tel. (7-395) 242 63 21 (L I Vereshchagin)

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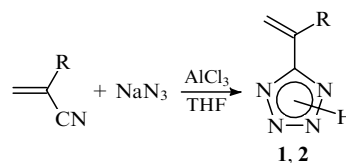
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II. Synthesis of vinyltetrazoles

The choice for a procedure for the synthesis of vinyltetrazole derivatives depends on the position of the vinyl group in the ring, but two main approaches stand apart among other methods. One of them consists of the formation of the tetrazole ring by cyclisation of open-chain compounds containing a vinyl group, while the second approach, which is more common, includes the formation of a double bond at the heterocycle.

1. Synthesis of *C*-vinyltetrazoles

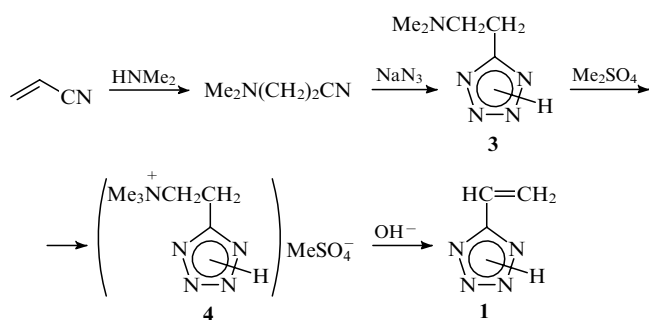
Reaction of acrylonitrile with sodium azide in the presence of aluminium chloride occurs in one step and results in 5-vinyltetrazole (**1**) (conversion 55%). However, the yield is low and unstable due to polymerisation of the starting and target vinyl compounds. Using this approach, 5-isopropenylnitrazole (**2**) was prepared from methacrylonitrile in a somewhat better yield (conversion 71%, yield ~ 45%), since the C=C bonds in methacrylonitrile and isopropenylnitrazole are less prone to polymerisation.²¹



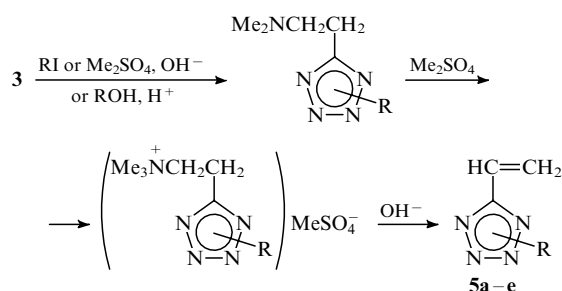
R = H (**1**), Me (**2**).

Cycloaddition of the azide ion to the C≡N bond of nitriles is significantly facilitated if the reaction is carried out in the presence of compounds able to form hydrazoic acid salts from sodium azide soluble in the solvent used. In addition, these salts increase the reactivity of the azide ion. They are prepared using ammonium chloride,^{22,23} alkylamine hydrochlorides,^{14,15} tetramethylguanidinium chloride,²⁴ boron trifluoride etherate²⁵ and aluminium chloride.²¹

Temporary protection of the double bond of acrylonitrile by addition of dimethylamine has made it possible to avoid polymerisation and resinification in the reaction of the azide ion with the nitrile group of 3-dimethylaminopropionitrile: 5-(2-dimethylaminoethyl)tetrazole (**3**) was prepared in high yield.^{14,15} The Hoffmann deamination of the quaternary salt **4** gives 5-vinyltetrazole (**1**).



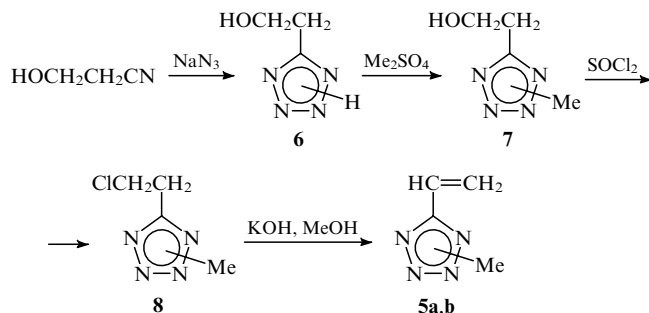
Preparation of *N*-alkyl-*C*-vinyltetrazoles **5a–e** is more difficult because of the impossibility of direct introduction of the alkyl substituent into 5-vinyltetrazole (**1**) due to spontaneous polymerisation under the reaction conditions. Therefore, the formation of the vinyl group by deamination of the quaternary ammonium salt is preceded by alkylation of the heterocycle in the tetrazole derivative **3**.^{14, 15, 26–28}



R = 1-Me (**a**), 2-Me (**b**), 2-Et (**c**), 2-Prⁱ (**d**), 2-Bu^t (**e**).

Hydrohalogenation of acrylonitrile resulting in 3-chloropropionitrile, its reaction with the azide ion and subsequent dehydrochlorination of the 5-(2-chloroethyl)tetrazole formed with potassium hydroxide in aqueous methanol is a more convenient approach to the synthesis of unsubstituted 5-vinyltetrazole (**1**).²¹ In order to increase the yield of the vinyl compound and to suppress its spontaneous polymerisation, it was proposed to perform dehydrochlorination with a twofold excess of an alkali in the presence of ionol as the polymerisation inhibitor.²⁹

Ethylene cyanohydrin can be used as a starting material in the synthesis of vinyltetrazoles **5a,b**. Cycloaddition of the azide ion to the nitrile group results in 5-(2-hydroxyethyl)tetrazole (**6**),^{16, 17} which is methylated with dimethyl sulfate and the hydroxyethyl group in compound **7** is further modified. Subsequent dehydrochlorination of the chloroethyl derivative **8** with methanolic KOH affords vinyltetrazoles **5a,b**.

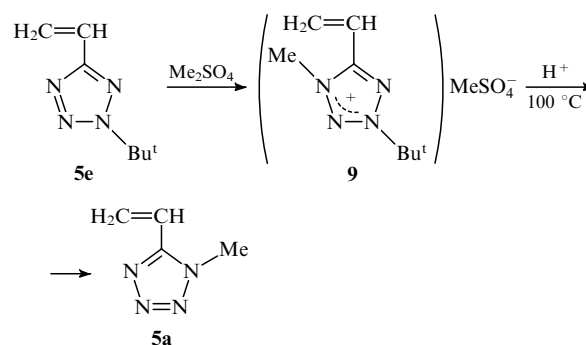


R = 1-Me (**a**), 2-Me (**b**).

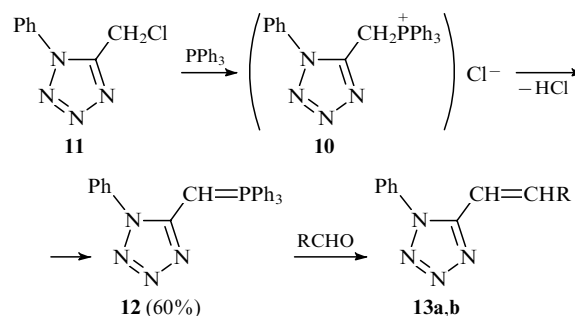
The use of dehydrochlorination for the synthesis of vinyltetrazoles has a number of advantages. Deamination of the quaternary salts of 2-dimethylaminoethyltetrazoles proceeds upon heating, while dehydrochlorination of 2-chloroethyl compounds is usually carried out with potassium hydroxide solutions at low temperatures, which significantly decreases the risk of polymerisation of the target product. This method ensures repro-

ducible and satisfactory yields of 5-vinyltetrazole (**1**) and its alkyl derivatives.^{1, 2, 16–19, 21, 29–31}

A procedure for the synthesis of 5-vinyl-1-methyltetrazole (**5a**) starting from 2-*tert*-butyl-5-vinyltetrazole (**5e**) via the quaternary salt **9** has been proposed.³²



The aforementioned methods cannot be extended to the synthesis of *N*-aryl-substituted *C*-vinyltetrazoles. The vinyl group was introduced into position 5 of the tetrazole ring containing a phenyl substituent at the nitrogen atom using the Wittig reaction.³¹ Phosphonium salt **10** was prepared from 1-phenyl-5-chloromethyltetrazole (**11**); its dehydrochlorination gave the ylide **12**. The latter readily reacts with various aldehydes according to a common scheme to give compounds **13a,b**.



R = H (**a**), Ph (**b**).

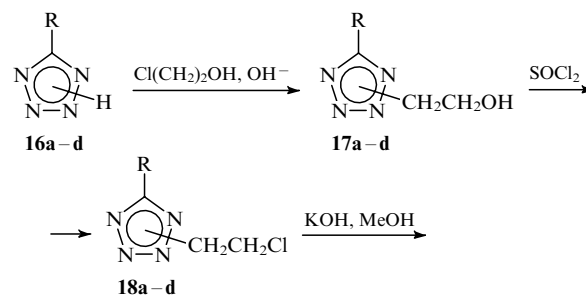
This reaction affords tetrazolyl-substituted alkenes in good yields.

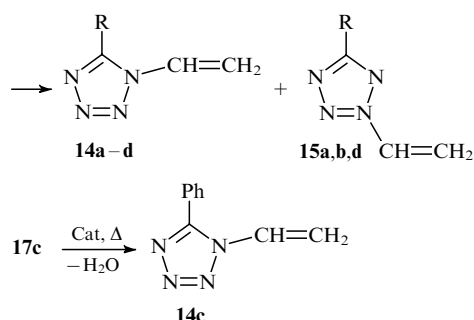
2. Synthesis of *N*-vinyltetrazoles

The major difference between the approaches used in the synthesis of *N*-vinyltetrazole derivatives and those described above is that the former makes use of compounds with preformed heterocycles as starting substrates.

N-Vinyltetrazoles **14** and **15** are synthesised from 2-chloroethyltetrazoles using three different approaches.

The first of them includes alkylation of tetrazoles **16a–d** with ethylene chlorohydrin with subsequent replacement of the hydroxy group in 2-hydroxyethyltetrazoles **17a–d** by chlorine under the action of thionyl chloride^{1, 2, 17, 18} and dehydrochlorination of 2-chloroethyl derivatives **18a–d**. Vinyltetrazole **14c** can be prepared by dehydration of compound **17c**.³³

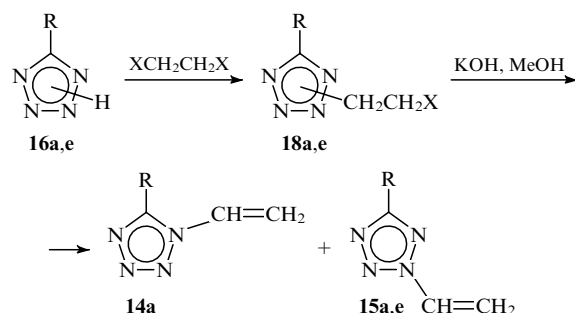




R = H (**a**), Me (**b**), Ph (**c**), NH_2 (**d**).

As in the case of *C*-vinyltetrazoles, dehydrochlorination is more preferable for the formation of the vinyl group.

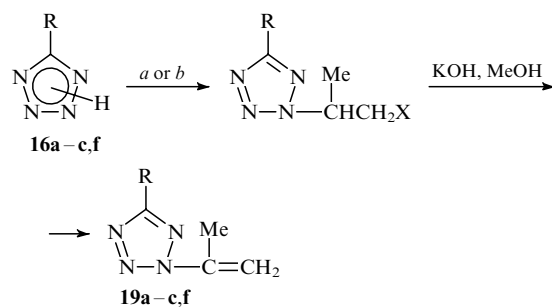
The second approach to the synthesis of *N*-vinyltetrazoles has been described in the studies,^{34–36} where 1- and 2-(2-halogenoethyl)tetrazoles were synthesised by alkylation of tetrazole (**16a**) and 5-nitrotetrazole (**16e**) with 1,2-dichloro- or 1,2-dibromoethane under conditions of phase-transfer catalysis.



R = H (**14a**, **15a**, **16a**), NO_2 (**15e**, **16e**); X = Cl, Br.

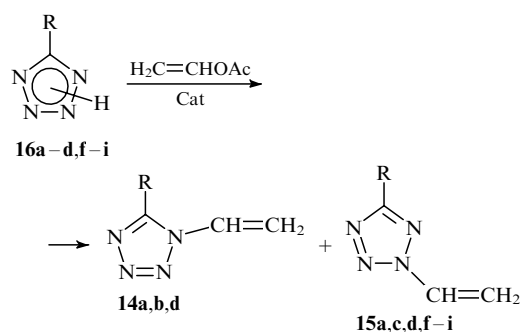
2-(2-Halogenoethyl)-5-nitrotetrazoles are prepared from the nitro derivative **16e**; their dehydrohalogenation was used for the synthesis of 2-vinyl-5-nitrotetrazole (**15e**).³⁶ It is of note that the alkylation yields a mixture of isomers in the majority of cases, the separation of which is often problematic.

The third approach to the synthesis of 2-(2-halogenoethyl)tetrazoles has recently been proposed.³⁷ This consists of selective alkylation of tetrazole and its 5-substituted derivatives with halo-substituted alcohols or allyl halides. Subsequent dehydrohalogenation of the intermediate compounds yields 2-isopropenyltetrazoles **19a-c,f**.



R = H (**a**), Me (**b**), Ph (**c**), CF_3 (**f**);
(a) $\text{MeCH}(\text{OH})\text{CH}_2\text{X}$ (X = Cl, Br), H_2SO_4 ;
(b) $\text{CH}_2=\text{CHCH}_2\text{Br}$, H_2SO_4 .

Reaction of vinyl acetate^{31,38–43} or butyl vinyl ether⁴² with tetrazoles **16a-d,f-i** is a convenient approach to the synthesis of *N*-vinyltetrazoles.



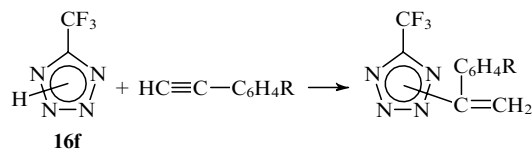
R = H (**a**), Me (**b**), Ph (**c**), NH_2 (**d**), CF_3 (**f**), NO_2Ph (**g**), CH_2Cl (**h**), $\text{CH}=\text{CH}_2$ (**i**).

The synthetic procedures proposed by different authors utilise different catalytic systems, but all of them make use of mercuric acetate in the presence of acetic^{31,38–42} or sulfuric acids,³¹ boron trifluoride etherate⁴¹ and palladium – sodium acetate mixture as a catalyst.⁴² The yields of the vinylation products and the position of the vinyl group in the substituted tetrazoles depend on the nature of the substituent at the carbon atom. Small-size or potent electron-withdrawing substituents direct the vinyl group to position 1 of the tetrazole ring predominantly. Electron-withdrawing substituents shielding the vicinal nitrogen atom favour the formation of 2-vinyltetrazoles **15**. In addition, such substituents decelerate or fully inhibit the reaction.

The catalytic system $\text{Hg}(\text{OAc})_2 - \text{CF}_3\text{CO}_2\text{H}$ was recommended for the preparation of 1-vinyltetrazole (**14a**).⁴³ The use of trifluoroacetic acid prevents secondary polymerisation. If the reaction time is small, the yield of the vinylation product is close to quantitative; the target product contains predominantly 1-vinyltetrazole (**14a**) and only a small amount (no more than 10%) of 2-vinyltetrazole (**15a**). Irrespective of the catalytic system used, vinylation of unsubstituted tetrazole gives two isomeric vinyltetrazoles **14a** and **15a** which are readily separated by vacuum distillation. A method for separation of 1- and 2-vinyl-substituted tetrazoles has been developed^{40,44–46} which entails selective formation of CuCl_2 complexes; their subsequent degradation affords 1-vinyl-substituted tetrazoles.

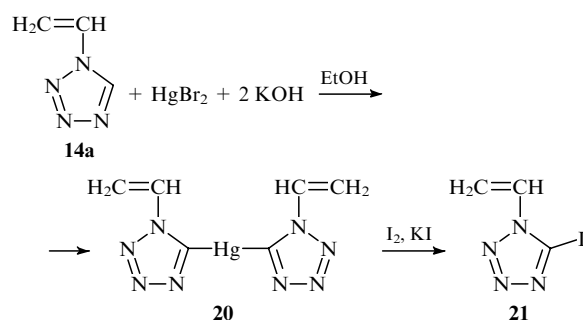
Vinylation of tetrazoles under the action of isopropenyl acetate was used in the synthesis of 1-isopropenyltetrazole in 30% yield.⁴³

Some tetrazolyl-substituted alkenes were prepared by reaction of 5-trifluoromethyltetrazole **16f** with arylacetylenes. This reaction proceeds vigorously upon mixing of the reagents in the absence of the solvent and the catalyst.⁴⁷



R = H, 4-Cl, 4-Me.

In contrast to the 5-vinyl derivative where the double bond must be protected, the synthesis of 1-vinyltetrazole allows the introduction of substituents into the heterocycle without preliminary protection of the vinyl group. Thus mercuration of 1-vinyltetrazole (**14a**) yields the mercury derivative **20**. Subsequent replacement of the mercury atom by iodine gives 1-vinyl-5-iodotetrazole (**21**).⁴⁸



Several other approaches to the synthesis of vinyltetrazoles exist. These are based on reaction of vinyl isocyanide⁴⁹ or vinyl-oxazolones⁵⁰ with hydrazoic acid, reaction of *N*-methylacrylonitrile fluoroborate²⁵ with sodium azide, reactions of acrylonitrile with organotin azides⁵¹ or cross-coupling of 1-benzyl-2-bromotetrazole with vinylboronic acid.⁵² However, these methods have no preparative significance.

III. Electronic structures and geometry of vinyltetrazoles

Vinyl derivatives of five-membered nitrogen-containing heterocycles including vinyltetrazoles can be regarded as bifunctional compounds containing two unsaturated fragments, *viz.*, the vinyl group and the azole ring. The intramolecular interactions in vinyltetrazoles and their effects on the electronic structure have been documented in numerous papers.^{27, 53–59} In many of them, the authors did not restrict themselves to consideration of charge and energy characteristics of interacting molecules, but attempted to estimate their reactivities on the basis of calculations.

The distribution of the total charges ($\sigma + \pi$) calculated by the SINDO/S method based on the planar structure of vinyltetrazole molecules is shown in Figure 1.⁴³

Calculations of total ($\sigma + \pi$) electron densities have shown^{60, 61} that both carbon atoms in the vinyl group of *C*-vinyltetrazoles bear a negative charge, while the charge of the α -carbon atom of *N*-vinyltetrazoles is positive due to σ -electron-withdrawing properties of the nitrogen atom at the double bond. In both cases, the total electron density on the β -carbon atom of the vinyl group is higher than that on the α -atom. The π -electron distribution is characterised by reverse polarisation^{60, 61} (the negative π -electron charge is concentrated on the α -carbon atom of the C=C bond), which testifies to the π -electron-withdrawing effect of the tetrazolyl substituent. Polarisation of the vinyl group ($\Delta q_{\beta\alpha}$) in *N*-vinyltetrazoles is more pronounced than in *C*-vinyltetrazoles. Introduction of electron-donor substituents, such as Me and NH₂, into position 5 of the tetrazole **14a** (compounds **14b,d**) reduces the electron-withdrawing effect of the tetrazolyl substituent on the vinyl group. Consequently, the total ($\sigma + \pi$) negative charge of the α -carbon atom and complete polarisation of the double bond of the vinyl group are increased. Similar changes in the distribution of electron density are induced by introduction of an alkyl substituent (compounds **5c** and **5b**) into position 2 of the tetrazole **1**; this effect does not depend on the size or structure of the alkyl group.²⁷

Introduction of a methyl substituent into the vinyl group changes drastically the charge distribution pattern. The total ($\sigma + \pi$) negative charge of both 1-isopropenyl- (**22**) and 5-isopropenyltetrazole (**2**) is concentrated on the β -carbon atom, whereas the positive charge on the α -atom of the isopropenyl group. Special mention should be made of the much higher polarity ($\Delta q_{\beta\alpha}$) of the C=C-bond of isopropenyl derivatives in comparison with the corresponding vinyl compounds.

An analysis of distribution of the electron density in the heterocyclic fragment has shown that, in contrast to unsubstituted tetrazole, the vinyl group at C(5) has virtually no effect on the atomic charges in the ring.^{55, 62} The carbon and the 'pyrrole' nitrogen atoms both bear positive charges, whereas 'pyridine'

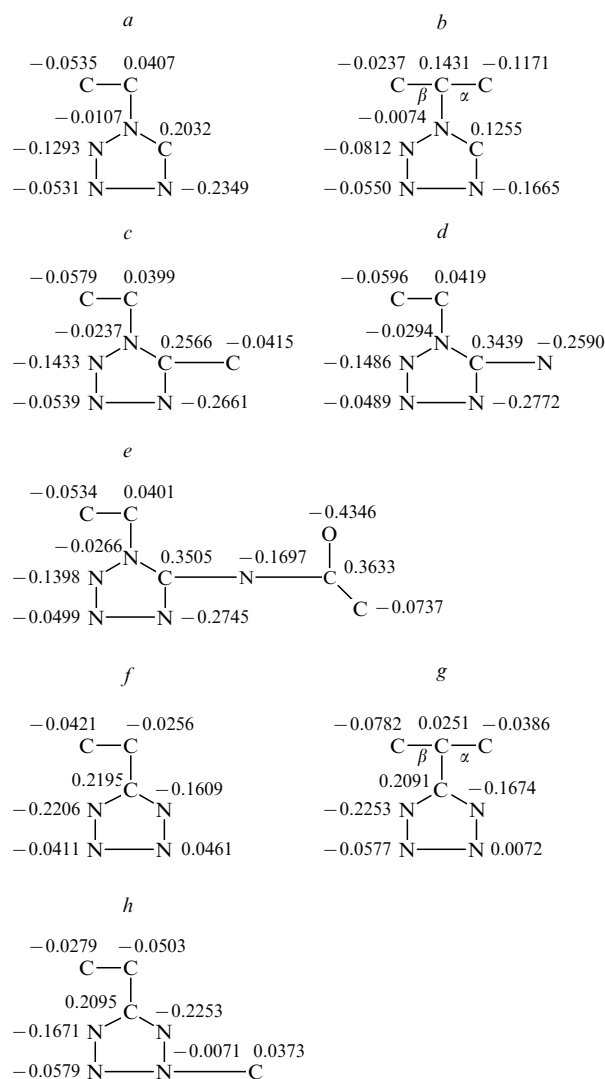
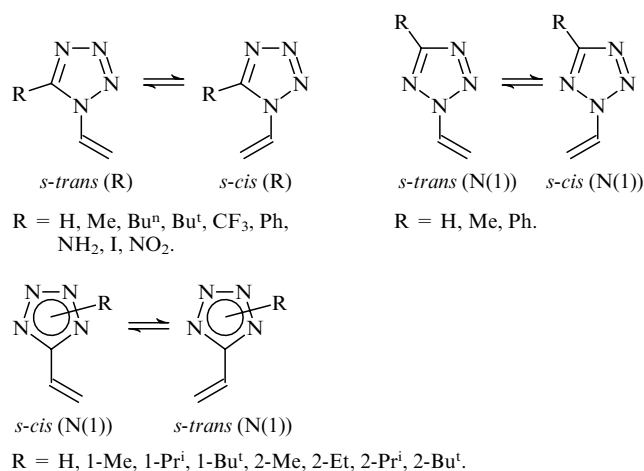


Figure 1. The distribution of total charges in vinyltetrazole molecules.⁴³ (a) 1-Vinyltetrazole (**14a**); (b) 1-isopropenyltetrazole (**22**); (c) 5-methyl-1-vinyltetrazole (**14b**); (d) 5-amino-1-vinyltetrazole (**14d**); (e) 5-acetyl-1-vinyltetrazole (**14f**); (f) 5-vinyltetrazole (**1**); (g) 5-isopropenyltetrazole (**2**); (h) 2-methyl-5-vinyltetrazole (**5b**).

nitrogen atoms are charged negatively. The vinyl group at N(1) slightly changes the distribution of electron density in the tetrazole ring. As the 'pyrrole' nitrogen atom manifests σ -electron-withdrawing properties, the vinyl group localised in this position imparts a small negative charge to it. The positive charge of *N*-vinyltetrazole molecules is accumulated predominantly on the carbon atom, while in 1- (**14a**) and 5-vinyltetrazole (**1**) it is concentrated on the N(4) atom. Introduction of electron-donor substituents, such as Me and NH₂, into position 5 of 1-vinyltetrazole (**14a**) further increases the electron density at N(4). In contrast to 5-vinyltetrazole (**1**), the presence of a methyl substituent in position 2 of 5-vinyl-2-methyltetrazole (**5b**) slightly diminishes the negative charge on N(4), but increases it on N(1).

Studies of mutual effects of two unsaturated fragments in vinyltetrazole molecules should include an analysis of their spatial structures. According to quantum-chemical calculations, the optimised geometry of the monomers is planar. *s-cis/s-trans*-Isomerism is more characteristic of compounds in which the heteroaromatic nuclei are conjugated with the acyclic unsaturated fragment. Both conformers are typical of *C*- and *N*-vinyltetrazoles.^{63–72}



A correlation dependence has been found between integral intensities of stretching vibrations of the C=C bond in the vinyl group of some unsubstituted *N*-vinylazoles and the difference in the electron charges on their carbon atoms.⁶⁴ This finding has allowed the authors to conclude that these compounds exist predominantly in the *s-trans*-conformation. At the same time, data from ¹³C NMR spectroscopy do not exclude the *s-cis*-conformation.⁶⁵ More recent studies of stereochemical dependences of direct spin–spin coupling constants of ¹³C–¹H in the vinyl group of vinylazoles revealed that the proportion of the *s-trans*-form in the conformer mixture increases with an increase in the number of nitrogen atoms in the heterocycle.^{67,68} It may thus be concluded that 1-vinyltetrazole (**14a**) exists predominantly in the *s-trans*-conformation. Introduction of substituents into position 5 of the heterocycle results in stabilisation of the *s-trans*-conformation of *N*-vinyltetrazoles.^{68,73} Both conformers of unsubstituted 5-vinyltetrazole (**1**) are equivalent as can be judged from the IR spectroscopic data.⁷² The effect of the alkyl substituent in position 2 of *C*-vinyltetrazole on the conformer ratio is interpreted differently by different authors. According to study,⁶⁹ 5-vinyl-2-methyltetrazole (**5b**) represents a mixture of *s-cis* and *s-trans*-conformers whose ratio varies depending on the temperature and the nature of the solvent. According to electron-diffraction analysis data, 5-vinyl-2-methyltetrazole (**5b**) exists exclusively in the *s-cis*-conformation in the gas phase.⁶⁶ Quantum-chemical calculations have shown that the content of 5-vinyl-2-R-tetrazole rotamers has virtually no dependence on the substituent size, whereas the conformation equilibrium of 5-vinyl-1-R-tetrazoles is mainly determined by the steric effect of the substituent: the amount of the *s-trans*-conformer increases with an increase in the size of the alkyl substituent.⁶³

IV. Physicochemical and spectroscopic properties of vinyltetrazoles

Recent advances in the synthesis of vinyltetrazole derivatives have stimulated studies into their physicochemical and spectroscopic properties. These studies and quantum-chemical methods may help establish a quantitative correlation between structural, physicochemical and spectroscopic properties and reactivities of vinyltetrazoles, including their radical polymerisation. It is from this standpoint that spectroscopic characteristics on vinyltetrazoles are considered in the overwhelming majority of published papers.^{27, 53, 55, 65, 69, 74, 75}

1. Dipole moments of vinyltetrazoles

The experimental values of dipole moments of vinyltetrazoles (μ) (Table 1) significantly exceed those of vinylazole derivatives containing fewer nitrogen atoms in their rings. For example, the dipole moments of 1-vinylimidazole, 1-vinylpyrazole and 1-vinyl-1,2,4-triazole are equal to 3.2, 1.9 and 3.05 D, respectively.^{76,77} These data point to a higher polarity of vinyltetrazole molecules in

Table 1. Dipole moments (μ), polarographic reduction potentials ($E_{1/2}$) and characteristics of the absorption bands in the UV spectra of vinyltetrazoles (MeCN).⁴³

Compound	μ /D	$E_{1/2}$ /V	UV spectra	
			$\lambda_{\max}$ /nm	$10^{-3} \epsilon$
1-Vinyltetrazole (14a)	5.34	−2.52	223 (224) ^a	7.30 (6.10) ^a
5-Methyl-1-vinyltetrazole (14b)	5.71	−2.59	218	6.45
5-Amino-1-vinyltetrazole (14d)	7.10	−2.70	242	6.0
5-Acetylamino-1-vinyltetrazole (14f)	4.05	−2.67	228, 196	8.78, 7.63
5-Phenyl-1-vinyltetrazole (14c)	—	—	239 ^a	11.80 ^a
1-Isopropenyltetrazole (22)	—	—	232.5	5.0
5-Vinyltetrazole (1)	5.21	−2.0	218	10.75
2-Methyl-5-vinyltetrazole (5b)	2.34	−2.42	218	10.30
5-Isopropenyltetrazole (2)	4.77	−2.03	223	8.60

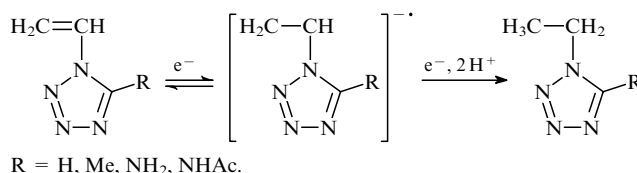
^a Data from Ref. 33.

comparison with other vinylazoles. High values of dipole moments of unsubstituted tetrazoles are usually assigned to the polarising effect of unshared pairs of nitrogen atoms and the resulting nonuniform distribution of electron density in the tetrazole ring.⁶² Introduction of a vinyl group further enhances the nonuniformity of the charge distribution. The values of dipole moments of unsaturated tetrazole derivatives (see Table 1) usually exceed those of the corresponding non-vinylated substituted tetrazole derivatives. Thus the μ values for tetrazole, 5-methyltetrazole and 5-aminotetrazole are equal to 5.14, 5.17 and 5.71 D, respectively.^{4,5} Contrariwise, introduction of the isopropenyl group into position 5 decreases the polarity of a molecule in comparison with unsubstituted tetrazole. 2-Methyl-5-vinyltetrazole (**5b**) has a low dipole moment characteristic of tetrazole derivatives (including 2,5-disubstituted ones) with a substituent in position 2 of the heterocycle.⁷⁸ The hypothesis on the 1*H*-tautomeric conformation of unsubstituted tetrazole is based on the significant difference in the polarities of 1- and 2-substituted tetrazoles. A comparison of the experimental dipole moment of tetrazole (5.14 D) with theoretically calculated values of μ for the 1*H*- and 2*H*-tautomeric forms of tetrazole (4.8–5.23 and 1.63–2.35 D, respectively) corroborates this hypothesis.⁵ Taking into account high values of μ for 5-vinyl- (**1**) and 5-isopropenyltetrazole (**2**) and their comparison with the corresponding value for unsubstituted tetrazole, one may conclude that both vinyltetrazoles exist predominantly in the 1*H*-conformation.

2. Polarographic analysis of vinyltetrazoles

The mutual effect of two unsaturated fragments in the vinyltetrazole molecule is especially pronounced in their polarographic analysis.^{43,60,79} Vinyltetrazoles are polarographically active, but the mechanisms of reduction of *N*- and unsubstituted *C*-vinyl derivatives are different.

The vinyl group in *N*-vinyltetrazoles, as in other alkenes,⁸⁰ in particular vinylazoles,⁸¹ is completely reduced by a two-electron mechanism in the presence of proton donors.



Introduction of various groups, such as Me and NH₂, into position 5 of the tetrazole ring increases the electron density on the vinyl group and causes a shift of $E_{1/2}$ for the vinyl group towards more negative values in comparison with 1-vinyltetrazole (**14a**) (see Table 1). Under these conditions, the change in $E_{1/2}$ correlates with the electronic effects of the substituents present in the ring. Thus a satisfactory correlation was found between $E_{1/2}$ and the charge of the β -carbon atom (q_β), the difference of charges on the carbon atoms of the vinyl group ($\Delta q_{\beta\alpha}$)⁴³ and the values of induction constants (σ_1) (see Ref. 82) of the corresponding tetrazolyl substituents.

$$E_{1/2} = (-1.04 \pm 0.10) + (27.33 \pm 2.77)q_\beta \quad (r = 0.93, n = 3),$$

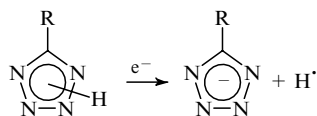
$$E_{1/2} = (-5.02 \pm 0.48) + (24.66 \pm 0.79)\Delta q_{\beta\alpha} \quad (r = 0.99, n = 3),$$

$$E_{1/2} = (-4.32 \pm 0.43) + (2.71 \pm 0.51)\sigma_1 \quad (r = 0.97, n = 3),$$

where r is the correlation coefficient and n is the number of compounds tested.

A quite unexpected [in comparison with 1-vinyltetrazole (**14a**)] shift of $E_{1/2}$ for 5-acetylamino-1-vinyltetrazole (**14f**) towards the negative region testifies to the electron-donor nature of the AcNH group.

A completely different reduction mechanism is observed in the case of 5-substituted tetrazoles, particularly 5-vinyltetrazole derivatives. In contrast to *N*-vinyltetrazoles, the double bond of the vinyl fragment in 5-vinyl- (**1**) and 5-isopropenyltetrazole (**2**) is not reduced. The polarographic activity of tetrazole ($E_{1/2} = -2.13$ V) and its 5-substituted derivatives is determined by their acidic properties; the polarographic wave is associated with proton reduction⁷⁹ which proceeds by a single-electron mechanism. Substitution of the methyl substituent for the acid proton favours reduction of the vinyl group in compound **5b**. It is of note that this process is characterised by a lower value of the negative potential in comparison with *N*-vinyltetrazoles (see Table 1).



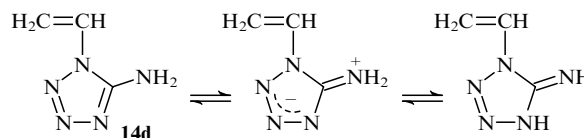
R = CH=CH₂, CMe=CH₂.

3. Ultraviolet spectra of vinyltetrazoles

The conjugation between the π -systems of the heterocycle and the vinyl group determines the presence of intense absorption bands of both *N*- and *C*-vinyltetrazoles in the near UV-region (see Table 1). Introduction of substituents into position 5 of 1-vinyltetrazole (**14a**) results in slight reduction of the extinction coefficient (ϵ), which can be attributed to the decrease in the conjugation between unsaturated fragments in compounds **14b,d** due to deviation of the vinyl group from the plane. A similar effect is observed after introduction of a methyl substituent into the α position of the vinyl group, the values of extinction coefficients ϵ of isopropenyltetrazoles being lower than those of vinyltetrazoles. Introduction of a methyl substituent into position 2 of tetrazole **1** has virtually no effect on the wavelength and intensity of the UV absorption band which testifies to the lack of conformational changes.

It is known that 5-dialkylamino-substituted tetrazoles undergo amine-imine rearrangements.^{4,5} Evidence for the existence of the imine form can be derived from a more significant bathochromic shift of the UV absorption bands of these compounds in comparison with tetrazoles with unsubstituted amino groups which are thought to exist exclusively in the amino form. The absorption maximum in the UV spectrum of 5-amino-1-vinyltetrazole (**14d**) is noticeably shifted towards the longwave region relative to other vinyltetrazoles⁴³ and lies in the region close to the absorption band of the imino (rather than the amino) form (see Table 1). It may thus be concluded that in contrast to

other tetrazole derivatives containing an unsubstituted amino group, 5-amino-1-vinyltetrazole (**14d**) undergoes amine-imine rearrangement.



The parameters of UV absorption bands of *N*-vinyl- and substituted *C*-vinyltetrazoles do not depend on the nature of the solvent, the concentration and pH of the reaction medium. The dependence of spectroscopic characteristics on the aforementioned parameters was observed for 5-vinyltetrazole (**1**) which can be ionised: in aqueous solutions, a change in the concentration of a compound or an increase in pH caused a further shift of the absorption band towards the longwave region. In the ionised form, 5-vinyltetrazole (**1**) is absorbed at $\lambda = 226$ nm ($\epsilon = 9900$).⁴³ In contrast to aqueous solutions, the position of the absorption band in acetonitrile and ethanol did not change with concentration. This finding suggests that 5-vinyltetrazole does not dissociate in these solvents.

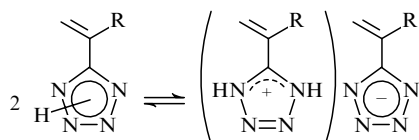
4. Infrared spectroscopy of vinyltetrazoles

There is little evidence on vibrational spectra of vinyltetrazoles. Among a variety of other studies, only two papers devoted to a detailed analysis of IR spectra of unsubstituted 1- and 5-vinyltetrazoles^{71,72} and a few publications where spectral analysis of vinyltetrazole compounds was used to confirm the structures of the polymers prepared from them deserve mention.^{79,83,84}

The IR spectra of vinyltetrazoles contain three main regions. The shapes and positions of low-frequency absorption bands around 600–1000 cm⁻¹, induced by extraplanar vibrations of C–H or by deformation and torsion vibrations of the tetrazole ring⁸⁵ change appreciably depending on the place of attachment of the vinyl group and the nature of the substituent in the heterocycle. Skeletal vibrations of the tetrazole rings are observed around 1000–1500 cm⁻¹ and are characterised by several intense absorption bands around 1030–1090, 1125–1150, 1250–1270, 1320–1390 and 1430–1470 cm⁻¹ irrespective of the vinyltetrazole structure. There is no unanimous opinion about the origin of the intense absorption band around 1560–1580 cm⁻¹ in the IR spectra of tetrazole (**16a**) and its 5-vinyl derivative (**1**). Judging from quantum-chemical calculations,^{72,85} this band has been assigned to the C=N vibrations of the ring. However, analysis of the IR spectra of vinyltetrazoles, model 1-, 2-, 1,5- and 2,5-substituted tetrazoles and 5-substituted tetrazolium salts revealed⁸³ that these spectra contain no band around 1560–1580 cm⁻¹. This finding led us to suggest that this band should be assigned to deformation vibrations of the tetrazole ring induced by the N–H bond characteristic exclusively of non-ionised forms of 5-substituted tetrazoles.

Vibrations of the double bond of the vinyl group in the IR spectra of all vinyltetrazoles under study are manifested as a narrow band around 1645–1655 cm⁻¹. The absorption intensity of various vinyl-substituted tetrazoles correlates with the previously observed dependence of integral intensities of stretching vibrations of the C=C bond on the polarity of the vinyl group.⁶⁴ Higher polarity of the vinyl fragments of *N*-vinyltetrazoles determines higher intensity of the absorption bands around 1645–1655 cm⁻¹ in comparison with those in *C*-vinyltetrazole derivatives. A more detailed analysis of absorption spectra of 2-methyl-5-vinyltetrazole (**5b**) revealed two absorption bands in the region of C=C bond vibrations: a singlet band around 1656 cm⁻¹ and a doublet band around 1648 and 1645 cm⁻¹ (see Ref. 69). These bands were assigned to stretching vibrations of the vinyl groups of two different rotamers of compound **5b**. Deformation vibrations of the =CH-bond of the vinyl group are observed around 960–980 cm⁻¹.

The difference between the IR spectra of vinyltetrazoles is especially pronounced in high-frequency regions (2200–3700 cm⁻¹). The simultaneous presence of an acid proton and ‘pyridine’ nitrogen atoms in 5-vinyl- (**1**) and 5-isopropenyltetrazole (**2**) rings gives rise to intermolecular interactions typical of NH-unsubstituted azoles.^{4,86} The IR spectra of *C*-vinyltetrazoles contain a broad absorption band around 3000–3500 cm⁻¹ corresponding to stretching vibrations of NH⋯N and a band around 2300–2800 cm⁻¹ assigned to the quaternary nitrogen atom, ≡N⁺H (see Ref. 87). No such bands are observed in the IR spectra of *N*-vinyltetrazoles. This suggests that condensed forms of compounds **1** and **2** contain, along with molecular forms, two additional forms, one of which is bound by hydrogen bonds and the other one is ionised as a result of complete proton transfer.



The IR spectra of *N*-vinyltetrazoles and *N*-alkyl-5-vinyltetrazoles contain absorption bands around 2900–3200 cm⁻¹ due to stretching vibrations ν(CH). The complex structure of the absorption band in this particular region of the IR spectrum of 1-vinyltetrazole (**14a**) is attributed to association of molecules *via* the ≥CH⋯N bond.⁷¹

The high-frequency region of the IR spectrum of 5-amino-1-vinyltetrazole (**14d**) contains absorption bands corresponding to the amino group (3150 and 3330 cm⁻¹). The existence of amine–imine rearrangement in compound **14d** is confirmed by IR (see Ref. 43) and UV spectral data: the presence of an absorption band in the IR spectrum around 1670–1680 cm⁻¹ can be assigned to vibrations of the exocyclic C=N bond of its imino form.

5. NMR spectra of vinyltetrazoles

Structural studies of vinyltetrazole derivatives widely employ ¹H and ¹³C NMR spectroscopy. Chemical shifts (δ) of the characteristic proton signals for the vinyl groups of all *N*-vinyltetrazoles studied lie in the range of δ 7.20–7.40 (H_A, q), 5.96–6.05 (H_B, d) and 5.30–5.50 (H_C, d), while signals for the carbon atoms lie around δ 126–128 (C_α) and 106–114 (C_β).^{41,43,53,88,89} Greater shielding (relative to the carbon atom in ethylene) of the C_β atom [δ(C) = 123.3] testifies to effective conjugation of the vinyl group and the tetrazole ring.⁶⁷ Introduction of electron-donor substituents into the tetrazole ring induces a regular upfield shift of the C_β signal commensurate with an increase in the calculated total electron density on the β-carbon atom. The changes in δ(C_β) correlate with the values of the induction constants of σ_I of the tetrazolyl substituents.⁴³

$$\delta(\text{C}_\beta) = (70.1 \pm 10.2) + (60.9 \pm 8.8)\sigma_I \quad (r = 0.999, n = 3).$$

Of special note are parallel changes in *E*_{1/2} and ¹³C_β chemical shifts in the ¹³C NMR spectra. This dependence is described by equation:⁶⁰

$$E_{1/2} = (0.044 \pm 0.016)\delta(\text{C}_\beta) - (7.360 \pm 1.780) \quad (r = 0.883, n = 4).$$

The effect of the tetrazolyl substituent on the chemical shifts of the vinyl group atoms is also determined by its position in the heterocycle. However, it is difficult to establish the difference between the δ values of the vinyl group in the ¹H and ¹³C NMR spectra of 1- and 2-vinyltetrazoles.⁴¹ An insignificant (1–3 ppm) upfield shift of the C_β signal was observed⁶⁷ for 2-vinyltetrazole (**15a**) and its derivatives in comparison with the corresponding 1-vinyl derivatives. In the presence of a vinyl group in position 5, the pattern of the ¹³C NMR spectra of vinyltetrazoles changes considerably: the signal for the β-carbon atom of 5-vinyltetrazole (**1**) is more appreciably shifted downfield [δ(C_α) = 119.99 and δ(C_β) = 124.70]. The polarity of the C=C bond in the vinyl group

(Δ*q*_{αβ}) of compound **1** is much lower than that of the 1-vinyl derivative **14a**.^{60,61} As a result, the difference between the chemical shifts (Δδ_{αβ}) diminishes correspondingly.^{27,31,43,53} Introduction of an alkyl substituent into position 1 of 5-vinyltetrazole (**1**) has virtually no effect on the δ values of the vinyl group [δ(C_α) = 118.87 and δ(C_β) = 126.85].^{53,89} The signal of the C_α atom [δ(C_α) = 122.49, δ(C_β) = 121.48] in the ¹³C NMR spectra of 2-alkyl-5-vinyltetrazoles and 1-vinyltetrazoles is shifted downfield, but the difference in the chemical shifts Δδ_{αβ} is even less pronounced than in the case of unsubstituted 5-vinyltetrazole (**1**).²⁷ The methyl group in the α-position of the vinyl substituent strongly increases the polarity of the C=C bond in both *C*- and *N*-isopropenyl derivatives resulting in a drastic increase in Δδ_{αβ} (see Ref. 43).

The shapes of the proton signals in the ¹H NMR spectra of 5-vinyl- and 1-vinyltetrazoles are similar; the signals of 5-vinyltetrazoles lie in a narrower range (δ 5.62–6.91).^{27,31,43,53} The H_B (δ 6.05 and 5.74, respectively) and H_C (δ 5.58 and 5.23, respectively) signals in the ¹H NMR spectra of isopropenyltetrazoles **2** and **22**, which represent a superposition of two quadruplets, are shifted upfield in comparison with the corresponding signals of the vinyl derivatives. The signals of the methyl group in the NMR spectra of compounds **2** and **22** are manifested as a superposition of two doublets (δ 2.24 and 2.40, respectively).⁴³

The electronic effect of the vinyl group on the heterocycle is manifested in ¹H and ¹³C NMR spectra of vinyltetrazoles. Thus the difference in the position of the vinyl group of 1- and 2-vinyltetrazoles determines the difference in the shielding of C(5), being by 12 ppm more protected in 1,5-disubstituted tetrazoles in comparison with 2,5-isomers. This effect was used for identification of isomeric vinyltetrazole derivatives.⁴¹

¹⁵N NMR spectra of vinyltetrazole derivatives are less studied. A linear correlation was found⁸⁸ between δ and the electron density on nitrogen atoms, which allowed unambiguous interpretation of signals in the NMR spectra of vinyltetrazoles (Table 2). According to quantum-chemical calculations, the nuclei of ‘pyrrole’ nitrogen atoms of vinyltetrazoles resonate in a higher field in comparison with ‘pyridine’ nitrogen atoms.

Table 2. Chemical shifts in the ¹⁵N NMR spectra of vinyltetrazoles (MeNO₂ as a standard).⁸⁸

Compound	δ ¹⁵ N /ppm			
	N(1)	N(2)	N(3)	N(4)
1-Vinyltetrazole (14a)	−135.3	−19.1	10.1	−52.4
1-Methyl-5-vinyltetrazole (5a)	−157.6	−10.3	8.4	−56.6 ^a
2-Methyl-5-vinyltetrazole (5b)	−79.8	−103.7	0	−52.0 ^a

^a In DMSO.

6. Acid–base properties of vinyltetrazoles

Acid–base properties of nitrogen-containing heterocyclic compounds are related to their most essential characteristics, which determine in many respects their reactivities and physiological activities. Unfortunately, vinylazoles fall out of this area of research. The values of basicity (p*K*_{BH⁺}) and acidity (p*K*_a) constants of azoles and their vinyl derivatives are given in Table 3. Acidic properties of azole rings are increased with an increase in the number of nitrogen atoms, tetrazole being the strongest acid. As mentioned above, introduction of a vinyl group into position 5 of the tetrazole ring further increases the acidity of the heterocycle. Contrariwise, the basicity of azoles decreases with an increase in the number of nitrogen atoms in the ring, tetrazole being the weakest base among other azoles. An analysis of experimental data on basicities of various vinylazoles allows one to establish certain regularities in reactions between heterocyclic

Table 3. The values of pK_{BH^+} and pK_a for azoles and vinylazoles.^{90–92}

Compound	pK_{BH^+}	pK_a
Imidazole	7.05	14.17
1-Vinylimidazole	7.32	—
1,2,4-Triazole	2.45	10.04
1-Vinyl-1,2,4-triazole	2.97	—
Tetrazole	−2.68	4.89
1-Vinyltetrazole (14a)	−3.43	—
5-Methyl-1-vinyltetrazole (14b)	−2.56	—
5-Vinyltetrazole (1)	−2.91 ^a	4.10 ^a
2-Methyl-5-vinyltetrazole (5b)	−2.77	—

^a Data from Ref. 43.

and vinyl fragments. First, introduction of a vinyl group into imidazole and 1,2,4-triazole rings increases their basicities, while the vinyl group present in the tetrazole ring decreases it. This suggests that the mode of transfer of electronic effects changes on going from vinylimidazole and -triazole to vinyltetrazole derivatives. Second, like alkyl derivatives,⁹⁰ the corresponding *N*-vinyltetrazoles are weaker bases than *C*-vinyltetrazoles. On the whole, vinylazole derivatives are weaker bases in comparison with alkyl derivatives, which is confirmed by polarographic and NMR spectroscopic data. Third, introduction of a methyl substituent into 1- and 5-vinyltetrazoles enhances basic properties of the heterocycle, which is especially pronounced in the former case.

Numerous studies into protonation of various tetrazole derivatives provide support that the nitrogen atom in position 4 is the most basic site in the heterocycle.⁹⁰

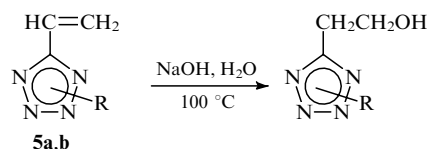
V. Reactions of vinyltetrazoles

The chemistry of vinyltetrazoles has not been studied in depth. One possible reason is that vinyltetrazole derivatives are used as monomers for preparation of high-energy polymeric products and are seldom used as starting compounds for other chemical reactions. Modification of the heterocycle is usually confined to reactions which have no appreciable influence on the energy characteristics of the tetrazole ring; reactions involving the vinyl group have not been sufficiently studied either. However, despite the obvious paucity of experimental data, certain conclusions can be made about the correlation between the structural and chemical properties and reactivities of vinyltetrazoles in order to compare them with those of vinyl derivatives of other five-membered nitrogen-containing heterocycles.

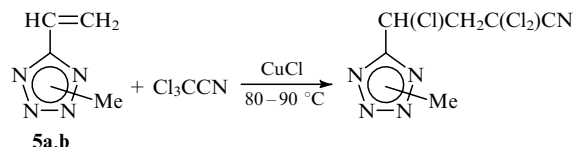
1. Reactions involving the vinyl group

As mentioned above, conjugation of the tetrazole ring with the vinyl group results in its pronounced polarisation. Taking into account the electron-withdrawing character of the heterocycle, it may be expected that the vinyl group will manifest higher (in comparison with alkenes) reactivity towards the nucleophilic reagents and lower reactivity in an electrophilic attack. However, it has been shown that the reactivity of the vinyl group is largely determined by its position in the ring. Whereas 5-vinyltetrazoles readily enter into addition reactions at the double C=C bond under the action of both nucleophilic and electrophilic reagents, the vinyl group of 1-vinyltetrazoles is virtually inert to both types of reagents.

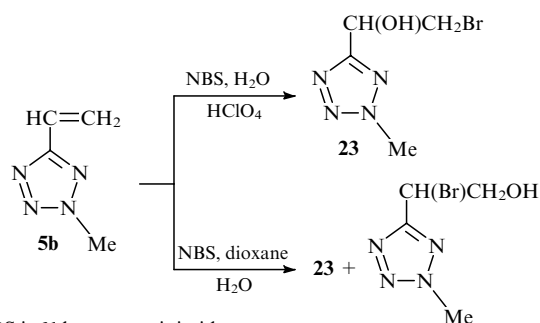
Hydration of the vinyl group of 1-methyl-5-vinyl- (**5a**) and 2-methyl-5-vinyltetrazoles (**5b**) resulting in the corresponding alcohols is an example of nucleophilic addition to the double bond.¹⁹

R = 1-Me (**a**), 2-Me (**b**).

In the presence of copper catalysts, compounds **5a,b** add trichloroacetonitrile surprisingly smoothly.⁹³



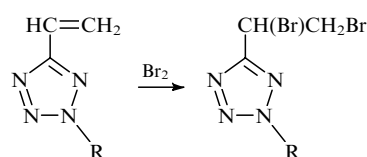
It is known that 2-methyl-5-vinyltetrazole (**5b**) reacts with hypobromous acid. Slow addition of an aqueous suspension of *N*-bromosuccinimide to compound **5b** in the presence of perchloric acid occurs regiospecifically and gives rise to 5-(2-bromo-1-hydroxyethyl)-2-methyltetrazole (**23**) in quantitative yield.⁹⁴

NBS is *N*-bromosuccinimide.

Reaction of vinyltetrazole **5b** with *N*-bromosuccinimide in aqueous dioxane yields an equimolar mixture of isomeric bromohydrins,⁹⁵ presumably as a result of stabilisation of the bromonium ion by dioxane as an electron donor.

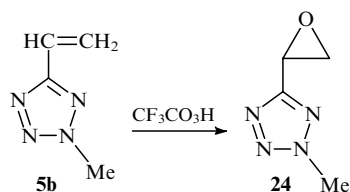
Reaction of 1-methyl-5-vinyltetrazole (**5a**) performed under analogous conditions yields polymerisation products, which is attributed⁹⁵ to higher ability of the isomer **5a** for radical polymerisation in comparison with compound **5b**.

Electrophilic addition of bromine to the vinyl group of 5-vinyltetrazole (**1**) and its homologues proceeds rather smoothly.³⁰

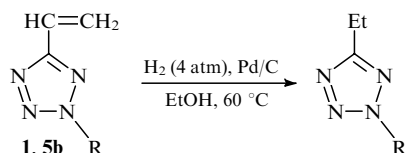


R = H, Me, Et.

Selective oxidation of the vinyl group in vinyltetrazoles has been studied with a view to obtaining epoxy derivatives of tetrazoles.^{96,97} It was found that 2-methyl-5-vinyltetrazole (**5b**) is not oxidised by hydrogen peroxide, *tert*-butyl hydroperoxide or hydrogen peroxide in the presence of sodium tungstate as a catalyst or by sodium hypochlorite in alkaline media under conditions of phase-transfer catalysis. Compound **5b** is also inert with respect to hypochlorous acid. The C=C bond of vinyltetrazole **5b** could only be oxidised with trifluoroperacetic acid. Epoxide **24** was obtained in 25%–30% yield.



Selective hydrogenation of 5-vinyltetrazoles at the vinyl group occurs under relatively mild conditions.⁴³



R = H (**1**), Me (**5b**).

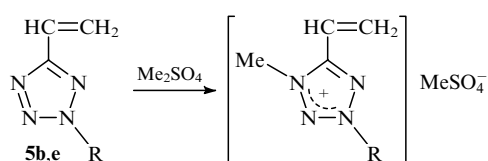
These few examples of chemical reactions of 5-vinyltetrazoles do not reveal any unusual behaviour of the vinyl group substituted by an aromatic heterocycle. The oxidation of the double bond resulting in epoxide **24** is the only exception.

2. Reactions involving the tetrazole ring

Reactions of vinyltetrazoles involving the heterocyclic fragment are more extensively documented in the literature. The tetrazole ring has several reaction centres, *viz.*, the 'pyrrole' nitrogen atom (in unsubstituted 5-vinyltetrazoles), 'pyridine' nitrogen atoms, the carbon atom of unsubstituted 1- and 2-vinyltetrazoles manifesting CH-acidic properties. The diversity of reactions involving this heterocycle significantly expands the range of vinyltetrazole-containing monomers as starting materials for the synthesis of polymeric products. Therefore, reactions involving the heterocyclic fragment have attracted more attention than reactions involving the vinyl group.

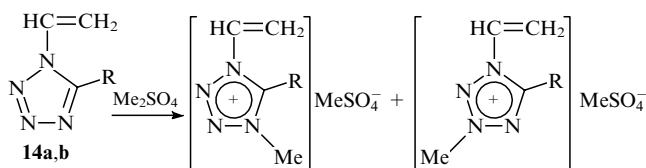
a. Reactions involving the nitrogen atom

Quaternisation reactions of tertiary nitrogen atoms of azole compounds and their vinyl derivatives by alkyl halides or dimethyl sulfate are well known.^{98–100} It was found that the ability to undergo quaternisation reactions decreases with an increase in the number of nitrogen atoms in the heterocycle: quaternisation of tetrazole derivatives occurs under more drastic conditions than that of imidazoles or triazoles. Introduction of electron-donor substituents into the tetrazole ring increases slightly the reactivity of vinyltetrazoles in this reaction. Thus introduction of NH_2 or Me groups makes it possible to prepare quaternary salts of 5-amino-1-vinyl- (**14d**) and 2-methyl-5-vinyltetrazole (**5b**) by reaction with methyl iodide or dimethyl sulfate.^{43, 88} At the same time, 1-vinyltetrazole (**14a**) can form salts exclusively under the action of dimethyl sulfate. A wide variety of quaternary salts of 5- and 1-vinyltetrazoles have been prepared by treatment with Me_2SO_4 in the presence or absence of solvents (20–80 °C).⁸⁸ Notably, 5-vinyl-2-R-tetrazoles are quaternised much more easily than 1-vinyl- and 5-vinyl-1-R-tetrazoles. ¹³C and ¹⁵N NMR spectroscopic studies revealed another interesting peculiarity, *viz.*, selective formation of 1,3-dialkyl-5-vinyltetrazolium salts in reactions of 5-vinyl-2-R-tetrazoles with dimethyl sulfate.⁸⁸

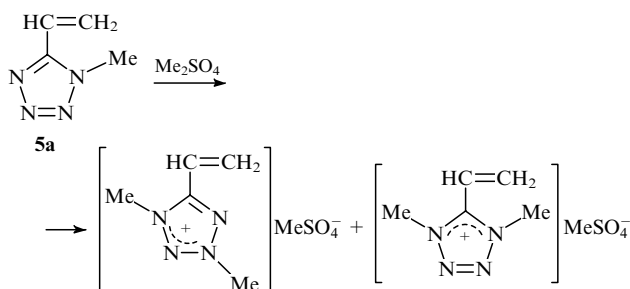


R = Me (**b**), Bu^t (**e**).

1-Vinyl- and 5-vinyl-1-R-tetrazoles yield a mixture of isomeric salts.⁸⁸

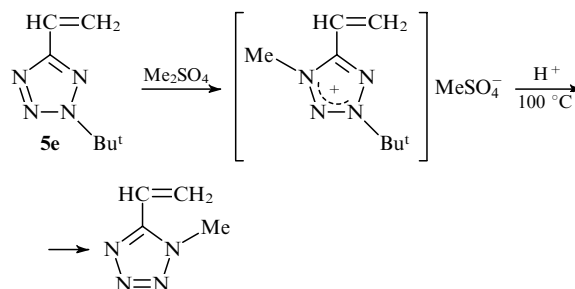


R = H (**a**), Me (**b**).



The isomeric ratio of the reaction product strongly depends on the structure of the starting vinyltetrazole.

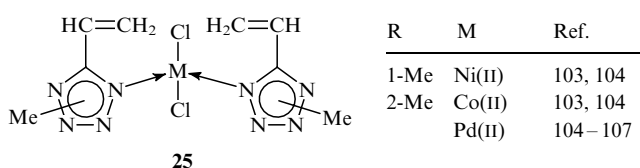
Quaternary salts of 2-*tert*-butyltetrazole derivatives, *e.g.*, those prepared from compound **5e**, are readily transalkylated upon heating with the loss of the *tert*-butyl substituent. This reaction occurs regioselectively with intermediate formation of trisubstituted tetrazolium salts to give 1,5-disubstituted tetrazoles in 78%–96% yields.³²



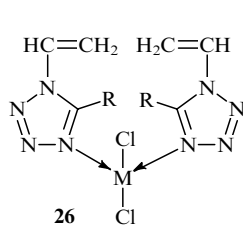
The salts prepared by reaction of vinyltetrazoles with Me_2SO_4 are prone to spontaneous polymerisation upon standing.⁸⁸ In contrast, the salts prepared by quaternisation of vinyltetrazoles with methyl iodide are not polymerised even under radical initiation conditions.

Vinyltetrazoles are as prone to complexation with metal ions as vinylazoles containing two or three nitrogen atoms in their rings. In most cases, such complexation occurs smoothly even at the stage of mixing of vinyltetrazole solutions with metal salts and does not require long-term heating. The structure and properties of the complexes formed depend on the nature of the ligand and the metal ion.

Reactions of 1-vinyl- (**14a, d**) and 5-vinyltetrazoles (**5a, b**) with Cu(II), Ni(II), Co(II) and Pd(II) chlorides yield donor–acceptor complexes (**25, 26**) of the composition ML_2Cl_2 irrespective of the ratio of the starting reagents.



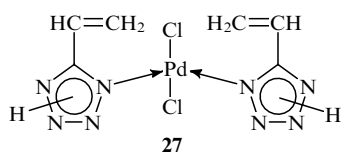
R	M	Ref.
1-Me	Ni(II)	103, 104
2-Me	Co(II)	103, 104
	Pd(II)	104–107



R	M	Ref.
H	Cu(II)	40, 46, 101, 102
	Cu(SCN) ₂	40
	Ni(II)	101, 102
	Co(II)	102
	Pd(II)	101
	Pd(II)	101
NH ₂	Cu(II)	101
	Ni(II)	101
	Pd(II)	101

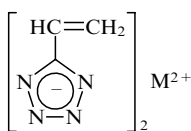
A complex of the composition CrL_3Cl_3 was prepared using chromium(III) chloride.¹⁰³ Complex derivatives of 1-methyl- (**5a**) and 2-methyl-5-vinyltetrazoles (**5b**) with Rh(III), Ti(IV) and V(IV) ions have been prepared and characterised¹⁰⁴ using NMR and IR spectroscopy and X-ray diffraction analysis. It was found that in all cases studied coordination of the metal ion occurs to the nitrogen atom in position 4 of the heterocycle.^{101, 105, 106} The vinyl group is not involved in the complexation: the positions of the signals for the carbon atoms of the $\text{C}=\text{C}$ bond in the ^{13}C NMR spectra and the position of the absorption band in the IR spectra did not change upon complexation.^{101, 103, 105, 106} The 1-methyl-5-vinyltetrazole (**5a**)– PdCl_2 complex in which the vibration frequency of the $\text{C}=\text{C}$ bond of the vinyl group decreased from 1642 to 1625 cm^{-1} was the only exception (see Ref. 105).

The behaviour of 5-vinyltetrazole (**1**) is similar to that of above-mentioned compounds. This forms complex **27** [PdL_2Cl_2 with palladium(II) chloride] due to a donor–acceptor interaction with the formation of an $\text{N}–\text{Pd}$ bond.^{101, 107}



The low-frequency region of the IR spectrum of the complex **27** contains an absorption band around 365 cm^{-1} which is characteristic of the $\text{Pd}–\text{Cl}$ bond where the metal ion is coordinated to another atom (in our case, the nitrogen atom).¹⁰⁸

A different situation is observed in reaction of 5-vinyltetrazole (**1**) with copper and nickel chlorides in water.¹⁰¹ In this case, reaction products appear as salt-like complexes; the vinyltetrazole anion plays the role of a ligand.



M = Cu, Ni.

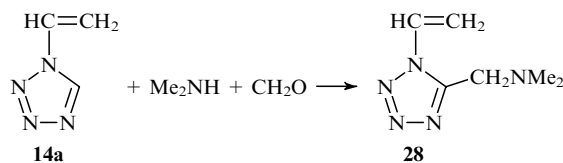
An unusual effect was observed in reactions of 5-vinyltetrazole with CuCl_2 in organic solvents: complexation was accompanied by elimination of the vinyl group; the metal–unsubstituted tetrazole complex was formed as the final product.

Preservation of the vinyl group in the aforementioned complexes determines the interest in these compounds as candidate monomers for the synthesis of metal-containing polymers. Polymeric complexes prepared by polymerisation of PbCl_2 complexes with 2-methyl-5-vinyltetrazole have been studied.¹⁰⁷

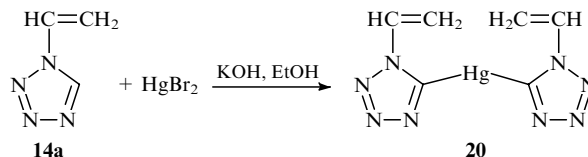
b. Reactions involving the carbon atom of the heterocycle

It has recently been shown that reactions of vinyltetrazoles involving the carbon atom of the heterocycle are possible. By virtue of their high CH-acidities ($\text{p}K_a$ 23–25), 1-substituted tetrazoles enter into the Mannich reaction. Thus 1-vinyltetrazole

(**14a**) is aminomethylated under mild conditions as a CH-acid to give 5-dimethylaminomethyl-1-vinyltetrazole (**28**).^{63, 109}



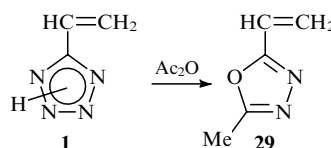
Like other compounds with pronounced CH-acidities, 1-vinyltetrazole (**14a**) is mercured by mercury(II) salts at the carbon atom of the tetrazole ring in the presence of bases to give symmetrical bistetrazolymercurials (**20**).^{48, 63}



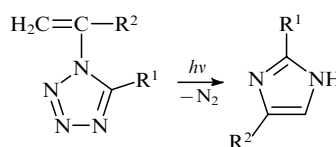
c. Recyclisation reactions

Some reactions of vinyltetrazole derivatives are accompanied by recyclisations; the heterocyclic products of these reactions contain fewer nitrogen atoms in their rings.

For the first time, such a reaction was described for 5-vinyltetrazole (**1**) by Arnold *et al.*²¹ Reaction of compound **1** with acetic anhydride gives the corresponding 2,5-disubstituted 1,3,4-oxadiazole **29** in good yield.

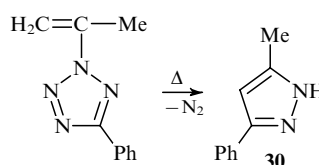


Some 1- and 2-vinyltetrazoles eliminate nitrogen upon photolysis or thermolysis to give diazole derivatives. 1-Vinyl-substituted tetrazoles afford imidazole derivatives.³³



$\text{R}^1, \text{R}^2 = \text{H, Ph.}$

Heating of 2-isopropenyl-5-phenyltetrazole results in pyrazole **30**.¹¹⁰



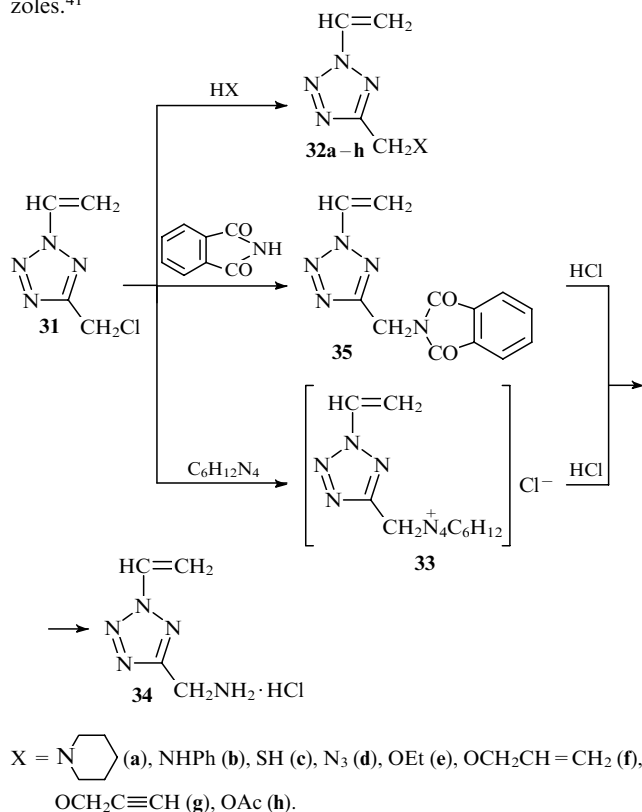
In certain cases, chemical transformations lead to destruction of the tetrazole ring. Several thermal degradation reactions of vinyltetrazoles are known. Kinetic parameters of monomolecular thermal degradation of a series of isomeric tetrazoles including 1-methyl-5-vinyl- (**5a**) and 2-methyl-5-vinyltetrazoles (**5b**) under isothermal conditions were studied using manometric methods.¹¹¹ It was found that the degradation of both isomers is characterised by high values of entropy of activation (on average, $33.5\text{ J mol}^{-1}\text{ K}^{-1}$). The activation energies of compounds **5a** and **5b** are equal to 180.0 and 198.9 kJ mol^{-1} , respectively. In the authors' opinion, monomolecular degradation occurs stepwise. For 1,5-disubstituted tetrazoles, reversible formation and subsequent degradation of intermediate azidoazomethines is the limit-

ing step, whereas the limiting step in the case of 2,5-disubstituted isomers is degradation of azodiazocompounds.

The rate of self-propagating high-temperature decomposition of 5-amino-1-vinyltetrazole (**14d**) was estimated to be equal to 0.5 mm s^{-1} , *i.e.*, virtually coincides with the combustion rate of unsubstituted tetrazole.¹¹²

3. Reactions of substituents in the ring

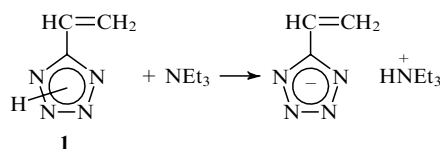
Substitution of the halogen in 5-chloromethyl-2-vinyltetrazole (**31**) by reactions with phthalimide, urotropin and other nucleophiles was used for the synthesis of functionalised 2-vinyltetrazoles.⁴¹



Thus reactions of compound **31** with secondary amines and aniline afford 5-aminomethyl-2-vinyltetrazoles (**32a,b**) in good yields. 5-Mercaptomethyl-2-vinyltetrazole (**32c**) was prepared by reaction with thiourea with subsequent decomposition of the thiuronium salt. The chloromethyl derivative **31** readily forms salt **33** with urotropin; treatment of compound **33** with hydrochloric acid yields the primary amine hydrochloride **34**. Substitution of the primary amino group for chlorine in the Gabriel reaction proceeds successfully: treatment of chloromethyltetrazole **31** with sodium phthalimide gives 5-phthalimidomethyl-2-vinyltetrazole which is hydrolysed into amine **34** upon treatment with hydrochloric acid. Substitution of the azido group for the chlorine atom and the formation of the derivative **32d** occur under conditions of phase-transfer catalysis in the presence of benzyltriethylammonium chloride. Treatment of the chloromethyl derivative **31** with sodium alkoxides under conditions of phase-transfer catalysis yields ethers **32e-g**, while its reaction with sodium acetate affords an ester (**32h**).

4. Reactions of 5-vinyltetrazole with amines

Tetrazole and its 5-substituted derivatives manifest acidic properties and give salts upon reactions with bases including organic bases.^{4,5} It was expected that 5-vinyltetrazole (**1**) would also react with bases to give monomeric salts. This reaction was studied in more detail with triethylamine as an example.¹¹³ The formation of monomeric salts in the first step was confirmed by conductometric, UV spectroscopic and ^1H NMR data.



However, this reaction is accompanied by an increase in the viscosity of the reaction system and a drastic decrease in the relative intensities of signals for the protons of the vinyl group in ^1H NMR spectra. This suggests that polymerisation occurs in the system. Treatment of the reaction mixture with diethyl ether yields a viscous mass; its storage (and vacuum drying) leads to resinification or vitrification. Reactions of 5-vinyltetrazole (**1**) with ammonia, hydrazine, trimethylamine, diethylamine and pyridine proceed in a similar way.^{114,115} Depending on the nature of the amine and reaction conditions, one can prepare polymeric 5-vinyltetrazole salts which are readily soluble or moderately swelling in water.

VI. Polymerisation of vinyltetrazoles

Vinyltetrazoles constitute a relatively novel class of monomers. The first vinyltetrazole derivatives were synthesised in the early 1960's in an attempt to construct promising polymeric materials. High polymerisability of these monomers and valuable properties of polymers prepared from them have stimulated further progress in the chemistry of vinyltetrazoles. Owing to high intrinsic energy and unique physicochemical and operation characteristics, polyvinyltetrazoles have attracted attention as promising to give impetus to organisation of large-scale production of some monomeric and polymeric tetrazole-containing products.^{12,116,117}

Despite the high polymerisability of vinyltetrazoles reported in the very first publications, in-depth studies into polymerisation activities and properties of polymers prepared from them began in the 1980's. Both *N*- and *C*-vinyltetrazole derivatives manifest high polymerisability under conditions of radical initiation. Bulk polymerisation or polymerisation in solvents is carried out in the presence of thermally unstable initiators [*e.g.*, azobisisobutyronitrile (AIBN) and benzoyl peroxide (BP)],^{1,16,17} ammonium persulfate (AP),⁷⁹ H_2O_2 ,¹¹⁸ transition metal acetylacetonates⁴² and redox systems [H_2O_2 - FeSO_4 ,¹¹⁸ FeSO_4 -(NH_4)₂ $\cdot\text{S}_2\text{O}_8$ - $\text{K}_2\text{S}_2\text{O}_5$ (see Refs 1 and 17)]. Radical polymerisation of vinyltetrazoles induced by γ -irradiation¹¹⁹ and electrochemically^{120,121} has been described. The possibility of polymerisation of 5-vinyl-2-methyltetrazole under the action of cationic and anionic catalysts has been demonstrated.¹²² A method for solid-phase polymerisation of 5-vinyltetrazole by exposure to high pressure has been developed.¹²³ Preparation of polymers from 1-methyl-5-vinyl- and 2-methyl-5-vinyltetrazoles grafted onto cellulose is also possible.¹¹⁸

The diversity of structural variants of vinyltetrazole derivatives and the vast body of evidence on quantitative aspects of their radical polymerisation have made it possible to study the effects of the structure of the vinyl monomer, the nature of the reaction medium and the initiator on the polymerisabilities of vinyltetrazoles.

1. Structures and activities of vinyltetrazoles in radical polymerisation

a. Effect of the position of the vinyl group on the activity of vinyltetrazoles in polymerisation

A comparative study of polymerisabilities of unsubstituted *C*- and *N*-vinyltetrazole derivatives has been carried out.^{43,124} Acetonitrile was selected as a medium, since unsubstituted 5-vinyltetrazole behaves as a non-ionisable monomer in this solvent. In the presence of AIBN, polymerisation of 1- and 5-vinyltetrazoles proceeds as a steady-state reaction without an induction period with initial rates depending on the concentration of the reactants and the temperature. The orders of the reaction rates with respect

Table 4. Kinetic parameters of the polymerisation of vinyl-^{43, 124} and isopropenyltetrazoles^{43, 61} in MeCN (AIBN, 60 °C).

Monomer	E_{ef} (see ^a)	$10^4 K_{\text{ef}}$ (see ^b)	$10^5 K_{\text{in}}$ /s ⁻¹	$K_{\text{p}}/K_{\text{t}}^{0.5}$ (see ^c)	$E_{\text{p}} - 0.5 E_{\text{t}}$ (see ^a)
5-Vinyltetrazole	74.5	22.42	1.12	0.67	16.7
1-Vinyltetrazole	80.4	12.5	1.33	0.34	20.6
5-Isopropenyl- tetrazole (2) ^d	85.6	3.4	0.35	0.18	—
1-Isopropenyl- tetrazole (22)	84.3	0.32	1.30	0.009	—

Note. E_{ef} is the effective activation energy of polymerisation; K_{ef} is the effective rate constant of polymerisation; K_{in} is the initiation rate constant; E_{p} and E_{t} are the activation energies for the propagation and termination of the polymeric chain.

^a kJ mol⁻¹; ^b litre mol^{-0.5} s⁻¹; ^c litre^{0.5} (mol s)^{-0.5}.

^d The polymerisation kinetics was studied in water in the presence of AP.

to the monomer and the initiator are 1 and 0.5, respectively, which suggests a bimolecular chain termination mechanism.

The reactivity criterion $K_{\text{p}}/K_{\text{t}}^{0.5}$ (where K_{p} and K_{t} are the rate constants for chain propagation and termination, respectively) (Table 4) suggest the higher activity of the *C*-vinyl monomer in the radical polymerisation; in addition, polymerisation of 5-vinyltetrazole is less energy-consuming.¹²⁴ A similar ratio of activities of *C*- and *N*-vinyltetrazole derivatives in the polymerisation reaction is consistent with the existing criteria for the estimation of polymerisation activities of vinyl monomers.^{125–127} The electronic structure of 5-vinyltetrazole is characterised by a smaller charge, q_{β} , and a lower charge difference, $q_{\alpha} q_{\beta}$, in comparison with 1-vinyltetrazole.^{60, 61} Moreover, a small reduction of the acceptor induction effect of the substituent at the double bond of 5-vinyltetrazole is accompanied by a considerable decrease in the donor mesomeric effect in comparison with 1-vinyltetrazole. Thus, the tetrazolyl substituent in the *C*-vinyl monomer manifests stronger acceptor properties which accounts for higher activity of 5-vinyltetrazole.

The difference in the reactivities of *C*- and *N*-isopropenyltetrazoles is even more pronounced.⁶¹ Polymerisation of 1- (**22**) and 5-isopropenyltetrazole derivatives (**2**) and their vinyl analogues occurs as a steady-state process without an induction period and is described by the kinetic equation:

$$W = K[M][I]^{0.5}.$$

The $K_{\text{p}}/K_{\text{t}}^{0.5}$ values (see Table 4) suggest that the activity of 5-isopropenyltetrazole (**2**) in radical polymerisation is 20 times higher than that of its isomer **22**.⁶¹ As in the case of vinyltetrazoles, the polymerisation activity correlates with the smaller charge q_{β} and the smaller charge difference, $q_{\alpha} q_{\beta}$, of 5-isopropenyltetrazole (**2**) in comparison with 1-isopropenyltetrazole (**22**).

A comparison of kinetic and energetic characteristics of polymerisation of vinyl- and isopropenyltetrazole derivatives demonstrates a significant decrease in the activities of the latter in radical polymerisation. A 4–10-fold change in the polymerisation activity (*i.e.*, the $K_{\text{p}}/K_{\text{t}}^{0.5}$ ratio for the vinyl and isopropenyl derivatives⁶¹) of 5-vinyl- vs. 5-isopropenyltetrazole is, in general, typical of the transition from *C*-vinyl to *C*-isopropenyl compounds.¹²⁵ A change in the activity in the polymerisation of *N*-substituted vinyltetrazoles [1-vinyl- (**14a**)–1-isopropenyltetrazole (**22**) pair] is more pronounced (see Table 4). These differences are attributed⁶¹ to the regular changes in the electronic structures of the monomers on going from 1-vinyl- to 1-isopropenyltetrazole or from 5-vinyl- to 5-isopropenyltetrazole. Introduction of a methyl substituent into the α -position of the vinyl group both decreases the reactivities of both 5- and 1-isopropenyltetrazoles in comparison with vinyl monomers and reduces the molecular masses (MM) of the polymeric products.

b. Effect of substituents in the heterocycle on the polymerisation activities of vinyltetrazoles

Polymerisation of vinyltetrazole methyl derivatives differing in the position of the substituent in the heterocycle has been studied in the greatest detail.^{43, 124, 128–130} Introduction of a methyl group into the tetrazole ring of 1- and 5-vinyltetrazoles does not change the character of the polymerisation of the monomers: as for unsubstituted vinyltetrazoles, the orders of the reaction with respect to the monomer and the initiator remain equal to 1 and 0.5, respectively.^{43, 124, 128–130} However, the polymerisabilities of substituted vinyltetrazoles vary considerably. The methyl group in position 1 has virtually no effect on the activity of the monomer in comparison with unsubstituted 5-vinyltetrazole: the value of $K_{\text{p}}/K_{\text{t}}^{0.5}$ changes only insignificantly in the polymerisation in CHCl₃, whereas polymerisation in DMF is characterised by a slight increase in the activity despite the increase in the efficient polymerisation energies (Table 5). This does not contradict the results of quantum-chemical calculations of 5-vinyl- and 1-methyl-5-vinyltetrazole,⁵⁵ which points to the lack of the electron-donor effect of the methyl group in position 1. Moreover, the results of ¹³C NMR studies and the values of induction and resonance constants^{27, 131} testify to a slight enhancement of the electron-withdrawing properties of the tetrazolyl substituent upon the introduction of the methyl group into position 1, which enhances the polymerisability of 1-methyl-5-vinyltetrazole in comparison with unsubstituted 5-vinyltetrazole.

Table 5. Kinetic parameters of the polymerisation of methyl-substituted *C*- and *N*-vinyltetrazoles (AIBN, 60 °C).

Monomer	Solvent	E_{ef} (see ^a)	$K_{\text{p}}/K_{\text{t}}^{0.5}$ (see ^b)	$E_{\text{p}} - 0.5 E_{\text{t}}$ (see ^a)	Ref.
1-Methyl-5-vinyl- tetrazole (5a)	DMF	87.95	0.85	—	130
	without solvent	—	0.69	20	129
2-Methyl-5-vinyl- tetrazole (5b)	MeCN	81.3	0.31	19.9	43
	DMF	82.3	0.46	—	130
5-Methyl-1-vinyl- tetrazole (14b)	MeCN	81.8	0.21	21.3	43, 124

^a kJ mol⁻¹; ^b litre^{0.5} (mol s)^{-0.5}.

In contrast, the introduction of a methyl group into position 2 of *C*-vinyltetrazole or into position 5 of *N*-vinyltetrazole decreases the activities of methyl-substituted monomers in radical polymerisation (see Table 5). The difference in the $K_{\text{p}}/K_{\text{t}}^{0.5}$ values for the 5-vinyltetrazole–2-methyl-5-vinyltetrazole pair is 2.2, while that for the 1-vinyltetrazole–5-methyl-1-vinyltetrazole pair is 1.6.^{43, 124} Reduced activities of methyl-substituted monomers are also explicable in terms of the electronic effect of the methyl group, which being present in position 2 or 5, behaves as a potent electron donor. As a result, the electronic structures of 2- and 5-substituted monomers differ from those of unsubstituted vinyltetrazoles. This difference is more pronounced for the 5-vinyl- and 2-methyl-5-vinyltetrazole pair than for the 1-vinyl- and 5-methyl-1-vinyltetrazole pair, which probably determines the greater difference in the radical polymerisability of the former monomer pair.

The effects of substituents in the heterocycle on polymerisation activities of vinyltetrazoles have been clearly demonstrated for the polymerisation of *N*-vinyltetrazoles in water in the presence of AP.^{60, 84} According to kinetic data, polymerisation activities of *N*-vinyltetrazoles decrease in the following order: 1-vinyltetrazole (**14a**) > 5-methyl-1-vinyltetrazole (**14b**) > 5-amino-1-vinyltetrazole (**14d**) > 5-acetylamino-1-vinyltetrazole (**14f**) (Table 6). The changes in the activities of the first three compounds correlate with the decrease in the electron-withdrawing properties of the tetrazolyl substituent with respect to the

Table 6. Kinetic parameters of the polymerisation of *N*-vinyltetrazoles in water (AP, 60 °C).^{43, 60, 84}

Monomer	E_{ef} /kJ mol ⁻¹	$10^4 K_{\text{ef}}$ /litre ^{0.5} mol ^{-0.5} s ⁻¹	$10^5 K_{\text{in}}$ /s ⁻¹	$K_{\text{p}}/K_{\text{t}}^{0.5}$ /litre ^{0.5} (mol s) ^{-0.5}	$E_{\text{p}} - 0.5 E_{\text{t}}$ /kJ mol ⁻¹	σ_{I}	σ_{R}
1-Vinyltetrazole (14a)	90.9	95.9	1.42	2.54	23.9	0.65	-0.33
5-Methyl-1-vinyl-tetrazole (14b)	84.3	73.3	1.29	2.09	22.2	0.64	-0.34
5-Amino-1-vinyl-tetrazole (14d)	75.2	48.0	1.46	1.46	19.0	0.59	-0.37
5-Acetylamino-1-vinyl-tetrazole (14f)	85.0	41.4	1.40	1.16	24.2	—	—

double bond (*i.e.*, σ_{I} and σ_{R} values), which results in regular changes in their electronic structures. 5-Acetylamino-1-vinyltetrazole (**14f**), the polymerisation activity of which would not differ from that of unsubstituted 1-vinyltetrazole, falls out of this series. Presumably, the presence of such a bulky substituent as NHCOMe in position 5 creates steric hindrance in the act of chain propagation. It should be noted that $K_{\text{p}}/K_{\text{t}}^{0.5}$ values depend not only on charge characteristics and σ_{I} and σ_{R} of substituents, but also on the values of polarographic reduction potentials ($E_{1/2}$) and chemical shifts of signals for β -carbon atoms of the vinyl group in ¹³C NMR spectra.^{57, 81} The dependences of $\log(K_{\text{p}}/K_{\text{t}}^{0.5})$ on σ_{I} , $E_{1/2}$ and $\delta(\text{C}_{\beta})$ for 1-vinyl-, 5-methyl-1-vinyl- and 5-amino-1-vinyltetrazoles are linear.⁸⁴ The activity of 5-acetylamino-1-vinyltetrazole (**14f**) in polymerisation reactions is much lower than that expected based on these correlations. The reason is the aforementioned steric hindrance in the chain propagation step.

As regards their activities in radical polymerisation, vinyltetrazoles stand with methyl acrylate, acrylonitrile and acrylamide. Their high reactivities do not contradict the general concepts on the activating effect of electron-withdrawing substituents at the double bond. However, there exist other viewpoints as to high polymerisation activities of vinyltetrazoles. In terms of the chemical structures, 1-methyl-5-vinyl- and 2-methyl-5-vinyltetrazoles are considered to be similar to styrene,^{128, 129} although at 40 °C $K_{\text{p}}/K_{\text{t}}^{0.5}$ values for 1-methyl-5-vinyltetrazole and 2-methyl-5-vinyltetrazole exceed that of styrene 25- (see Ref. 129) and 17.5-fold, respectively. This is explained¹²⁸ by either a significant decrease in the chain termination rate in the polymerisation of vinyltetrazoles or, alternatively,⁶⁹ by rotational isomerism of 2-methyl-5-vinyltetrazole which is absent in styrene and helps favourable orientation of the vinyl group in the chain propagation. However, the first assumption is not experimentally proved and the reason for the significant difference between the K_{t} values for styrene and vinyltetrazoles is unclear. The second assumption does not stand up to criticism, because despite hindered rotational isomerism of 1-methyl-5-vinyltetrazole, its reactivity is high. The most probable reason for the enhanced activity of vinyltetrazoles in comparison with styrene is higher electron-withdrawing activity of tetrazolyl substituents at the double bond compared to the phenyl group. As is known, electron-withdrawing substituents with the same degree of conjugation increase the activity of monomers in homopolymerisation.¹²⁵

2. Effect of the nature of the solvent on radical polymerisation of vinyltetrazoles

Vinyltetrazole derivatives are related to polar (and, in the majority of cases, water-soluble) monomers. Heterocyclic substituents at the double bond contain nitrogen atoms of both 'pyrrole' and 'pyridine' types. Depending on the position of the vinyl group in the heterocycle, vinyltetrazoles manifest the properties of ionisable (unsubstituted *C*-vinyltetrazoles, such as 5-vinyl- and 5-isopropenyltetrazoles) or non-ionogenic monomers (protected *C*-vinyl- and *N*-vinyltetrazoles) because of their low basicities. However, even the latter compounds are not inert with respect to the reaction medium owing to the presence of unshared electron pairs of nitrogen atoms and an aromatic π -system of the hetero-

cycle. This determines the existence of different interactions between the monomer and the solvent which is manifested in the polymerisation activities of vinyltetrazoles. There is evidence that self-association of 1-vinyltetrazole and 1-methyl-5-vinyltetrazole in various solvents affects the polymerisation activity of the monomers^{86, 124} along with accelerating effects of water^{124, 130, 132} and some low-molecular-weight additives¹³³ on polymerisation of vinyltetrazoles. The nature of the polymerisation medium also significantly affects the MM characteristics of the polymers synthesised. Thus MM of the polymeric products prepared in water-containing systems were found to be substantially increased.^{79, 124, 130} Varying the nature of the solvent is the most efficient way to achieve control over polymerisation of vinyltetrazoles and of the effect on the structures and properties of the polymers obtained. The data listed in Table 7 confirm the important role of the solvent in the polymerisation of both the ionogenic (5-vinyltetrazole) and non-ionogenic (*C*- and *N*-vinyltetrazoles) monomers. A transition from the solvent-free polymerisation to the solution polymerisation favours, as a rule, higher yield of the polymeric product but differently affects the reactivities of the monomers. Thus the activities of 2-methyl-5-vinyltetrazole in solvent-free polymerisation and in polymerisation in chloroform were practically identical,¹²⁸ while characteristic viscosities of the polymers obtained significantly decreased with a decrease in the initial concentration of the monomer in the polymerisation system. Polymerisation in more polar solvents, especially in water, increases the activities of vinyltetrazoles and MM of the polymers formed.^{43, 124} The activating effect of water is also manifested in the polymerisation in mixed solvents. The addition of water to DMF or acetonitrile causes a monotonic increase in the polymerisation rate and $K_{\text{p}}/K_{\text{t}}^{0.5}$ parameters for 5-vinyl-, 1-methyl-5-vinyl- and 2-methyl-5-vinyltetrazoles^{43, 124, 130, 132} and increases the degree of polymerisation of the polymers obtained (Fig. 2). A sharp increase in $K_{\text{p}}/K_{\text{t}}^{0.5}$ was

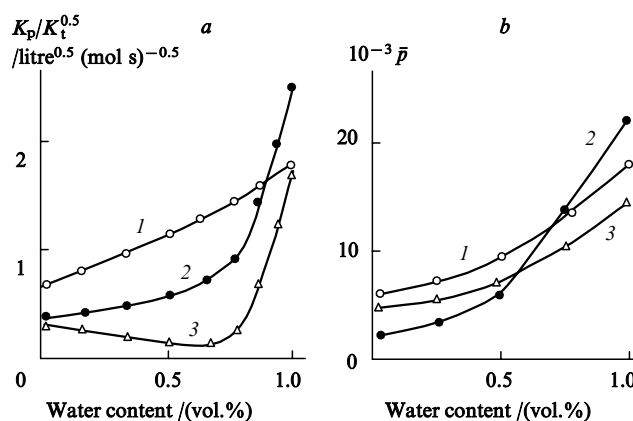


Figure 2. The dependence of the relative rate constant for chain propagation, $K_{\text{p}}/K_{\text{t}}^{0.5}$ (a) and the degree of polymerisation of the polymeric products ($\bar{p}$) obtained (b) by polymerisation of 5-vinyltetrazole (1), 1-vinyltetrazole (2) and 2-methyl-5-vinyltetrazole (3) on the composition of the MeCN–H₂O mixture (60 °C).^{43, 124}

Table 7. The effect of the solvent on the kinetic parameters of the polymerisation of *C*- and *N*-vinyltetrazoles (60 °C).

Monomer	Solvent	$E_{\text{ef}}/\text{kJ mol}^{-1}$	$K_p/K_t^{0.5}/\text{litre}^{0.5}(\text{mol s})^{-0.5}$	$E_p - 0.5 E_t/\text{kJ mol}^{-1}$	Ref.
5-Vinyltetrazole (1)	AcOH	—	0.65	—	43, 124
	MeCN	74.8	0.67	16.7	43, 124
	EtOH	83.3	0.90	19.4	43, 124
	H ₂ O	65.8	1.82	14.8	43, 124
1-Methyl-5-vinyl-tetrazole (5a)	without solvent	—	0.69	20.0	129
	DMF	87.95	0.85	—	130
	DMF–H ₂ O ^a	—	1.02	—	130
2-Methyl-5-vinyl-tetrazole (5b)	MeCN	81.3	0.31	19.9	43
	DMF	82.3	0.46	—	130
	DMF–H ₂ O ^a	85.1	0.75	—	130
	H ₂ O	77.6	1.86	—	43
1-Vinyltetrazole (14a)	MeCN	80.4	0.34	20.6	43, 124
	H ₂ O	90.9	2.54	23.9	43, 124
5-Methyl-1-vinyl-tetrazole (14b)	MeCN	81.8	0.21	21.3	43, 124
	H ₂ O	84.3	2.09	22.2	43, 124

Note. AIBN was used as the initiator in organic solvents; AP was used as the initiator in water. ^a Water content was 9.2 mol litre^{−1}.

observed in the AIBN-induced polymerisation of 1-vinyltetrazole and 2-methyl-5-vinyltetrazole in an H₂O–MeCN system with the water content > 0.8 vol.% (see Fig. 2a).^{43, 124} In aqueous solutions, the polymerisation activities of nonionogenic 2-methyl-5-vinyl-, 1-vinyl- and 5-methyl-1-vinyltetrazoles characterised by the parameter $K_p/K_t^{0.5}$ exceed those in acetonitrile 6-, 7.5- and 10-fold, respectively (see Table 7). In acetonitrile, the activities of the aforementioned monomers are lower than that of unsubstituted 5-vinyltetrazole, while the $K_p/K_t^{0.5}$ values of *N*-vinyltetrazoles in H₂O are higher than that of *C*-vinyltetrazole. Apparently, the most probable reason for enhanced polymerisation activity of non-ionogenic vinyltetrazoles in water is the increase in the concentration of the monomer in the microenvironment of the active centres of the growing macroradicals as a result of sorption of the hydrophobic monomer.¹²⁴ Selective sorption of organic monomers by polymeric coils and the resulting increase in polymerisation rates have repeatedly been observed for other water-soluble monomers.^{134, 135} In water, the molecular masses of polyvinyltetrazoles formed increase severalfold (see Fig. 2b).

Of special note is the effect of water on polymerisation of ionisable 5-vinyltetrazoles. The values of $K_{\text{ef}} = W[M_0]^{-1}$ and the initiation rate constant K_{in} for reactions performed in acetonitrile and water depend differently on the monomer concentration (Fig. 3).¹²⁴ The initial concentration of 5-vinyltetrazole does not affect K_{in} and K_{ef} in acetonitrile, but for polymerisation in water in the presence of AP, these constants depend on the monomer

concentration. Moreover, the formal kinetic expression for the rate of polymerisation in water and the energy characteristics of the reaction depend on the monomer concentration. The classical equation $W = K[M][I]^{0.5}$ is observed only at the initial concentrations of 5-vinyltetrazole below 0.3 mol litre^{−1}. In this case, the effective activation energy, E_{ef} , is equal to 65.8 kJ mol^{−1} (see Ref. 124). K_{in} and K_{ef} values increase with an increase in the initial concentration of the monomer from 0.5 to 2.0 mol litre^{−1}. The formal order of the reaction with respect to the monomer in the given concentration range is > 1, whereas the effective activation energy is 49.3 kJ mol^{−1} (see Refs 43 and 136). With these concentrations of the monomer, redox initiation involving 5-vinyltetrazole takes place.

5-Vinyltetrazole manifests the properties of a weak acid; therefore, its polymerisability, *e.g.*, expressed through the reduced polymerisation rate, depends on the pH of the reaction medium (Fig. 4).^{124, 136} The maximum reaction rates and the molecular masses of the polymers formed are observed at pH values corresponding to self-dissociation of the monomer, whereas their minimum values are observed at pH close to the point of complete neutralisation of the NH-acid. Such a parallel dependence of the kinetic and molecular-mass characteristics on pH is also observed for unsaturated carboxylic acids and is determined by changes in the electronic structures of the polymerising monomers in the course of ionisation.¹³⁷

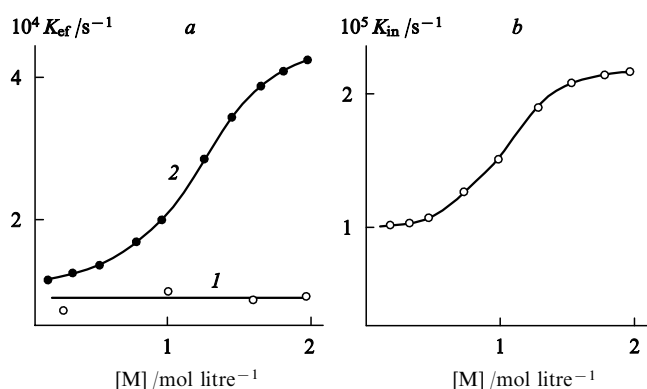


Figure 3. The dependences of the effective rate constant (K_{ef}) for the polymerisation of 5-vinyltetrazole (a) in acetonitrile (1) and water (2) and of the initiation rate constants (K_{in}) in water (b) on the concentration of the monomer (60 °C).

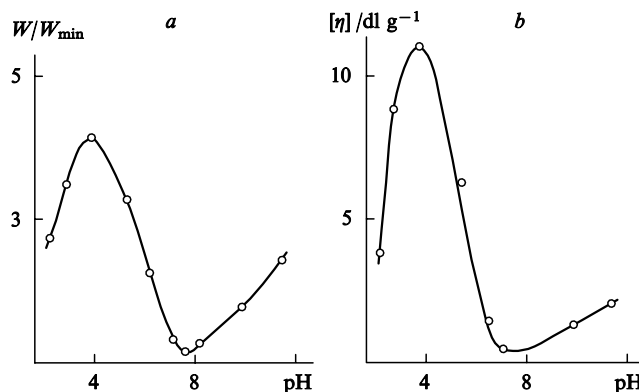


Figure 4. The pH dependence of the reduced rate constant (W/W_{min}) for the polymerisation of 5-vinyltetrazole (a) and the intrinsic viscosity $[\eta]$ of the polymers formed (b) (H₂O, 60 °C). $W_{\text{min}} = 0.13 \times 10^{-4}$ mol litre^{−1} s^{−1}. Concentrations: monomer, 0.25 mol litre^{−1}; AP, 10^{-3} mol litre^{−1}.

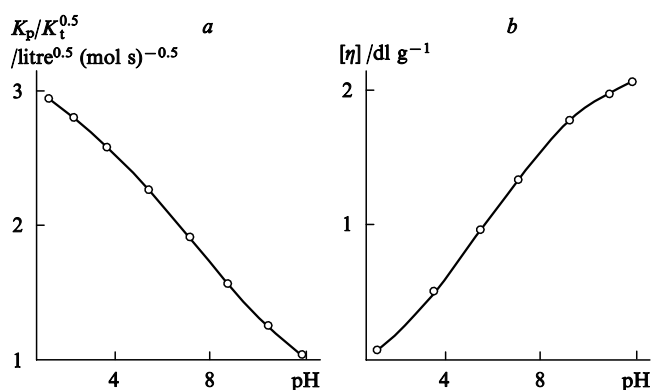
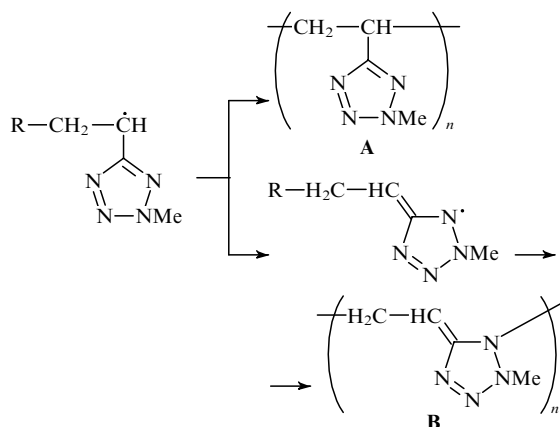


Figure 5. The effect of pH of the aqueous solution on the relative rate constant for chain propagation, $K_p/K_t^{0.5}$ (a) and the intrinsic viscosity $[\eta]$ of the polymeric products obtained (b) upon polymerisation of 5-amino-1-vinyltetrazole (60 °C).

Among other *N*-vinyltetrazoles, 5-amino-1-vinyltetrazole is the most sensitive to pH changes in the course of polymerisation, which is probably related to the enhancement of the basic properties of the tetrazole ring and its ability to be protonated in acidic media. The $K_p/K_t^{0.5}$ values for this monomer increase with a decrease in pH (Fig. 5).⁴³ In contrast, the characteristic viscosities of the polymers formed increase with pH. The polymers synthesised at pH > 11 are insoluble.

Polymerisation of vinyltetrazoles is also affected by addition of some low-molecular-weight salts, *e.g.*, sodium thiocyanate.¹³³ In aqueous solutions of this salt, 1-vinyl-, 5-methyl-1-vinyl- and 2-methyl-5-vinyltetrazoles yield polymeric products of much higher molecular masses than in the absence of solvents or in organic media.

The structures of synthetic polymers also depend on the nature of the reaction medium. Under conditions of radical initiation, the polymerisation of 2-methyl-5-vinyltetrazole occurs by an isomerisation mechanism with simultaneous cleavage of the C = C bond of the vinyl group and the C = N bond of the tetrazole ring and formation of the C = C bond in the main polymeric chain.



An increase in the solvent polarity leads to the predominant formation of form **A**, while the proportion of form **B** in the final polymeric product increases in less polar solvents.

Thus, by varying the nature of the reaction medium one can gain reliable control over polymerisation of vinyltetrazoles and MM characteristics of the polymers synthesised.

3. Effect of the method of initiation on the polymerisation of vinyltetrazoles

The use of various methods of initiation for the polymerisation of vinyltetrazole derivatives allows control over polymerisation and

modification of structural and molecular-mass characteristics of the polymeric products.

Polymerisation of 5-vinyl-2-methyltetrazole under conditions of anionic catalyst, BuONa, and cationic catalyst, $\text{Ph}_3\text{C}^+\text{ClO}_4^-$, initiation afforded a polymer with a high content of structures **B**.¹²² The molecular masses of the polymers synthesised are $(5-50) \times 10^3$, *i.e.*, by one order of magnitude lower than those of polymers prepared under the conditions of the radical initiation. In addition, ionic polymerisation leads to the opening of the tetrazole ring with cleavage of the C = N bond and formation of cross-linked structures. High-molecular-weight poly(5-vinyltetrazole) was prepared by electrochemical radical polymerisation of the monomer in water at 20 °C in the presence of potassium persulfate using a glass electrode.¹²¹ A chelate-type polymeric complex of poly(5-vinyltetrazole) with Fe^{2+} (see Refs 138 and 139) was synthesised under analogous conditions using an iron electrode. γ -Radiation-induced polymerisation of 2-methyl-5-vinyltetrazole occurs by a radical mechanism: the reaction rate is proportional to the dose rate to the power 0.5.¹¹⁹ All other factors being the same, the reactivity of the tetrazole-containing monomer in the radiation polymerisation exceeds those of styrene, acrylonitrile, methyl methacrylate and vinyl acetate.^{119, 140} Varying the irradiation conditions in the polymerisation of 2-methyl-5-vinyltetrazole allows preparation of polymeric products in a broad range of molecular masses ($2 \times 10^4 - 20 \times 10^5$). Radiation polymerisation was accompanied by radiolytic degradation of the tetrazole ring with elimination of nitrogen.¹¹⁹

Radical polymerisation of vinyltetrazoles in the presence of initiators which enables a high degree of conversion and formation of high-molecular-weight products ($\text{MM} \sim 10^6$) is of particular practical interest. For the majority of monomers, the highest yields and MM were achieved by polymerisation in water in the presence of AP. In some cases, the use of redox systems permits one to increase the yields of the polymers with simultaneous reduction of the reaction time and the temperature. The increases in the reaction rates and conversion are especially pronounced in the case of 1-vinyl- and 5-methyl-1-vinyltetrazoles in the presence of redox systems in water: at 20 °C, polymerisation occurs virtually instantaneously with high self-heating and quantitative yields of the polymers.⁷⁹ In the presence of AP and BP, the polymerisation of 5-vinyltetrazole occurs even at 20 °C (where no thermolysis of the initiator occurs) and affords polymers of the highest MM.¹⁴¹ The structures of tetrazole-containing monomers enable their donor–acceptor interactions with compounds containing a peroxide O–O fragment, which affects the polymerisation of vinyltetrazoles in the presence of peroxide initiators.

a. Polymerisation of 5-vinyltetrazole under the action of peroxide initiators

It was noted in one of the early papers¹¹⁸ that the polymerisation of 1-methyl-5-vinyl- and 2-methyl-5-vinyltetrazoles with simultaneous grafting onto cellulose initiated by H_2O_2 is characterised by extraordinarily low values of activation energies (49.6 and 43.2 kJ mol⁻¹, respectively). This is also typical of polymerisation reactions occurring under redox initiation conditions. As mentioned above, the K_{in} and E_{ef} values for the polymerisation of 5-vinyltetrazole in water under the action of AP depend on the concentration of the monomer.¹²⁴ Obviously, the tetrazole-containing monomer is involved in the initiation step in the presence of peroxide initiators. As expected, 5-vinyltetrazole containing both nitrogen atoms with an unshared electron pair and a proton-donor NH bond interacts with the initiator the most actively.

The results of kinetic studies of the polymerisation of 5-vinyltetrazole induced by various initiators are presented in Table 8. Under conditions of thermolysis of BP, the reaction of the monomer with the initiator does not influence the polymerisation kinetics of 5-vinyltetrazole. As can be seen from Table 8, the polymerisation induced by BP under identical conditions is more energy-consuming and occurs at a lower rate than that in the presence of AIBN due to a much lower (*ca.* fivefold) initiation rate

Table 8. Kinetic parameters of the polymerisation of 5-vinyltetrazole in the presence of AIBN, BP and AP.^{43, 141}

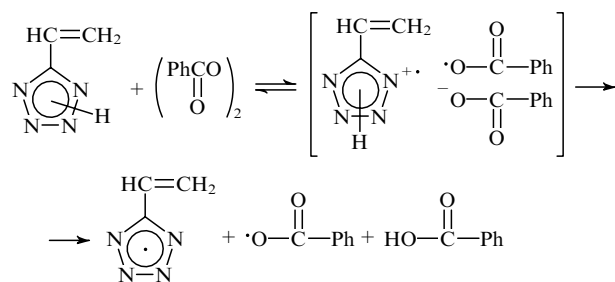
Initiator	Solvent	$T/^{\circ}\text{C}$	Kinetic orders		$E_{\text{ef}}/\text{kJ mol}^{-1}$	$10^4 K_{\text{ef}}/\text{litre (mol s)}^{-1}$	$10^5 K_{\text{in}}/\text{s}^{-1}$
			[M]	[I]			
AIBN	EtOH	60	1.5	0.5	83.3	28.0	0.96
BP	EtOH	60	1.5	0.6	92.0	12.9	0.20
	EtOH	20	1.9	0.8	22.1	0.87	0.007
AP	H ₂ O	60	1.8	0.26	49.3	16.4	1.67
	H ₂ O	20	1.85	0.5	25.4	2.2	0.16

constant. Such a correlation of K_{in} for the polymerisation initiated by BP and AIBN is characteristic of vinyl monomers.¹²⁵

A different situation is observed in the polymerisation of 5-vinyltetrazole in water at 50–70 °C in the presence of AP as the initiator. In addition to the concentration dependence of K_{in} and K_{ef} in the range of the monomer concentrations of 0.5–2 mol litre⁻¹ (see Table 8), the kinetic order with respect to the monomer is increased, while the E_{ef} value is commensurate with the values of the activation energies for the reactions initiated by redox systems. In this case, K_{in} exceeds the corresponding value for the polymerisation in the presence of AIBN and BP (two- and eightfold, respectively), which ensures higher reaction rates. These data suggest the feasibility of an interaction of 5-vinyltetrazole with AP, which is manifested in the polymerisation kinetics.

Polymerisation of the vinyl monomer in the 5-vinyltetrazole–BP and 5-vinyltetrazole–AP systems occurs at the temperatures where no thermolysis of the initiators takes place.¹⁴¹ The AP-induced low-temperature (10–30 °C) polymerisation of 5-vinyltetrazole in water proceeds at significantly higher rates than that in the presence of BP, which can be attributed to higher values of the initiation constant, K_{in} , for the 5-vinyltetrazole–AP system (see Table 8). This suggests that the donor–acceptor interaction of 5-vinyltetrazole with AP, which results in the formation of radicals initiating the polymerisation, proceeds more smoothly than with organic peroxides.

A mechanism of involvement of 5-vinyltetrazole in the generation of radicals initiating the polymerisation of the monomer in the presence of BP at reduced temperatures has been proposed.^{43, 141}



Tetrazole derivatives are weaker electron donors than tertiary amines, therefore, 5-vinyltetrazole is less prone to donor–acceptor interactions with peroxide than, *e.g.*, alkylamines or *N,N*-dimethylaniline. However, the presence of an acid proton in the tetrazole ring favours decomposition of the charge-transfer complexes formed to yield radical species initiating the polymerisation. If a heterocycle contains no acid proton (*e.g.*, as in the cases of *N*-methyl- or *N*-vinyl derivatives), no polymerisation in the presence of AP or BP in aprotic solvents at 20 °C occurs. The addition of water to these systems induces polymerisation of both 2-methyl-5-vinyltetrazole and 1-vinyltetrazole. This fact points to the crucial role of the proton in reactions of tetrazole-containing compounds with AP or BP.

b. Spontaneous polymerisation of 5-vinyltetrazole

A characteristic feature of 5-vinyltetrazole is its spontaneous polymerisability in the absence of initiators at 20 °C and lower

temperatures upon dissolution in water, ethanol, formamide, DMF and DMSO.¹⁴² No spontaneous polymerisation of the monomer occurs in acetone or acetonitrile. The rate of spontaneous polymerisation of 5-vinyltetrazole and the polymer yields depend on the nature of the solvent and pH of the medium, reaching maximum values in water at pH 4.3. The logarithmic dependence of the polymerisation rate of 5-vinyltetrazole in water at 60 °C on the monomer concentration appears as:

$$\log W = (-5.79 \pm 0.05) + (1.90 \pm 0.11) \log [M].$$

The E_{ef} value for spontaneous polymerisation of 5-vinyltetrazole determined from the temperature dependence of K_{ef} [1.13×10^{-6} (at 50 °C), 1.49×10^{-6} (at 60 °C), 1.98×10^{-6} litre (mol s)⁻¹ (at 70 °C)] is 25.8 kJ mol⁻¹ (see Refs 43 and 142), which accounts for the occurrence of this reaction at 20 °C and lower temperatures.

The molecular masses of the polymeric products synthesised by spontaneous polymerisation of 5-vinyltetrazole in water do not depend on the initial concentrations of the monomer and are commensurate with those of poly(5-vinyltetrazole) specimens prepared by initiator-induced polymerisation.

VII. Copolymerisation of vinyltetrazoles

Copolymerisation, like chemical modification, is used for changing physicochemical, physicomachanical, chemical and other properties of polymeric compounds as well as for conferring novel properties that are sometimes atypical of homopolymers. Vinyltetrazole derivatives are promising starting compounds for the synthesis of novel polymeric products by copolymerisation with other vinyl monomers. The activities of vinyltetrazoles in copolymerisation reactions allow easy variation of the composition, and, correspondingly, properties of the polymeric products obtained.

An analysis of results of copolymerisation studies involving vinyltetrazoles should be started from the consideration of reactivities of vinylazoles, which are thought to depend on the number of nitrogen atoms in the heterocycle.

An analysis of a vast body of experimental (often, contradictory) data on copolymerisation of vinylazoles^{53, 54, 143–158} revealed that these compounds manifest lower activities in the copolymerisation with standard comonomers, such as styrene and methyl methacrylate (MMA). At the same time, an increase in the number of nitrogen atoms in the heterocycle of vinylazoles, which enhances the π -electron-withdrawing effect of the azolyl substituent on the double bond, is accompanied by enhancement of activities of vinylazoles in the reaction with a macroradical having a terminal styrene fragment.⁵³ In the copolymerisation with MMA, an opposite trend is observed.¹⁵⁸ In our opinion, the most correct approach to the study of structure–activity relationships of vinylazoles in copolymerisation was proposed by Smirnov *et al.*^{54, 144} Thus for the *N*-vinylazole–diethyl maleate (DEM) and *N*-vinylazole–1-vinylpyrrolidone (VPD) systems, the activities of the monomers in the reaction of vinylazoles with the DEM radical are the higher the higher is the polarity of the C=C bond and the negative charge of the β -carbon atom of the vinyl group of the vinylazole. In contrast, the activities of vinylazoles in the reaction with the VPD radical increase with a decrease in polarity

Table 9. Constants of copolymerisation of vinyltetrazoles with other vinyl monomers in the presence of AIBN.

Vinyltetrazole	r_1	Comonomer	r_2	Solvent	Temperature /°C	Ref.
5-Vinyltetrazole (1)	0.29 ± 0.05	acrylic acid	0.67 ± 0.11	DMF	60	159
	2.93 ± 0.23	vinyl acetate	0.07 ± 0.03	DMF	60	160
	0.44 ± 0.03	<i>N</i> -vinylpyrrolidone	0.30 ± 0.07	DMF	60	150
	0.44 ± 0.09	maleic acid	0.21 ± 0.02	DMF	60	161
	0.61 ± 0.18	2-methyl-5-vinyltetrazole	0.52 ± 0.16	acetonitrile	60	162
	0.31 ± 0.02	styrene	0.78 ± 0.03	DMF	60	152
	0.36 ± 0.04	"	0.97 ± 0.03	DMF	—	63
5-Isopropenyltetrazole (2)	0.37 ± 0.02	<i>N</i> -vinylpyrrolidone	0.27 ± 0.05	DMF	60	154
	0.27 ± 0.01	"	0.10 ± 0.02	ethanol	60	154
	3.60 ± 0.50	"	0.25 ± 0.08	water (pH 2.3)	60	154
	0.70 ± 0.11	1-vinyltetrazole	1.78 ± 0.28	DMF	60	163
	0.90 ± 0.07	maleic acid	0.13 ± 0.06	DMF	60	161
	0.42 ± 0.02	styrene	0.45 ± 0.04	DMF	60	161
	0.99 ± 0.04	acrylonitrile	0.068 ± 0.05	DMF	60	156
1-Methyl-5-vinyl-tetrazole (5a)	2.12 ± 0.07	"	0.013 ± 0.01	DMF	60	164
	0.98 ± 0.06	methyl methacrylate	0.64 ± 0.06	DMF	60	53
	1.36 ± 0.06	2-methyl-5-vinyltetrazole	0.65 ± 0.05	DMF	65	165
	0.50 ± 0.07	"	0.49 ± 0.03	without solvent	65	164
	0.57 ± 0.07	styrene	0.28 ± 0.09	DMF	60	157
	0.86 ± 0.02	"	0.48 ± 0.04	DMF	65	164
	0.18 ± 0.03	chloroprene	2.94 ± 0.5	chloroform	60	155
	0.22 ± 0.01	acrylonitrile	0.37 ± 0.07	DMF	60	156
	2.39 ± 0.20	"	0.07 ± 0.03	without solvent	65	153
	2.18 ± 0.18	"	0.02 ± 0.01	aqueous emulsion ^a	40	153
2-Methyl-5-vinyl-tetrazole (5b)	1.49 ± 0.08	butyl methacrylate	0.51 ± 0.05	without solvent	—	166
	2.5	vinyl acetate	0.1	water ^{a, b}	—	167
	23.0	"	0.01	chloroform	65	86
	0.52 ± 0.16	5-vinyltetrazole	0.61 ± 0.18	acetonitrile	60	162
	0.76 ± 0.07	"	0.49 ± 0.03	DMF	65	63
	0.59 ± 0	hydroxyethyl methacrylate	0.54 ± 0.03	without solvent	65	153
	0.19 ± 0	glycidyl methacrylate	1.04 ± 0.06	chloroform	60	153
	0.60 ± 0	methacrylic acid	1.0 ± 0.12	acetone	60	153
	0.65 ± 0.05	1-methyl-5-vinyltetrazole	1.36 ± 0.06	DMF	65	165
	0.49 ± 0.03	"	0.50 ± 0.07	without solvent	65	164
	0.48	methyl methacrylate	1.0	chloroform	65	86
	0.51 ± 0.02	"	1.47 ± 0.07	without solvent	—	166
	0.77	styrene	1.18	chloroform	65	86
	0.64	"	1.07	without solvent	65	27
	0.08 ± 0.02	chloroprene	10.76 ± 0.8	chloroform	65	155
	0.83	styrene	1.04	without solvent	65	27
2-Ethyl-5-vinyl-tetrazole (5c)						
2-Isopropyl-5-vinyl-tetrazole (5d)	0.64	"	0.99	the same	65	27
	0.37	methyl methacrylate	1.01	"	65	27
2- <i>tert</i> -Butyl-5-vinyl-tetrazole (5e)	0.53	styrene	1.12	"	65	27
	0.43	methyl methacrylate	1.05	"	65	27
1-Vinyltetrazole (14a)	0.34 ± 0.01	acrylonitrile	0.57 ± 0.05	DMF	65	149
	0.23	<i>N</i> -vinylpyrrolidone	0.03	without solvent	60	54
	9.55	diethyl maleate	0.19	the same	60	54
	1.78 ± 0.28	5-isopropenyltetrazole	0.70 ± 0.11	ethanol	60	163
	0.29 ± 0.01	methyl methacrylate	6.68 ± 0.09	DMF	65	149
	0.20 ± 0.02	styrene	3.74 ± 0.09	DMF	65	149
	0.95	butyl methacrylate	1.04	DMF	—	168
5-Amino-1-vinyl-tetrazole (14d)	1.24 ± 0.10	vinyl acetate	0.55 ± 0.06	DMF	60	160
	0.15	<i>N</i> -vinylpyrrolidone	0.78	DMF	—	168
	0.69 ± 0.07	"	0.51 ± 0.05	DMF	60	150
	0.83 ± 0.05	maleic acid	0.27 ± 0.05	water ^c	60	161
	0.23	methacrylic acid	1.30	DMF	—	168
	0.42 ± 0.05	styrene	1.20 ± 0.05	DMF	60	151
	0.72 ± 0.09	methyl methacrylate	1.19 ± 0.15	without solvent	65	63
2-Isopropenyl-5-methyltetrazole	0.32 ± 0.01	styrene	1.19 ± 0.02	the same	65	63

^a The redox system Fe²⁺ – H₂O₂. ^b Graft copolymerisation onto cellulose. ^c In the presence of AP.

and q_B . Thus, the activities of *N*-vinylazoles in reactions with electron-withdrawing radicals (DEM and MMA) decrease with

an increase in the number of nitrogen atoms in the heterocycle, while those in reactions with donor radicals (VPD) increase. This

suggests that the activity of *N*-vinyltetrazole is the lowest (compared to those of other vinylazoles) in the copolymerisation with electron-withdrawing monomers and the highest in the copolymerisation with electron-donating monomers. However, the *N*-vinylazole–styrene system does not fit into this series. The activities of vinylazoles in the reaction with a macroradical containing a terminal styrene unit characterised by parameter $1/r_2$ (where r are effective relative activity constants) decrease in the following order: 1-vinylimidazole [0.1 (see Ref. 145)] < 1-vinyltetrazole [0.27 (see Ref. 149)] < 1-vinyl-1,2,4-triazole [0.67 (see Ref. 148)].

C-Vinyltetrazoles are more reactive in copolymerisation with styrene and MMA than *N*-vinyl derivatives (Table 9); their activities depend critically on the presence and positions of substituents in the molecule of the monomer. The presence of a methyl group in the vinyl fragment or in position 1 of *C*-vinyltetrazole changes the reaction pattern so that 5-isopropenyltetrazole is as active as styrene in the copolymerisation and the activity of 1-methyl-5-vinyltetrazole exceeds those of styrene and MMA (see Table 9). 2-Methyl-5-vinyltetrazole is less reactive towards the styrene radical ($1/r_2 = 0.84$)⁸⁶ than unsubstituted 5-vinyltetrazole ($1/r_2 = 1.28$).¹⁵² In this case, the size of the alkyl substituent in position 2 does not affect the activities of the monomers in the copolymerisation.²⁷

The interest of investigators in tetrazole-containing polymers has long been determined by the possibility of technological applications of these high-energy compounds. However, the properties of polymers based on tetrazole are very diverse owing to the presence of several reactive sites in the tetrazole ring. In some copolymers of vinyltetrazoles with other vinyl monomers, these properties are more pronounced. For this reason, copolymerisation reactions hold especially great promise in the synthesis of novel tetrazole-containing polymeric materials of practical importance.

VIII. Practical applications of vinyltetrazole derivatives

Despite diverse properties of vinyltetrazoles and their polymeric derivatives, their practical applications are not an issue of broad discussion. In this section we consider the prospects of practical applications of vinyltetrazoles.

Vinyltetrazoles present interest for organic synthesis as intermediates. They were used in the synthesis of tetrazole-containing bromohydrins,⁹⁴ epoxytetrazoles,⁹⁴ hydroxyethyltetrazole,¹⁹ aziridine derivatives,⁹⁷ 2-(tetrazol-5-yl)bicyclo[2.1.2]hept-5-ene and 2-methyl-5-vinyl-1,3,4-oxadiazole.²¹ The approaches to the synthesis of 5-iodo- and mercury-substituted vinyltetrazoles⁴⁸ have been outlined and the possibility of alkylation of 5-vinyltetrazole under electrophilic conditions has been demonstrated.³² Various functionalised derivatives based on 5-chloromethyl-1-vinyltetrazole have been synthesised; for some of them biological activity is anticipated.⁴¹ As vinyltetrazoles can easily form complexes with metal ions including Ni^{2+} and Pd^{2+} , it may be expected that these complexes will manifest catalytic activity in hydrogenation reactions.¹⁰¹

The construction of novel polymeric materials endowed with unique properties on the basis of tetrazole derivatives is the most promising line of research. High-energy characteristics of tetrazole polymers, their relatively low sensitivity to shock and friction, rather high thermal stability, low toxicity and evolution of a large volume of neutral gas upon decomposition make polymers and copolymers based on vinyltetrazoles promising components for gunpowders, explosives and propellants.^{1, 14–20, 28} The majority of published papers confirm the fact that tetrazole-containing polymers used in various fuel systems differ favourably from analogous polymeric materials in enhanced intrinsic energy, good compatibility with other composition components and handling safety.

Meanwhile, other properties of vinyltetrazole-containing polymers are currently attracting the attention of investigators. Thus ternary copolymers of 2-methyl-5-vinyltetrazole with acrylic acid and its esters were recommended as components of rubber compositions possessing high mechanical characteristics.¹⁶⁹ Preparation of a film-forming substance for cosmetics based on hydroxyethylammonium salt of poly(5-vinyltetrazole) has recently been claimed.¹⁷⁰ A copolymer of 2-methyl-5-vinyltetrazole with 1-vinylpyrrolidone, methyl methacrylate and α,ω -hexamethacryloyl oligoacrylate has been recommended for the production of vision correcting lenses.¹⁷¹ A cellulose acetate composition comprising polyvinyltetrazole can be used for the preparation of ultrafiltration membranes.¹⁷² A copolymer of 2-methyl-5-vinyltetrazole with *N,N*-diallyl-*N,N*-dimethylammonium chloride has been patented as a film-forming substance possessing semiconducting and antistatic properties.¹⁷³ Graft copolymerisation of 2-methyl-5-vinyltetrazole was recommended to improve absorption properties of cotton and cellulose fibres.¹⁷⁴ A copolymer of butyl acrylate with acrylonitrile and 5-vinyltetrazole can be used as a polymeric binder of operating layers of magnetic storage media and an adhesive.¹⁷⁵ Taking into consideration high complex-forming ability of polyvinyltetrazoles with respect to heavy metal ions in aqueous media,^{43, 176–178} it may be expected that these polymers will find use as efficient sorbents for the solution of various environmental problems or for the isolation of precious metals. Sodium salt of poly-5-vinyltetrazoles forms hydrogel compositions in the presence of Cr^{3+} ions; this polymer has been patented as a thickening agent in water-filled explosives.^{179, 180}

The results of studies of physiological activities of tetrazole-containing polymers are promising, which opens new opportunities for the preparation of novel medicinal drugs based on them.

Unsubstituted poly-*C*-vinyltetrazoles manifest acidic properties and enter into interpolymeric reactions with natural high-molecular-weight compounds, which determines their anticoagulant properties.^{181, 182} The anticoagulant activity can be varied significantly by combining structural fragments of vinyltetrazoles with other comonomers in the polymeric chain.^{183, 184} Quaternary salts of polyvinyltetrazoles exert an opposite effect: they bind heparin in the circulating blood and thus favour blood coagulation.¹⁸⁵ The antiheparin activity of tetrazole-containing polycations compares favourably with that of currently employed medicinal drugs. Sodium salt of poly(5-vinyltetrazole), a polyelectrolyte endowed with pronounced antiinflammatory and aseptic properties, accelerates wound healing and suppresses cicatrization.^{43, 186, 187}

Tetrazole-containing polyelectrolytes manifest pronounced, sometimes extraordinarily high, immunoadjuvant activity towards a vast range of antigens.^{183, 188–190} Homo- and copolymers of poly-5-vinyl- and poly-5-isopropenyltetrazoles were recommended for the construction of antigenic diagnostic preparations surpassing in activity those currently in practice.^{191–194}

Thus, the broad spectrum of properties of vinyltetrazole-based polymers leaves hope that these compounds will soon find application in miscellaneous areas of human activity. In our opinion, studies aimed at the preparation of tetrazole-containing monomers and polymers will eventually lead to reduction of their production costs, which is undoubtedly important for the practical application of these novel products.

* * *

This review deals with generalisation of the known methods for the synthesis of *C*- and *N*-vinyltetrazole derivatives based on the formation of the tetrazole ring from open-chain compounds containing a vinyl group and formation of an unsaturated fragment in the preformed heterocycle. Some of these methods have been implemented in the flexible production system 'Tetrazoles' designed and launched at the pilot plant of St Petersburg State

Technological Institute (the Engineering and Design Department 'Tekhnolog', Russian Federation).

An analysis of structures and geometry of vinyltetrazole molecules, generalisation of their physicochemical and spectral properties and study of mutual effects of the two unsaturated fragments, viz., the vinyl group and the heterocycle, make it possible to predict chemical properties of these compounds in addition reactions involving the vinyl group as well as in alkylation, quaternisation, complexation, etc.

The radical polymerisability of vinyltetrazoles is one of their most essential features. A detailed analysis of effects of various factors (monomer structure, reaction medium, initiation procedure, etc.) on the polymerisation of vinyltetrazoles allows development of novel polymeric materials. Pilot-plant production of polyvinyltetrazoles has been started in two enterprises in Russia. A broad spectrum of valuable properties of vinyltetrazoles and their polymers leaves hope that this class of compounds will find application in various branches of science and technology.

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Non-traditional applications of NMR tomography

I V Koptug, R Z Sagdeev

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Abstract. Applications of NMR imaging to studies of chemical reactions including polymerisation reactions and the Belousov–Zhabotinsky oscillating reaction are considered. Publications concerning applications of NMR imaging to studies of the temperature and electric current density distributions in various specimens are discussed. NMR investigations of hyperpolarised gases and gases with equilibrium nuclear spin polarisation are described. NMR imaging studies of solids (in particular, polymers and elastomers) are briefly outlined. The bibliography includes 275 references.

I. Introduction

Investigations of chemical reactions *in situ* is a promising field of application of NMR tomography (or magnetic-resonance imaging, MRI). Currently, this field has attracted considerable attention of researchers. In this review we present a detailed consideration of the studies concerned with applications of NMR imaging to the determination of the temperature and electric current density distributions within various objects. Most of these studies were carried out to address biomedical problems; however, experimental MRI techniques can undoubtedly be useful for physicochemical investigations and chemical technology. A large section of this review concerns MRI of gases. A vast area of MRI studies of solid materials is only briefly outlined owing to specific features of solid-state NMR spectroscopy. However, some solid materials, such as polymers and elastomers, allow liquid-phase NMR techniques to be employed. In this connection mention may be made that applications of NMR imaging to studies of liquid-containing materials and mass transfer investigations have been the subject of our recent reviews.^{1,2}

I V Koptug, R Z Sagdeev International Tomography Centre, Siberian Branch of the Russian Academy of Sciences, ul. Institutskaya 3A, 630090 Novosibirsk, Russian Federation. Fax (7-383) 233 13 99. Tel. (7-383) 233 35 61. E-mail: koptug@tomo.nsc.ru (I V Koptug). Tel. (7-383) 233 14 48. E-mail: itc@tomo.nsc.ru (R Z Sagdeev)

II. Chemical reactions

1. General remarks

Currently, NMR spectroscopy is widely used in studies of chemical reactions. However, there are only a few reports on the use of NMR imaging for these purposes despite a steady interest in this kind of experimental research.

Currently, there are only two fields of application that have attracted considerable attention of researchers. One of them is the application of NMR microimaging, or magnetic resonance microimaging (MRM), to studies of polymerisation processes. Polymerisation is often accompanied by slowing down the molecular mobility, which can lead to substantial reduction of the spin–spin relaxation times (T_2) of the nuclei under study. This allows one to selectively follow variations of the spatial distribution of the initial reagents with time. Usually, polymers are characterised by short T_2 times and, hence, NMR signals of these substances are not often observed. The polymer matrix reduces the mobility of the residual monomer, and the T_2 time of the latter shortens as well. To enhance the NMR signal of the polymer, one can use the fact that an increase in temperature accelerates the molecular mobility. In the case of gel formation the system can be imaged using the signal of the more mobile, liquid dispersion medium. Yet another approach involves introduction of various tracers into the initial mixture. Tracers are not involved in the reaction, but reflect variations of the local viscosity of the medium during polymerisation.

Another field of successful application of the MRM technique is the study of the Belousov–Zhabotinsky (B–Z) oscillating reactions, *i.e.*, metal ion-catalysed oxidation of organic compounds by bromate ions.³ In this case the water proton chemical shifts and relaxation times are linear functions of the concentration of the paramagnetic metal ion present in the aqueous solution and are affected by the oxidised and reduced states of the metal ion in a different manner.

Some other reactions have also been studied using MRI techniques. Of particular importance is the possibility of determining the local chemical composition of the reaction mixture by recording spatially resolved NMR spectra and selective NMR imaging using a particular NMR signal.

2. Thermal polymerisation

The formation of poly(methyl methacrylate) (PMMA) was monitored⁴ by the disappearance of the signal of methyl methacrylate (MMA) mixed with the initiator in a mould pre-heated to 60 °C.

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The two-dimensional (2D) NMR images obtained revealed mainly homogeneous propagation of the polymerisation process from the centre of the sample towards its periphery. However, the images clearly exhibit a small 'defect', namely, a region in which the polymerisation proceeds at a lower rate. The presence of this defect was confirmed visually.⁴ Homogeneous polymerisation of MMA was also reported by other authors (see, *e.g.*, Ref. 5). Polymerisation in the course of the formation of an aqueous gel of cross-linked poly(methacrylic acid) was investigated by recording T_2 -weighted 2D images.⁶ An increase in the sample viscosity with time was found to shorten the T_2 time of the sample.

Copolymerisation of methacrylamide with N,N' -methylene-bisacrylamide in water has also been studied.⁷ The process began upon the addition of ammonium persulfate (initiator) and tetramethylethylenediamine (accelerator). Polymerisation reduces the T_1 time of the signals observed. Two-dimensional NMR images obtained using the NMR signal of water revealed homogeneous gel formation throughout the sample (no polymerisation front was observed).⁷

When preparing epoxy resin based composites, it is of great importance to have a means for monitoring variations of the state of the composite during the cross-linking of polymer chains at elevated temperature.^{8,9} Raising the temperature causes an increase in the T_2 time of the resin; therefore, at temperatures above 55 °C one can obtain NMR images during the cross-linking of resin reinforced with carbon fibres using the signal from the resin protons.⁸ At times of the order of 5 min after heating to 100 °C, the cross-linking degree of the polymer chains is low and the viscosity of the sample is a function of the temperature only. Therefore, the use of corresponding calibration allows the viscosity or temperature distribution to be mapped throughout the sample. Analysis of a set of NMR images acquired at 90 °C revealed that the cross-linking at the periphery of the sample proceeds at a higher rate.

To prepare a composite material, layers of aligned carbon fibres soaked with partially cured polymer were stacked in such a manner that the fibres in each layer have different orientation.⁴ The stack obtained was placed in a mould and hot vulcanised. Before vulcanisation the polymer exhibited a short time T_2 which increased during the heat treatment procedure due to an increase in the polymer mobility. As a result, an NMR signal appeared in the corresponding regions of the 2D NMR image. Further vulcanisation led to a decrease in T_2 and to disappearance of the NMR signal. Such a signal variation in the case of unilateral heating allows one to observe how the vulcanisation process propagates throughout the sample as a single wave.⁴ Rubber vulcanisation has also been studied.^{10,11}

If a chemical reaction is coupled to molecular diffusion, a reaction front moving at a constant velocity can appear in the system. Autocatalytic polymerisation of methacrylic acid¹² is due to the exothermic character of free-radical polymerisation and to thermal decomposition of the initiator (benzoyl peroxide), which is accompanied by generation of free radicals. Polymerisation causes a substantial shortening of the T_2 time for both the polymer and the solvent. The reaction was initiated by adding accelerator (N,N -dimethylaniline) on the surface of the methacrylic acid–benzoyl peroxide mixture. Then, an induction period was observed, where the reaction front moved downward slowly with variable velocity. The duration of the induction period (4–14 min) appeared to be related to the mixing degree of the reagents in the surface layer upon addition of the accelerator. After the induction period the reaction suddenly accelerated, but rapid movement of the reaction front settled into a constant velocity of $\sim 0.6 \text{ cm min}^{-1}$. NMR imaging studies using the ^1H NMR signal of the monomer (and aniline) and companion experiments using the ^{19}F nuclei of 1,4-dibromotetrafluorobenzene (tracer) led to similar results. The front length exceeded 1 mm while its shape remained unchanged with time. An NMR signal with good signal-to-noise ratio was observed in the region immediately behind the reaction front. This indicated the presence of the residual mono-

mer after passage of the reaction front. The experiments were carried out at room temperature; the temperature near the reaction front increased to 176 °C. Attempts at detecting the effect of the magnetic field on the reaction rate failed.¹²

3. Photoinduced and radiation induced polymerisation

Various types of radiation induced polymerisation are widely used in technological processes. Fabrication of various polymeric coatings, use of photosensitive dental materials for stomatology, creation of relief images in lithography can serve as examples of practical implementation of photoinduced polymerisation. Flexible photopolymer printing boards comprise layers of a rubber-like polymer, bifunctional monomer, photoinitiator, dyes and stabilisers. The unexposed regions of the plate are usually removed by solvent. In this case NMR imaging can be used for visualisation of the irradiated region before developing the board.⁴

Photoinduced polymerisation of a resin containing methacrylic monomers has been studied (the process was induced by irradiation with visible light at 470 nm).¹³ This material is used in stomatology. Shrinkage of the material due to polymerisation can be as high as 10%, thus shortening its lifetime and deteriorating properties. The polymerisation kinetics of the resin was studied by spatially resolved NMR imaging techniques. It was found that the polymerisation rate increases with the distance from the irradiated free surface of the sample due to the inhibiting action of dioxygen. As a result, after irradiation the surface layer of the sample (layer thickness 500 μm) was found to contain a large amount of the monomer.

Photoinduced polymerisation of hexamethylene dimethylacrylate using various concentrations of benzyl-dimethyl ketal as photoinitiator has been studied¹⁴ by means of chemical shift selective NMR imaging techniques with different monomer proton groups. As the content of the initiator was 1.5%, the degree of conversion was 20% and a gel-like state was formed; the T_2 times for different proton groups varied in a different manner. Lengthening the exposure time led to a sharper boundary between the polymer and the rest of the sample. An NMR imaging study of photoinduced polymerisation of 1,6-hexanediol dimethacrylate using the same initiator has been reported.¹⁵ In this case NMR images were acquired at different exposure times. Polymerisation began at the centre of the ampoule because of light focussing at the bottom. The polymerisation front was $\sim 50 \mu\text{m}$ long. The residual monomer was observed in the near-wall region. In some instances a rather thick monomer layer (due to oxygen diffusion) was observed adjacent to the free surface through which it was irradiated.^{14,15}

Radiation-induced polymerisation can be used for dosimetry in the case of irradiation with X- or γ -rays, proton beams, *etc.* An important application of MRI is the determination of the spatial distribution of the absorbed dose when using stereotaxic irradiation in radiation therapy of various diseases. Modern experimental methods allow high irradiation doses to be delivered to a small volume of a complex shape. The MRM technique¹ permits spatial (3D) visualisation of the irradiated zones using various gel-based dosimeters.¹⁶ Applications of gels containing the Fricke dosimetric solution is based on the radiation-induced transformation of Fe(II) into Fe(III), which causes reduction of the spin–lattice relaxation time, T_1 , of the solvent (ferrous-based MRI dosimetry, or FeMRI). The amount of newly formed Fe(III) is a linear function of the irradiation dose. The 'null-point' technique, which allows one to follow the movement of the region with the prescribed concentration of the paramagnetic tracer, was used to study the diffusion of Fe^{2+} and Fe^{3+} ions in agarose gel.¹⁷ Due to fast diffusion displacements of the ions the irradiation dose distribution over the sample should be studied within several hours after the irradiation. The sensitivity of the FeMRI technique to irradiation is low. NMR images of the X-ray or proton beam irradiated samples have been obtained and an improved T_1 mapping procedure has been reported.¹⁸

MRI applications of polymer gels, whose properties are similar to those of tissues in living organisms, are based on irradiation-induced polymerisation of a monomer dispersed in the gel (the so-called 'Polymerisation Based Dosimeter Gel Evaluated Using MRI' procedure, or PoMRI). This kind of dosimeter can be based on, *e.g.*, an aqueous gelatin gel with the addition of acrylic comonomers and cross-linking agents. Irradiation causes the generation of free radicals that initiate both polymerisation and cross-linking of the monomer molecules.^{19,20} Analysis of the T_2 maps obtained for irradiated polyacrylamide gels showed that polymerisation is not complete even several weeks after irradiation. Oxygen inhibits polymerisation; however, this was observed only in the near-surface layer due to slow oxygen diffusion. For thoroughly prepared samples the relaxation rates $1/T_1$ and $1/T_2$ appeared to be linear functions of the irradiation dose in the range from 0 to 10 Gy.²⁰ In the non-irradiated gels the T_2 value also decreased with time, which seems to be due to the presence of impurities in freshly prepared samples (radicals capable of initiating polymerisation).¹⁹ For N,N' -bisacrylamide gels the relaxation rate $1/T_2$ is a linear function of the irradiation dose up to saturation levels of 10 to 15 Gy.^{16,21} The T_2 maps obtained for these gels were converted into the spatial irradiation dose maps using the formula

$$\frac{1}{T_2} = 6.0 + 0.48 D,$$

where D is the irradiation dose (in Gy).¹⁶ N -Vinylpyrrolidone-based gels (VIPAR) exhibit lower toxicity; however, they are less sensitive to radiation.²¹

$$\frac{1}{T_2} = \frac{1}{T_{20}} + 0.09 D,$$

where T_{20} is the T_2 time of the gel before irradiation. A linear response was observed up to 32 Gy doses. The spatial distribution of the irradiation dose in these gels has also been studied.

4. The Belousov–Zhabotinsky reaction

A number of publications have been concerned with the NMR imaging studies of 'chemical' (concentration) oscillations and waves observed in the manganese-catalysed oxidation of malonic acid by bromate ion (Fig. 1). The system under study is optically transparent, which makes visual monitoring of various processes difficult. However, there is a linear correlation between the water proton chemical shift and relaxation times and the concentration of the paramagnetic metal ion in the aqueous solution. The reduced state of the manganese ion (Mn^{2+}) is known to affect these parameters more than the oxidised state (Mn^{3+}).²² The spin–spin relaxation time is most sensitive to the change in the oxidation state of manganese. Therefore, usually T_2 -weighted NMR images are used, in which the regions with higher concentrations of Mn^{3+} ions (reaction front or oxidation stage) give a stronger NMR signal compared to the regions with lower concentrations of Mn^{3+} ions. Instability of manganese in the $3+$ state in aqueous solutions can lead to a loss of image contrast; therefore,



Figure 1. Travelling concentration waves in the oxidation of malonic acid in an ampoule 5 mm in diameter filled with glass beads 0.5 mm in diameter.

A spherical wave is created in the bottom region of the sample (see the right side of the NMR image) and then partially annihilated upon collision with the ampoule wall. The remaining part of the wave front continues to propagate through the medium (see the left side of the NMR image). The 2D NMR image was obtained using the axial slice selection technique.

the reaction mixture is doped with orthophosphoric acid ($\sim 1 \text{ mol litre}^{-1}$) to stabilise the Mn^{3+} ion due to the formation of the metal–phosphate complex.²² The formation of more stable chelate complexes in the case of polydentate phosphate ligands causes a substantial increase in the T_2 time of the water protons in the oxidation stage even when much smaller amounts of dopants ($\text{Na}_4\text{P}_2\text{O}_7$ or $\text{Na}_5\text{P}_3\text{O}_{10}$) are used. This offers some advantages.²³ At the same time, the water proton relaxation time T_1 also increases, thus leading to a loss of image contrast or to image inversion.²³ In addition, variation of stability of the metal–ligand complex can cause changes in the period of the concentration oscillations.²³ To prevent gas liberation (*via* bubbling), the experiments are often carried out in tightly closed containers.

When studying the behaviour of trigger waves in the excitable (non-oscillating) B–Z system, agar is added to the solution to form gels and to suppress undesired convective flows in the medium due to an increase in the medium viscosity. 2D NMR images of the spiral waves in pseudo-2D thin gel layers and the 2D cross-sections of spherical waves in a cylindrical ampoule acquired at different instants have been reported.²⁴ This allowed visualisation of wave propagation and collisional annihilation. The advantage of the NMR imaging technique is the possibility of obtaining 3D images of the wave front. In combination with the achievements of modern computer graphics this makes it possible to construct 3D images of complex waves (*e.g.*, a twisted scroll wave) and thus investigate the evolution of the organising filamentary singularities of the wave concentration structures.²⁵

A simple procedure for fast imaging of the wave front propagation has been proposed by Tzalmona *et al.*²⁶ taking cerium-catalysed oxidation of citric acid by potassium bromate as an example. The technique involves 1D slice selective NMR imaging with slice projection on an axis in the slice plane. One-dimensional NMR images are successively acquired at a constant time delay (Fig. 2). By stacking the 1D NMR images one can obtain a 2D image in the displacement–time coordinates, where the regions of highly intense signals form inclined bands, their slopes being a measure of the wave front propagation velocity. If a concentration wave propagates at a constant velocity, the bands look like slant lines. Menzinger *et al.*²⁷ studied chemical waves in the Belousov–Zhabotinsky reaction in a non-viscous solution containing no agar. They found that the ascending portion of the spherically expanding wave becomes unstable and drastically accelerates, being developed in a plume-like cloud. At the same time, the descending portion of the wave travels unperturbed and at a constant velocity. The reason for instability of the ascending wave is an isothermal decrease in the medium density in the region after the oxidation front, resulting in the appearance of convective flows. Simultaneously, subsidiary pacemakers appear in the instability region, emitting new waves.²⁷ The 1D projection

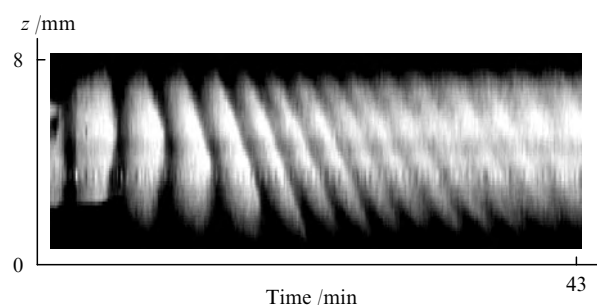


Figure 2. Concentration oscillations and concentration waves in the oxidation of citric acid.

Bright bands correspond to higher concentrations of Ce(III) and dark bands correspond to the oxidised state, Ce(IV). The reaction was conducted in water doped with starch (1%); the 1D projections of the reaction mixture on the axis of an ampoule 5 mm in diameter were obtained without slice selection.

technique was also employed to determine the activation energies for wave front propagation and wave emission by the pacemaker²⁸ and to obtain a dispersion curve that illustrates the interrelation between the wave propagation velocity and the pacemaker activity period.²⁹

Chemical waves in the B–Z system can also be used as an indicator of the fluid motion in the imaging of, *e.g.*, temperature-gradient driven convective flows. NMR imaging experiments using the 1D projection technique (see above) revealed wave-front distortions due to convection in a cylindrical sample which was heated and then allowed to gradually cool inside the probe of the NMR spectrometer.²⁸ An increase in the temperature gradient (Rayleigh number) due to the heating of the sample to higher temperatures led to the onset of the principal and then the lowest excited critical convection modes.

NMR imaging was also used for studying the self-oscillatory B–Z system in which not only trigger, but also phase waves are observed. The latter are not accompanied by mass transfer and represent a purely optical effect, which is due to the phase or frequency difference between the oscillations at different points of space. Kinematic waves (a kind of phase wave) originate from the temperature difference between different points of the sample. The 1D wave projection technique has been successfully employed in the investigations of the wave dynamics in the self-oscillatory B–Z system. Here, kinematic waves arose from frequency gradients in an anisotropically cooling sample.³⁰

An increase in the oscillation phase gradients is always accompanied by an increase in the concentration gradients in the sample. This gradually makes the role of diffusion increasingly important. As a result, conversion occurs of kinematic waves into diffusion-driven ones and the wave propagation velocity no longer decreases, thus reaching a limiting value corresponding to the velocity of chemical waves. A study of the interaction between trigger waves and kinematic waves showed that wave collision patterns can be incorrectly interpreted as a sudden acceleration of trigger waves.²⁶

Armstrong *et al.*³¹ reported an NMR imaging study of kinematic waves in the B–Z reaction catalysed by various metal ions. The technique requires that the effects of the oxidised and reduced states of the catalyst on the NMR parameters of water protons be different. In the case of cerium-catalysed oxidation of malonic acid the proton relaxation times of water in the presence of Ce(III) and Ce(IV) differ insignificantly, so only the 1D projections of the wave front were recorded. When ruthenium ($[\text{Ru}(\text{bipy})_3]^{2+}$, where bipy is bipyridyl) was used to catalyse the same reaction, the relaxation times of water varied over a somewhat wider range compared to the Ce-catalysed reaction and 2D NMR images of waves were also obtained. It should be noted that, in contrast to manganese and cerium, shorter relaxation times for the Ru-catalysed reaction were obtained for the oxidised state, Ru(III), rather than the reduced state, Ru(II). Therefore, the best contrast for the reaction with ruthenium should be expected for T_1 -weighted images. Attempts at NMR imaging a ferroin-catalysed B–Z reaction (ferroin is $[\text{Fe}(\text{phen})_3]^{2+}$, where phen is phenanthroline) failed despite considerably different effects of ferroin and ferriin ($[\text{Fe}(\text{phen})_3]^{3+}$) on the T_2 time of water. Armstrong *et al.*³¹ suggested that in this case the relaxation times are mainly affected by the Fe^{3+} ions that accumulate in the course of the reaction due to the decomposition of ferroin and ferriin; however, this does not correspond to actual wave dynamics of the medium.

5. Other reactions

Propagation of a single reaction front can also be observed in non-oscillating chemical systems, *e.g.*, in those characterised by rather large initial concentration gradients. The use of gels with high content of water allows one to suppress convection and, at the same time, permits experimental procedures typical of liquid-phase NMR studies to be employed for imaging using the proton signal of water. In particular, diffusion-controlled redox processes were studied using a hollow, thick-walled cylinder made of

polyacrylamide gel saturated with aqueous $\text{Fe}_2(\text{SO}_4)_3$ solution at pH 1.³² Filling the cylinder cavity with aqueous sodium bromate solution (pH 1) causes diffusion of the reagent into the cylinder walls and, as a consequence, oxidation of Fe^{2+} to Fe^{3+} . In the presence of Fe^{3+} ions the T_1 time of the water protons is shortened to a much greater extent compared to the Fe^{2+} ions. Because of this, T_1 -weighted NMR images obtained at different stages of the process exhibit a noticeable increase in the amplitude of the signal of water present in the cylinder walls as a result of propagation of the reaction front towards the outer surface of the cylinder.

In another series of experiments Fe^{3+} was reduced to Fe^{2+} with an aqueous ascorbic acid solution (pH 1), which led to a decrease in the signal amplitude. An identical cylinder made of polyacrylamide gel was used to obtain the 2D NMR image of the copper ion release process occurring upon variation of the pH value of the medium.³³ First, the material the cylinder was made of was doped with a chelate complex of copper with ethylenediaminetetraacetic acid. Then the cavity of the cylinder was filled with a sulfuric acid solution (pH 1.2). Proton diffusion into the bulk of the gel caused protonation of the ligand present inside the walls of the cylinder and shifted the complexation equilibrium towards the formation of free copper ions. In the presence of a chelate copper complex the T_1 time of water is shortened to a much lesser extent than in the presence of free Cu^{2+} ion due to poor contact of copper and the hydration shell. Therefore, the formation of free Cu^{2+} ions led to substantial enhancement of the NMR signal of water in the T_1 -weighted images. Analysis of a set of 1D profiles acquired during the propagation of the reaction front along the axis of the continuous cylinder showed that the displacement of the reaction front is proportional to the square root of the time, which is typical of a diffusion process.

Introduction of calcium ions into aqueous sodium alginate solution³⁴ causes cross-linking of the alginic acid molecules by calcium ions, resulting in the formation of a rigid gel. As a consequence, the T_2 time of the water molecules is shortened from 0.8 to 0.1 s. In the experiments sodium alginate and the solution of calcium ions were separated by a dialysis membrane. The process was studied with planar and cylindrical geometries at different concentrations of the reagents by acquiring the 1D and 2D NMR images. It was found that the reaction front moves in proportion to $t^{1/2}$ (t is time) and the diffusion coefficient of calcium ions depends on the concentration of calcium (due to different pore sizes and electrostatic interactions in the gel).

Gelation can be reversed by adding an aqueous solution of a sodium salt of ethylenediaminetetraacetic acid, since the acid favours removal of calcium owing to the formation of chelate complexes.³⁵ Depolymerisation-induced changes in the molecular mobility cause substantial variations of the spin–lattice relaxation times of the water molecules ($T_{1\text{sat}}$), measured at external saturation of the nuclear magnetic resonances of gel macromolecules, as a result of magnetisation transfer. This served as the basis for monitoring the movement of the sol/gel interface along the axis of a cylindrical sample during gel destruction. A combination of a 1D ‘null-point’ technique (here, the NMR signal of water molecules with prescribed time T_1 becomes zero due to incomplete magnetisation recovery after inversion) with selective saturation of the resonance signal from macromolecules was employed. The authors suggested that the process is controlled by diffusion transport of the acid towards the sol/gel interface. This technique allows one to selectively follow the movement of the region with any pre-selected gel concentration, since the $T_{1\text{sat}}$ time depends on the local concentration of gel. An increase in the initial gel concentration causes the movement of the sol/gel interface to slow down.³⁵

Studies of reactions in the solid phase require the use of solid-state NMR spectroscopy techniques. An anisotropic acid–base reaction of substituted benzoic acid with ammonia gas was investigated using a multipulse line-narrowing technique that allowed elimination of the dipolar coupling and chemical shift effects to second order.³⁶ The authors expected that

2D T_1 -weighted images of the molecular single crystal will correspond to very slow conversion of 4-bromobenzoic acid into ammonium 4-bromobenzoate on the (100) crystal face, where the carboxylic group is less accessible compared to other faces. However, the experiments revealed only weak anisotropy; this was rationalised by the poor quality of the crystal. In another experiment ammonium gas was blown over a thick layer of powdered toluic acid to give ammonium toluate. Using a series of 1D MRI projections acquired at different times, the authors showed that deeper layers of the acid sample begin to react later and at a lower rate than do the surface layers. Both experiments were carried out with the proton T_1 time governing the image contrast, since the T_1 time of the initial acid was much longer than the T_1 time of the reaction products.

A feature of some photoinduced radical reactions in solutions is the effect of chemically induced dynamic nuclear polarisation (CIDNP), or the nonequilibrium population of nuclear spin sublevels in the reaction products due to the spin dynamics in the short-lived radical pairs.^{37,38} As a result, the NMR signal of the reaction products can be substantially enhanced and even change its sign in the case of population inversion. Spatially resolved studies of this effect observed during the UV photolysis of *tert*-butyl methyl ketone in CCl_4 revealed spatially inhomogeneous variations of the signal amplitude in the sample due to inhomogeneous light absorption.³⁹ Intense irradiation of the sample initiated mixing of the solution. A possible reason is convection owing to heating of the sample.

Hydrogenation of unsaturated compounds with dihydrogen with nonequilibrium ratio of molecules with different total nuclear spin (ortho- and para-hydrogen) can cause dramatic enhancement of the NMR signal of the reaction product.^{40,41} Variation of the magnetic field can be used for polarisation transfer from the ^1H to the ^{13}C nuclei in the reaction product.⁴² In particular, this allowed an angiogram of a living rat to be generated in 0.9 s after introducing the reaction product in the caudal vein.⁴³ The experiments were carried out at the natural abundance level of the ^{13}C isotope (1.1%) and the NMR signal enhancement due to the polarisation of the ^{13}C nuclei was 10^4 .

Figure 3 presents the 2D images acquired during catalytic decomposition of hydrogen peroxide on a cylindrical catalyst granule ($\text{Pt}/\text{Al}_2\text{O}_3$) 3.6 mm in diameter. Figure 4 illustrates the capabilities of NMR imaging for studying the liquid phase distribution inside a catalyst granule during the evaporation of



Figure 3. A 2D NMR image of a cylindrical ampoule filled with a H_2O_2 solution. A catalyst granule ($\text{Pt}/\gamma\text{-Al}_2\text{O}_3$) is located at the centre of the ampoule.

Clearly seen are the gas bubbles formed on the ampoule walls and on the surface of the catalyst granule. A bright circle surrounding the catalyst granule corresponds to the domain with a strong NMR signal due to a decrease in the T_1 time in the near-surface region.

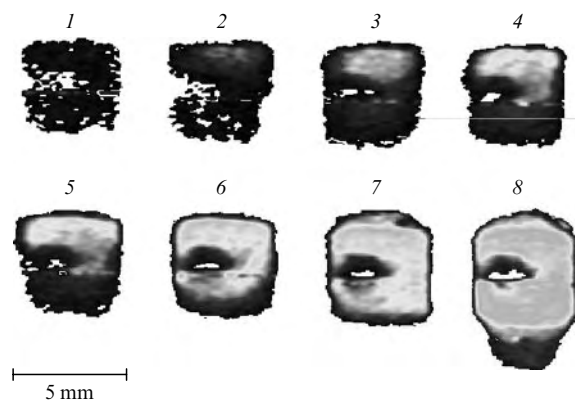


Figure 4. Liquid phase distribution inside a $\text{Pt}/\gamma\text{-Al}_2\text{O}_3$ granule during the evaporation of AMS accompanied by its vapour-phase hydrogenation.

The supply of liquid AMS increased from 0 to 0.71 mg s^{-1} . The temperature of the granule/ $^\circ\text{C}$: 109 (1, 2), 141 (3), 167 (4), 148 (5), 113 (6), 100 (7) and 64 (8). Brighter regions correspond to a higher content of liquid. The formation of an AMS droplet under the catalyst granule can be seen in the image (8).

α -methylstyrene (AMS) accompanied by its catalytic hydrogenation.[†]

III. Magnetic resonance thermometry

Variable-temperature NMR studies allow one to obtain a much greater body of information; however, this requires reliable methods for measuring the temperature of samples. In some experiments, this can be done using a thermocouple. However, this technique can introduce errors into the results of the NMR experiments. Pulsed field gradients induce eddy currents, thus increasing NMR signal distortion. In addition, variation of the geometry of the object under study in the presence of a thermocouple affects the temperature field distribution over the entire sample. Finally, experiments in nonzero magnetic fields can make the results of temperature measurements less reliable.

The NMR technique provides a means for using the molecules of the object under study as thermal sensors to measure the temperature inside the object. There is a set of reference samples for which the temperature dependencies of the chemical shift, linewidths or their splittings in the NMR spectra have been studied in detail. In particular, methanol and ethylene glycol serve as references in the case of ^1H NMR spectroscopy; these compounds are used in different temperature ranges.⁴⁴

A new era in the development of magnetic resonance thermometry is associated with the possibility of using the NMR imaging technique for constructing the spatial temperature distribution maps, which is of particular interest for biology and medicine. For instance, low-temperature hyperthermia involves heat treatment of tissues at elevated temperatures ($43\text{--}45^\circ\text{C}$) during tens of minutes either to kill malignant cells or to enhance their susceptibility to cytotoxic agents and/or irradiation. To induce necrosis of tissues due to protein denaturation after short-term heat treatment, even higher temperatures ($50\text{--}80^\circ\text{C}$) are used.⁴⁵ At 43°C , 100% necrosis occurs in several tens of minutes.^{45,46} On further increases in temperature the time taken to necrotise tissues nearly halves as the temperature increases by 1°C .

[†] See I V Koptug, A V Kulikov, A A Lysova, V A Kirillov, R Z Sagdeev, V N Parmon *Dokl. Akad. Nauk* **385** 205 (2002) [*Dokl. Phys. Chem. (Engl. Transl.)* **385** 158 (2002)]; I V Koptug, A V Kulikov, A A Lysova, V A Kirillov, V N Parmon, R Z Sagdeev *J. Am. Chem. Soc.* **124** 9684 (2002).

and reaches ~ 1 s at 57°C .⁴⁵ NMR imaging allows real-time assessment of temperature-induced variations in tissues in the course of thermal therapy procedures, which can be used for feedback creation in automated systems.⁴⁷ MRI also allows visualisation of changes in tissues after the completion of the therapeutical procedure. In addition, by using open-design devices one can also monitor the position of the applicator during the insertion in tissues.⁴⁸

NMR-Assisted temperature measurements are based on the fact that such parameters as the molecular diffusivity (D), nuclear magnetisation (signal amplitude), spin relaxation times and the resonance frequency of a nucleus (chemical shift) are sensitive to the local temperature. The characteristic temperature sensitivity of these parameters for tissues in living organisms and corresponding phantom objects in the physiological temperature range are of the order of $0.8\% - 2\% (\text{C}^\circ)^{-1}$ for T_1 , $2.4\% (\text{C}^\circ)^{-1}$ for D , -0.007 to -0.01 ppm $(\text{C}^\circ)^{-1}$ for the chemical shift of water molecules⁴⁹ and ~ 0.01 ppm $(\text{C}^\circ)^{-1}$ for both the ^{19}F nuclei in fluorinated hydrocarbons and ^2D nuclei (see Refs 50 and 51). The ^{13}C and ^{59}Co nuclei are also used.⁵¹ For Co(III) compounds the temperature coefficient of the chemical shift is $1.5 - 3$ ppm $(\text{C}^\circ)^{-1}$. Similarly to other types of experiments, the main problem of these studies is to select the temperature-induced contribution to overall variations of the parameters investigated. Therefore, methods based on variation of the NMR resonance frequency, which is less sensitive to side processes, are usually employed.

Many experiments have been carried out using the so-called proton resonance frequency (PRF) technique based on the resonance frequency variation when recording the ^1H NMR spectra of, e.g., water. Temperature-induced variations of the water proton resonance frequency are mainly due to variation of the shielding constant caused by the cleavage, stretch or bending of hydrogen bonds.⁵² There is a linear correlation between the chemical shift of water and the temperature at least up to 80°C . The advantage of the PRF technique is a constant value of the corresponding temperature coefficient for many samples, which was demonstrated in the studies of phantom objects and various types of tissues *in vivo*⁵² and *ex vivo*.⁴⁵ Low sensitivity can be compensated by mapping the phase of the magnetisation instead of acquiring the resonance frequency variations.⁵³⁻⁵⁶ To correct the phase of the signal (in particular, to include the magnetic field drift), the object under study is often surrounded by reference samples that are kept at room temperature.⁵⁷⁻⁵⁹ If a number of signals with comparable amplitudes is observed (in, e.g., water-fat systems), the chemical shift selective phase mapping allows one to avoid phase measurement errors for the total NMR signal and provides an internally referenced measurement tool (to this end, the signal of, e.g., fat can be used).⁶⁰ In some instances acquisition of a complete NMR spectrum is followed by numerical simulation to exactly determine the resonance frequencies.^{61,62}

In practice, the situation is complicated by the fact that the local magnetic field depends not only on the chemical shift, but also on the magnetic susceptibility of the sample, which in turn is a function of temperature. If temperature-induced variations of the volume magnetic susceptibility are large, variation of the local resonance frequency is not proportional to the local temperature and is determined by the temperature distribution over the entire sample.⁶³ In this case the heat source geometry and orientation in the magnetic field are of great importance.⁶⁴ In contrast to water, typical of fat is a relatively small temperature-induced variation of the resonance frequency, which is mainly due to local variations of the diamagnetic susceptibility rather than chemical shift.⁵³ On the one hand, this hampers temperature measurements in fatty tissues,⁵⁸ but, on the other hand, allows the fat tissue signal to be used as a reference,^{52,60,61} which can be of value in measuring the absolute temperature. However, it should be noted that magnetic susceptibility variations in fatty tissues can distort the local fields and introduce errors when measuring temperature in neighbouring muscle tissue.⁶³ For this reason one should also avoid the use

of paramagnetic substances (conventional water dopants for thermostating the object under study).

Other sources of errors in tissue temperature measurements can be:^{52,58,61,65} low signal-to-noise ratio, limited spectral resolution, inhomogeneity of the magnetic field, variation of the magnetic field due to eddy current magnetic field, field drift, variation of tissue perfusion and oxygen concentration in blood and temperature-induced variation of the magnetic susceptibility of tissues. Position shift, as well as a change in the size or geometry of the object under study (e.g., muscles) can introduce rather large errors into the results of temperature measurements.^{52,66-68} The drawbacks of the technique is low spatial and temperature resolution.⁵² Despite this fact the temperature map can be obtained using the proton phase shift imaging technique even on an open-configuration, low-field (0.2 T) scanner with a rather large field drift during the experiment.⁶⁹ The error of measurements can be less than 0.5°C for temperature variation by 10°C .⁵²

Stollberger *et al.*⁷⁰ reported separate measurements of the temperature coefficients of the diamagnetic susceptibility and chemical shift for water, gel, brain tissue and fat tissue. Both numerical simulation and test experiments showed that the contribution of temperature-dependent magnetic susceptibility to the variation of the NMR resonance frequency depends on the orientation of the laser applicator and on the distance from the applicator and can be large, especially for tissues with high fat content. In contrast to other authors, experiments with a human calf muscle revealed no effects due to variation of the diamagnetic susceptibility of fat.⁵⁷ At the same time, a complex response of living tissues to temperature variation was pointed out. The NMR signal of water in a living organism can be affected by both blood flow and magnetic susceptibility variations due to the change in the concentration of paramagnetic substances, e.g., the oxy/deoxy state ratio of hemoglobin and myoglobin in blood. As a result, the temperature dependencies of the NMR signal parameters have the shape of hysteresis curves.⁵⁷

De Poorter⁶³ evaluated the relative contributions of the temperature dependencies of the chemical shift and magnetic susceptibility to the temperature dependence of the proton resonance frequency in agarose gel and in porcine muscle tissue and fat tissue. In the experiments cylindrical gel samples were oriented both parallel and perpendicular to the magnetic field direction. The relative temperature-induced change in the magnetic susceptibility of fat tissue was shown to be close to the relative variation of the chemical shifts in muscle tissue and agarose gel. The temperature coefficients of the chemical shift in fat tissue and of the magnetic susceptibility in muscle tissue and gel appeared to be very small.

Temperature distribution studies during the heating of a rat hindleg⁵⁸ and cooling of a human leg⁶¹ ($5 - 37^\circ\text{C}$) using a water jacket have been reported. It was found that the temperature decreases to a greater extent in the regions with a thinner layer of fat tissue. The results obtained suggested that the cooling-heating cycle was accompanied by muscle deformation and/or muscle position shift.⁵⁸ Spatial temperature distributions were also monitored in the course of interstitial magnetic resonance-controlled laser-induced thermal therapy of head and neck tumours,⁷¹ human brain tumours⁵⁴ and during microwave-induced interstitial heating and thermal lesions in rabbit brain *in vivo*.⁵⁵ The methods employed were often tested on phantom objects (e.g., agarose gel⁵⁸); however, calibration of the water proton chemical shift for practical thermal surgery was carried out *in vivo* for ultrasound-heated rabbit tissues.⁷²

Fast MRI techniques allow mapping the temperature distribution in $1 - 2$ s.⁵⁶ Two-dimensional temperature maps for water-heated agarose gel were obtained in fractions of a second with an accuracy of 0.2°C .⁷³ The temperature distribution over the sample was calculated by converting the phase change relative to the initial NMR image acquired at the known temperature using a calibration curve.

NMR spectra exhibiting several signals with different chemical shifts allow internal-referenced (or self-referenced) temperature determination by measuring the chemical shift differences between two particular NMR lines.⁶² This approach was illustrated by the experiment with a double cylinder filled with ethylene glycol. The inner part of the cylinder was microwave heated. The local temperature in the sample was determined from the chemical shift difference between the OH and CH₂ groups of ethylene glycol molecules (the corresponding temperature dependencies are well known). A feature of an *in vitro* study of a porcine liver sample placed in a vessel filled with continuously heated water was the use of the effect of temperature on the chemical shift difference between the proton signals of lipids (polymethylene chain, $-\text{CH}_2-$) in water and in liver; the time for acquiring 2D temperature maps varied from 10 s to 3 min. The authors pointed out that, in contrast to other methods involving voxel-by-voxel comparison of two NMR images, their self-referenced method is less sensitive to translational motion of the sample in the course of the experiments.⁶²

Nott *et al.*⁵³ reported on mapping the temperature distributions induced in food by heating to 120 °C and even higher temperatures. To confirm that the changes in the signal phase were due to the variations of the temperature of the sample, additional experiments were carried out with a vessel containing pre-heated homogeneous gelated suspension of starch which was allowed to cool. The temperature distribution maps obtained revealed clearly seen radial temperature gradients in the vessel. In the experiment with less viscous agar gel the temperature distribution map was significantly distorted by stochastic convection effects. Food sauce was chosen as an example of an heterogeneous medium. The chemical shift was shown to be insensitive to structural inhomogeneities of the sample. The experiments provided data on both temperature distribution over the sample and structural inhomogeneity, which allows suggestions about interrelations between heat transfer processes and the structure of the product. The temperature dependencies of the spin relaxation times and diffusion coefficients have also been reported.⁵³

The possibility of acquiring separate NMR images of the volumes of water kept at different temperatures using the chemical shift difference between water protons was demonstrated taking two ampoules filled with water heated to 32 and 75 °C as an example.⁷⁴ The same study also reported separate NMR images of three coaxial cylinders containing an inorganic phosphate solution with different pH values (12, 7 and 3) obtained with the ³¹P NMR signal detection.

The chemical shifts of atomic nuclei in paramagnetic complexes are usually much more temperature sensitive compared to the chemical shifts of nuclei in diamagnetic compounds. In addition, the former substantially differ from the latter in magnitude, which allows one to avoid the overlap of lines in the NMR spectrum. For instance, the temperature sensitivity of the chemical shift of ¹H and ³¹P nuclei in a thulium complex with a macrocyclic cycloaza ligand is 0.89 ppm (°C)⁻¹ for the former and 2.18 ppm (°C)⁻¹ for the latter nucleus (two orders of magnitude higher than for water protons).⁷⁵ A method of simultaneous measurements of the temperature and the pH value of the medium using this paramagnetic thulium complex has been proposed.⁷⁶ This approach was practically implemented for the measurement of the temperature within the sample when thermostating the NMR probe or applying heteronuclear decoupling and was based on measuring the resonance frequency difference between two lines in the ¹H NMR spectrum of the water-soluble thulium complex.⁷⁷ In principle, the technique allows temperature variations of the order of 0.01 °C to be measured.

The advantage of a paramagnetic praseodymium complex is the large proton chemical shift (-24.1 ppm) relative to the conventional values.⁷⁸ The temperature sensitivity of the chemical shift, -0.131 ppm (°C)⁻¹, is independent of both the pH value of the medium ($5.6 \leq \text{pH} \leq 9.6$) and the concentration of the com-

plex. The possibility of using the complex was demonstrated in the *in vivo* experiments with rat liver. Yet another advantage of paramagnetic complexes is the short T_1 times of the magnetic nuclei. Aime *et al.*⁷⁹ developed a paramagnetic complex Yb-DOTMA [DOTMA is ($\alpha, \alpha', \alpha'', \alpha'''$)-tetramethyl-1,4,7,10-tetraazacyclodecane-1,4,7,10-tetraacetic acid] and studied its behaviour in human blood serum. They found that the chemical shift of the most intense line from four Me groups is -14.2 ppm, the temperature coefficient is 0.04 ppm (°C)⁻¹ and that the chemical shift difference between a prescribed pair of spectral lines is even more temperature sensitive [-0.42 ppm (°C)⁻¹].

Another method of temperature measurements is based on the temperature dependence of the spin relaxation time T_1 . For many types of tissues the T_1 time of water protons is a nearly linear function of the temperature in the range between 20 and 50 °C. However, the temperature coefficients of T_1 for different tissues are also different and therefore a preliminary calibration and knowledge of the chemical composition of tissues to be studied are required.⁶⁵ In addition, living organisms respond to temperature variations in a complex manner, so that the relation between T_1 and the temperature can be nonlinear.⁸⁰ Nevertheless, it was found that the temperature coefficient of the T_1 time is 13 ms (°C)⁻¹ ($T_1 \approx 1$ s) for sheep mammary glands and 3.2 ms (°C)⁻¹ ($T_1 \approx 360$ ms) for fatty tissues.⁸¹

A temperature distribution study using a fast T_1 mapping technique has been carried out with an agar-gel cylinder in which a radial temperature gradient was created.⁸² A calibration curve for converting the local T_1 values into temperature was obtained.

Signal amplitude in the T_1 -weighted image can also serve as a measure of temperature distribution over the sample. In this case one should take into account the fact that a decrease in the signal amplitude with an increase in temperature is a consequence of both the increase in T_1 and the decrease in the equilibrium magnetisation. To construct the temperature map, one should acquire the NMR image of the sample at ambient temperature and have a calibration curve, $T_1(T)$, for a particular type of tissue or use known data for this type of tissues. This method was used for construction of the temperature map in muscle tissue heated by placing the tissue in contact with a heated glass tube or by deposition of focussed ultrasound energy.⁸³ In the latter case the focal spot was inside the tissue, which was clearly seen in the NMR images acquired (region with very low signal intensity). All experiments were carried out at 20–45 °C. The difference between the MRI data and the temperature values measured using fibre-optic probes was at most 0.6 °C. The technique was also implemented in studies of the temperature distribution in gel or bovine muscle tissue *in vitro* or in rabbit muscle tissue *in vivo* during focussed ultrasound therapy treatment.^{84,85} The focal spot size and the thermal diffusivity were determined.⁸⁵ It was shown that temperature variation in the axial direction was asymmetric and that the near-field zone was heated to higher temperatures than the far-field zone. The near-field zone also cooled slower than the focal spot, which can lead to overheating upon repetition of ultrasound pulses.

Inversion–recovery T_1 measurements for a flowing fluid can be complicated since flow can cause additional changes in the signal amplitude.⁸⁶ It was proposed to create an inverted signal in a set of slices separated by slices with equilibrium nuclear magnetisation rather than in the entire sample. In this case the signal amplitude in the non-inverted regions in the immediate vicinity of the slice with inverted magnetisation can be used for normalising the signal amplitude. This approach is similar to the tagging technique employed in the studies of fluid flows;² single experiments additionally allow one to obtain information on the character of the flow. The method was implemented using a model comprising two tubes, a tube through which water was pumped ($T = 40.2$ °C at the inlet) and an external jacket through which a fluorinated cooling agent was pumped in a parallel direction ($T = 9.8$ °C). A 2D temperature distribution map was obtained. The accuracy of measurements was 15% of the temper-

ature difference between the inlet and outlet (which was equal to 15 °C).

The T_1 time of solid *cis*-polybutadiene at room temperature is 16 ms. This allows observation of the NMR signal of the polymer.⁸⁷ Based on the results of T_1 measurements, a temperature map was obtained for a *cis*-polybutadiene block through which cold (10 °C) and hot (70 °C) water was pumped using two tubes. The temperature coefficient of T_1 was $\sim 12 \text{ ms } (^\circ\text{C})^{-1}$ at the T_1 times ranging from 0.2 to 0.8 s. The maps obtained exhibited reasonable agreement with the results of calculations.

Local temperatures can also be determined from the molecular diffusion coefficients. Temperature variations upon heating of a polyacrylamide gel with an RF hyperthermia applicator were monitored using the 2D map of the diffusion coefficient of water molecules.⁸⁸ The local temperatures determined from the images averaged over a volume of 1 cm³ were found to be in good agreement with those recorded using implanted fibre-optic probes or a thermocouple (the difference was 0.2 °C). Temperature-related changes in the NMR signal intensity of agarose gel and rabbit brain tissue *in vivo* irradiated by a Nd:YAG laser were visualised by acquiring diffusion-weighted 2D images in 150 ms.⁸⁹ This method was also employed for *in vivo* temperature measurements of a human calf muscle.⁹⁰ The authors pointed out that the regional blood volume decreased by a factor of 3.5 on cooling and increased by a factor of 2.7 on heating as the temperature varied by several degrees.

A number of comparative studies of the above-mentioned temperature measuring techniques has been reported. Bertsch *et al.*⁶⁵ implemented and evaluated two methods based on the chemical shift and T_1 relaxation measurements taking external heating of samples in the range 22–50 °C using a water jacket and local (focal) laser heating in the range 22–35 °C as examples. MRI data were then compared with the results of fibre-optic temperature readings. The chemical shift method is usually more convenient than T_1 relaxation measurements for constructing more accurate 2D temperature distribution maps in shorter times. In agarose gel, the error was 0.6 °C; however, for more heterogeneous samples the error increased to 1–3 °C, especially in the presence of fat. In the latter case, the T_1 relaxation method gave better results. Cline *et al.*⁹¹ reported construction of temperature maps for heating of tissues *via* focussed deposition of ultrasound energy using simultaneous information on the chemical shift and T_1 variations (the error of measurements was 0.7 °C).

Comparison of the methods based on the chemical shift and water diffusion coefficient measurements revealed⁵⁹ higher accuracy of the former (the root-mean-square deviation was 0.1–0.15 °C) in the case of short-term measurements (measuring time less than 1 h) with inclusion of magnetic field drift correction (to this end, additional reference samples kept at a constant temperature in the course of the experiment were placed around the sample under study).

The sensitivity and other characteristics of the three above-mentioned methods have also been compared.^{49,53} Experiments were carried out with agarose gel in the temperature range 35–45 °C. It was shown that only two methods, namely, those based on the water proton chemical shift and T_1 relaxation measurements, permit construction of the temperature distribution map with an accuracy better than 1 °C at 15 s acquisition time, the former being more accurate than the latter.⁴⁹ Model calculations for the three methods have been reported.⁶⁷ The necessity of taking into account tissue perfusion variation and blood flow effects was pointed out.

Other parameters of the NMR signal can also be used for temperature measurements. For instance, the 1D temperature profile along the length of the NMR ampoule thermostatted by flowing air was constructed using variation of the ¹H NMR linewidth of dibromomethane dissolved in a nematic thermotropic liquid crystal as a 'thermometer'.⁹² It was shown that placing the NMR ampoule with the sample in a static bath

(perfluorinated oil of high heat capacity) causes no decrease in the longitudinal temperature gradient but makes it more uniform and, probably, eliminates transversal temperature gradients. The dipole and quadrupole splittings in the NMR spectra of molecules dissolved in nematic liquid crystals are also temperature sensitive.^{93,94} A 5% benzene solution in a nematic liquid crystal was used for temperature measurements in the range 290–330 K.⁹³ The frequency difference between the outermost spectral components varied from 7300 to 5300 Hz. The corresponding temperature coefficient increased from 52.5 Hz (K)^{−1} at 296 K to 111 Hz (K)^{−1} at 330 K. The linewidth can serve as a measure of the temperature field inhomogeneity within the sample.

The operating temperatures of cryosurgery can be as low as −180 °C. Obtaining information on the temperature distributions in frozen tissues using NMR spectroscopy seems to be highly improbable. Nevertheless, NMR imaging can be used for determining the cryoprobe position upon introduction into tissues as well as the position and displacement of the phase transition boundaries.⁹⁵ This permits assessment of the temperature distribution based on solution of the equations derived from inclusion of thermal conductivity, metabolism and blood flow effects.

MRI also allows imaging of frozen tissues during and after defrosting.⁹⁶

In conclusion, NMR spectroscopy of various nuclei is used in measuring low and ultralow temperatures.^{97,98}

IV. Magnetic resonance current density imaging

NMR imaging can be used for visualisation of static and radio-frequency magnetic fields produced within the sample by external sources.¹ In contrast to this, current density imaging (CDI) technique allows visualisation of local magnetic fields created within a sample by an electric current flowing through the sample. This permits calculations of the spatial current density distribution over the sample. It should be emphasised that, similarly to other experiments considered in this review, the CDI method is based on acquisition of NMR signals from certain types of atomic nuclei. Therefore, the electric current density can be determined only in those regions of the sample which produce observable NMR signals.

If a direct current flows through a sample, the phase of the precessing transverse magnetisation varies in proportion to the projection of the current-induced local magnetic field on the direction of magnet's field. Experiments are carried out using direct current pulses synchronised with the NMR pulse sequences.^{99,100} Generally, measurements of the three mutually perpendicular components of the local magnetic field require repetition of the experiments at three different orientations of the sample. However, usually it is sufficient to construct two-dimensional cross-sections of the spatial current density distribution maps in the plane perpendicular to the direction of the electric current flowing through the sample. To date, the sensitivity of corresponding experimental techniques, optimum current pulse duration and amplitudes^{99,100} and possible artifacts^{100,101} have been studied. Model experiments^{99,100,102} with a cylinder filled with aqueous NaCl solution confirmed theoretical conclusions. More rigorous tests of experimental methods involved measurements of the three spatial components of the electric current density around a spherical volume of the solution placed at the centre of the cylinder and encapsulated in an insulating sphere.¹⁰¹ The results obtained were in good agreement with the MRI data and current density calculations. The measured magnetic field amplitudes obeyed Maxwell's equations. The distribution of direct current flowing through plant stem fragments (*Pelargonium zonale*, *Rosa arvensis*) pre-soaked in a 10% saline solution in order to enhance the conductivity has been studied.⁹⁹

Electric current through a fragment of a hen thighbone immersed in physiological saline containing Gd–DTPA (DTPA is diethylenetriaminepentaacetic acid) has been studied in order to study osteoporosis and to evaluate the feasibility of electrical

stimulation of bone tissue growth to recover damaged regions in the case of bone fracture.¹⁰³ Changes in the current density upon artificial demineralisation or mechanical damage were visualised. The magnitude and spatial distribution of the current density are of great importance for electrotherapy and electrochemotherapy of tumours. Mice tumours and the effects of electrode geometry on the electric current distribution within the tumours have been studied.¹⁰⁴ Joy *et al.*¹⁰² detected a change in the signal phase in the NMR image of the cross-section of a human forearm (one of the authors of the study¹⁰² volunteered) in the experiments with application of a 2 mA electric current (pulse duration was 40 ms) flowing from the elbow towards the wrist.

Yet another possible application of the CDI technique is the investigation of chemical reactions and other physicochemical processes which are accompanied by changes in the electrical conductivity due to changes in the local concentration of ions (e.g., dissolution of a NaCl crystal in agar gel¹⁰⁵). The current density maps obtained revealed an increase in the concentration of mobile ions in gel followed by diffusion-induced redistribution of the ions during the dissolution of the crystal. The NMR images allowed changes in the size of the crystal to be monitored, which is NMR silent in contrast to the surrounding gel and looks at the region with very high noise level. The current density imaging technique was also employed to study the formation and subsequent dissolution of calcium carbonate.¹⁰⁵ Diffusion of carbon dioxide through a membrane into the bulk of agar gel doped with a saturated calcium hydroxide solution resulted in insoluble calcium carbonate. As a result, the conductivity of the sample reduced due to a decrease in the concentration of calcium ions and hydroxide ions. The dynamics of gas diffusion into the gel bulk was monitored by inhomogeneity of the conductivity within the sample. Further treatment of the gel with gaseous hydrogen chloride, which reacted with calcium carbonate to give soluble calcium chloride, led to recovery of gel conductivity.

Alternating currents flowing through samples at the Larmor frequency are studied by the RF-CDI method.^{106, 107} The RF field component with circular polarisation in the plane perpendicular to the external magnetic field affects the magnetisation analogously to the RF field of the spectrometer. The corresponding pulse sequence includes the alternating current pulse coherent to other RF pulses. Usually, the proton decoupling channel is used in the experiments with ¹H nuclei. Under particular conditions (e.g., in the experiments with cylindrical geometry) all the necessary components of the current-induced RF field can be determined at a single orientation of the sample. Further data processing allows mapping not only of the alternating current density, but also of the current phase which depends, in particular, on the relative contributions of the conduction and displacement currents. An RF-CDI study of a plastic cylinder filled with CuSO₄-doped aqueous NaCl solution has been reported.¹⁰⁶ Unambiguous determination of the matrix describing the rotation of the magnetisation vector during the current pulse requires a series of experiments at different initial orientations of the magnetisation vector (this extends the measuring time).

Similar to the above-mentioned method of mapping direct current density distribution is the rotating frame RF-CDI approach proposed to study alternating current density distributions.¹⁰⁸ In this case the current pulse is applied simultaneously with the RF pulse created by the transmitter coil. If the coil field amplitude is sufficiently large, only the projection of the current-induced field on the direction of the RF field of the spectrometer contributes largely to the nutation of the magnetisation vector. Scott *et al.*¹⁰⁸ reported the analysis of the problems concerning the finite amplitude and inhomogeneity of the RF field of the spectrometer as well as artifacts and of the sensitivity analysis. Trials have been performed using a three-compartment cylindrical model object containing an aqueous NaCl solution doped with CuSO₄ (mainly the conduction current was detected), a CuSO₄ solution (detection of the displacement current) and a mineral oil (no current was detected). In addition, the spatial distribution of

the current density and phase in the cross-section of a rat body *ex vivo* was obtained and the feasibility of the imaging procedure with tissue-dependent contrast (due to the electrical properties of biological tissues) was demonstrated. The experiments were carried out at 85.6 MHz.^{106, 108} It was pointed out that the technique can also be useful for the determination of the absorbed dose rate in the case of RF pyrotherapy and NMR imaging. The RF-CDI method was also employed in studies of the dynamics of changes in the brain conductivity of a living rat upon a decrease in the membrane potential due to the introduction of kainate into a lateral ventricle of the brain.¹⁰⁹ An increase in the alternating current density at a frequency of 100 MHz was mainly observed in the hippocampal area. Kainate affects the central nervous system inducing epilepsy; therefore the results of these experiments demonstrate the feasibility of the technique for studies of epileptic attacks and the action of antiepileptic pharmaceuticals.

Both CDI and RF-CDI investigations were mostly carried out at current densities ranging from 25 to 2500 A m⁻², however, theoretical estimates¹⁰⁰ suggest the possibility of measuring current densities of the order of 0.1 A m⁻².

Electric current can also be induced by the piezoeffect intrinsic in various animal and plant tissues and by neuronal firing. Taking a model sample (isolated copper conductor immersed in an aqueous NaCl solution doped with copper sulfate) as an example, the feasibility of detecting phase changes of the proton NMR signal images was demonstrated.¹¹⁰ The phase change detected corresponded to a change in the magnetic field by a value of 1.7 nT, which is equivalent to simultaneous firing of nearly a million neurons.

Finally, mention should be made that the magnetic field of electric current can be measured not only in the laboratory frame, but also in a moving frame of reference if the NMR signal is detected using the nuclei of the ions creating the electric current through the sample.¹¹¹

V. NMR imaging of gases

1. General remarks

The sensitivity and resolution of the MRI techniques employed in studies of gases is usually much lower as compared to fluids, since the gas density is three orders of magnitude lower than the density of water under normal conditions. In addition, for many gases efficient spin-rotational interactions cause the relaxation time T_2 ($T_2 \approx T_1$) to fall in the millisecond range¹¹² and be shorter than the minimum time needed to create the echo signal, which leads to a considerable loss of signal. Finally, the diffusion coefficients of gases at atmospheric pressure are 4–5 orders of magnitude higher than the self-diffusion coefficient of water. A decrease in the NMR signal amplitude due to stochastic molecular motion in inhomogeneous magnetic fields is well known and serves as the basis for a widely used method of measuring diffusion coefficients using NMR.² Since the imaging procedure requires the use of magnetic field gradients, fast gas diffusion causes further reduction of the signal-to-noise ratio. In addition, gas diffusion imposes limitations on the achievable spatial resolution, which cannot be better than the characteristic distance of the diffusion displacements of molecules over the time taken for spatial localisation of spins. High diffusion coefficients of gases can be the reason for substantial distortion of NMR images due to the edge enhancement effect.²

Fortunately, there are some ways to partially overcome these difficulties. Short relaxation times T_1 of many gases (SF₆, CF₄, C₂F₆, CH₄) allow multiple accumulation of the NMR signal over a relatively short time to improve the signal-to-noise ratio.^{112–114} In addition, the spin relaxation times of these gases are virtually insensitive to the presence of dioxygen and solid surfaces.¹¹³ Moreover, sometimes the relaxation times of gas molecules in porous media can increase due to frequent collisions of the gas molecules with the walls and/or due to the surface adsorption.^{115, 116} By recording the free induction decay (FID) or

implementing various versions of the single-point imaging technique (SPI, SPRITE) it is possible to compensate the loss of signal due to short relaxation times T_2 and fast diffusion¹¹² or flow effects.¹¹⁷

The spin relaxation times of relatively large gas molecules can approach those typical of many liquids. For instance, the relaxation times of butane are $T_1 = 1.27$ s and $T_2 = 0.75$ s at 1 atm and room temperature. Long relaxation times T_2 allow signal acquisition over a long period of time including multiple refocussing of the echo signal to improve the sensitivity or implement rapid imaging techniques. In addition, large molecules have smaller diffusion coefficients (for propane, $D = 6.6 \times 10^{-2}$ cm² s⁻¹ at 22 °C).

Experiments with molecules containing a large number of magnetic nuclei (*e.g.*, SF₆, C₄H₁₀) also permit improvement of the sensitivity of NMR imaging. In this case possible differences between the chemical shifts of nuclei are insignificant, since the chemical shift difference between inequivalent groups of atomic nuclei is often not resolved due to substantial line broadening. High adsorption of gases by porous materials also leads to substantial enhancement of the signal (Fig. 5); therefore, NMR imaging of adsorbed gases can be employed for measuring the local adsorption isotherms. By increasing the gas pressure one can increase the spin concentration and spin relaxation times and reduce the diffusion effects. However, this faces some problems, *e.g.*, one should use thick-walled ampoules or specially designed probes, an increase in the gas pressure can damage brittle samples (this also causes an increase in not only the relaxation time T_2 , but also T_1 , which requires the duration of the experiment to be extended due to the necessity of lengthening the relaxation delay between the pulse sequence repetitions).

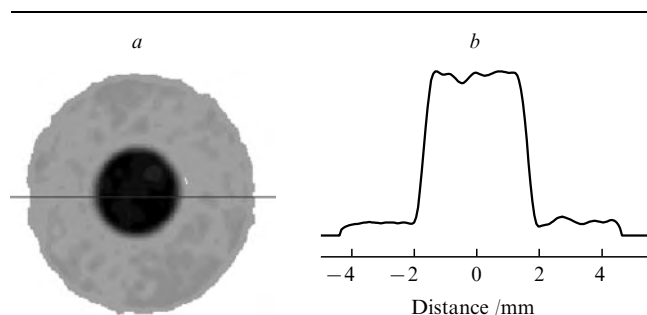


Figure 5. A 2D NMR image of the cross-section of a butane-filled cylindrical ampoule 10 mm in diameter with an alumina granule inside (a) and a 1D section of the NMR image (b); due to adsorption of butane the amplitude of the NMR signal from the alumina granule is an order of magnitude higher than the signal amplitude from the surrounding butane gas.

Another method of improving the sensitivity of NMR, which has recently gained wide acceptance, is the use of hyperpolarised gases¹¹⁸ for which the population difference between the spin sublevels much exceeds the equilibrium population in the magnetic field of a spectrometer. This is achieved using non-radioactive isotopes ¹²⁹Xe and ³He (for both the nuclear spin is 1/2). There are two approaches for creating the nonequilibrium population of nuclear spin sublevels. One involves optical pumping of the D1-transition of the optical absorption of rubidium vapours at a wavelength of 794.7 nm (the use of cesium can be even more efficient). Irradiation with circularly polarised light creates a nonequilibrium population of one of the two electron spin sublevels in the magnetic field and then the rubidium electron spin polarisation is collision transferred to the nuclear spins of noble gases. This technique allows one to achieve a 30% of polarisation of gas (in this case the signal of the gas at a pressure of 1 atm is an order of magnitude more intense than the ¹H signal of a water sample of the same volume). Often, mixtures of xenon

and other gases (N₂, ⁴He) are used at the natural abundance level of the ¹²⁹Xe isotope (26.44%) or using isotope enrichment. The natural abundance of the ³He isotope is very low (1.3×10^{-4} %); therefore, experiments are carried out only with isotopically enriched samples.

The other method for polarising the nuclear spins of ³He involves optical excitation (at a wavelength of 1083 nm) of metastable helium states created in the gas discharge, followed by collisional transfer of the nuclear polarisation to the ground state. Pumping occurs at a gas pressure of about 10^{-3} atm and then the pressure is increased to the operating values.¹¹⁹ Yet another method of NMR signal enhancement by a factor of 100 involves storage of helium at 2–4.2 K in a strong magnetic field (several T) followed by transfer in the magnetic field of the spectrometer and heating to room temperature.¹²⁰

Unlike many other gases, spin-rotational relaxation of monoatomic noble gas molecules is often inefficient due to spherical symmetry of the electron cloud; therefore, the spin relaxation times of these isotopes are rather long.^{121, 122} NMR studies of non-polarised noble gases are often carried out using their mixtures with oxygen to substantially reduce the relaxation time T_1 .^{123, 124} On the contrary, in the experiments with hyperpolarised gases long relaxation times T_1 allow one to appreciably extend the lifetime of the nuclear polarisation, which permits polarised xenon to be obtained in the solid, liquid¹²⁵ and supercritical¹²⁶ states and its transportation over long distances. Phase transitions cause no considerable loss of the spin polarisation while depolarisation of liquid xenon is insignificant even in the weak geomagnetic field.¹²⁵ Long relaxation times T_2 allow multiple refocussing of the magnetisation and acquisition of a large number of echo signals during each repetition of the pulse sequence.

Application of RF pulses causes irreversible loss of spin polarisation.^{127, 128} Therefore, experiments are designed in such a way that the loss of polarisation occurs portionwise due to the use of low-flip pulses. In some experiments the flip angle is gradually increased after each pulse as the longitudinal magnetisation decreases.¹²⁹ Fast gas diffusion can partially compensate the loss of magnetisation owing to the polarised gas present outside the slice under study.¹³⁰ A number of experimental setups has been designed to permit 'on-the-fly' polarisation of the ¹²⁹Xe nuclei up to 3% and thus to provide continuous circulation of the hyperpolarised gas through the sample and fast recovery of the magnetisation destroyed by the RF pulses.^{117, 131–133}

The nuclear magnetisation of hyperpolarised nuclear spins is independent of the applied magnetic field, B_0 . In this case the signal-to-noise ratio is proportional to B_0 instead of B_0^2 under the equilibrium polarisation conditions (see Ref. 134). Therefore, experiments with hyperpolarised gases are particularly efficient when operating in weak magnetic fields^{135, 136} that are used in, *e.g.*, biomedical studies. Lower magnetic fields cause substantially lower field gradients due to the difference between the volume magnetic susceptibility of materials and, hence, considerable reduction of NMR image distortion and the signal decay rate ($1/T_2^*$). In addition, one can use lower field gradient amplitudes, simpler and cheaper MRI scanners and operate at lower resonance frequencies. This causes an increase in the thickness of the skin layer for conducting materials and makes it possible to study, *e.g.*, gases in metallic containers, which cannot be done in strong-field experiments.

High spin magnetisation of hyperpolarised gases was shown¹³⁴ to induce radiation damping effects^{137–140} (the so-called RF maser effect¹⁴¹). In particular, placing a helium-filled cell (2.5 atm, 15% polarisation) into an RF coil in a homogeneous magnetic field caused fast spontaneous loss of polarisation despite the low Q -factor ($Q = 10$) and low filling factor (2%) of the RF coil.¹³⁵ Similar effects can introduce errors into the experimental results. After acquiring the NMR signal the magnetic field gradient pulses destroy the transverse magnetisation, thus weakening the radiation damping effects.¹³⁴

2. Gases with equilibrium nuclear polarisation

Despite the above-mentioned difficulties accompanying NMR imaging of gases, interesting results have been obtained in a number of studies using gases with equilibrium nuclear polarisation at both elevated and normal pressure. Rinck *et al.*¹⁴² seem to report a pioneering study concerning NMR imaging with gas signal acquisition. They studied dog lungs using a $\text{CF}_4 - \text{O}_2$ [80:20 (vol.%)] mixture and ^{19}F NMR signal acquisition in a weak magnetic field (938 G). The frontal, sagittal and transversal NMR images of the lung volume revealed poor ventilation of the upper part of the left lung induced by pneumonia. Considerable promise of the application of physiologically inert perfluorinated gases in real-time studies of perfusion and lung ventilation in stronger magnetic fields was pointed out.¹⁴²

A $\text{C}_2\text{F}_6 - \text{O}_2$ (80:20) mixture was used for forced ventilation of rat lungs. Lungs were imaged with a spatial resolution of 700 μm at 4.3 h acquisition time.¹¹⁴ The fluorine relaxation times at a rat body temperature of 39 °C were $T_1 = 5.9$ and $T_2 = 5.3$ ms. Two-dimensional NMR images of rat lungs were also obtained with a spatial resolution of 4.4 mm by acquiring a total of 64 successive echo signals of thermally polarised ^3He in 8 min.¹⁴³

Varying the concentration of oxygen in gas mixtures allows one to reveal regions of lungs with low alveolar ventilation-to-blood perfusion ratio.¹¹³ These regions are characterised by an increased relative concentration of the blood insoluble gas (a two- or threefold increase if gas mixtures with high concentration of oxygen are used). NMR imaging experiments with a $\text{SF}_6 - \text{O}_2$ mixture with different component ratios demonstrated a marked difference between the images of a normal rat lung and the lung partially blocked by inserting a glass bead with a lumen into the left bronchus.¹¹³

The SPRITE technique was employed to acquire a 1D NMR image of a methane-filled cylindrical glass ampoule divided by Teflon disks into cylindrical layers 2 and 3 mm thick and a 3D image of a fragment of the *Diploria labyrinthiformis* coral placed in a rubber balloon filled with SF_6 at a pressure that was somewhat higher than atmospheric pressure.¹¹² In the latter case the relaxation times ($T_1 = 1.8$ and $T_2^* = 0.6$ ms) were shorter than for pure SF_6 ($T_1 = 2$ and $T_2^* = 1$ ms at 1 atm), which was attributed to the interaction of gas with the developed surface of the porous sample.

The opposite trend was observed in studies of CF_4 and C_2F_6 in the pores of a layered composite ceramic material similar to mullite in chemical composition.¹¹⁵ The relaxation times T_1 of both gases in the pore space of the sample at gas pressures of 0.5 to 5 atm exceeded those of the bulk phase gases by more than an order of magnitude and became much less pressure dependent. The relaxation times T_2 exhibited similar changes. The decrease in the relaxation rate can be rationalised by the adsorption of gases and by reduction of the rotational correlation time of the molecules at small pore sizes, where the frequency of collisions with the ampoule walls becomes comparable with the frequency of intermolecular collisions. The 2D NMR images demonstrated the layered structure of the sample, delamination regions and inner voids. Considerable changes in the spin relaxation times, spin density and effective diffusion coefficient of the gas in the pore space ($D = 6 \times 10^{-3} \text{ cm}^2 \text{ s}^{-1}$ for the bulk phase C_2F_6 gas at 5 atm and 295 K and $D = 10^{-4} \text{ cm}^2 \text{ s}^{-1}$ for gas occluded in pores of the sample) allows the use of these parameters as the basis of the image contrast related to the characteristic dimensions of the morphology and to the local values of the specific surface of the pore space. In particular, an increase in the amplitude of the field gradients used for image acquisition causes suppression of the signal of the gas outside of the sample and allows selective visualisation of gas within the pore space characterised by relatively slow diffusion.¹¹⁵ The surface adsorption of C_2F_6 and C_4F_8 was also observed in studies of partially sintered, tetragonal Y-stabilised zirconia powders.¹¹⁶ The sample porosities were determined based on the results of relaxation time measurements.

Intercalation of AsF_5 into highly oriented pyrolytic graphite was studied using fluorine-detected NMR imaging.¹⁴⁴ The concentration of AsF_5 uniformly increased with time throughout the sample. After equilibration, the diffusion coefficients of the fluorine atoms involved in the exchange processes were measured.

Studies of the structure of mesoporous silica-based material (M41S) showed that the pores in the sample with strongly disordered structure are almost inaccessible to xenon, whereas the samples with more ordered structure exhibited the presence of physisorbed xenon.¹⁴⁵ The experiments revealed fast exchange of xenon in the interparticle space with physisorbed xenon.

Variation of the chemical shift of ^{129}Xe over a wide range (300 ppm depending on the environment) in combination with various selective NMR imaging techniques¹ permits chemical shift selective MRI investigations using the ^{129}Xe atoms in a particular environment. For instance, Gregory *et al.*¹²³ studied silica aerogel samples sealed in an ampoule filled with xenon (30 atm). The NMR images acquired using the lines at $\delta = 46$ and 52 corresponded to ^{129}Xe in aerogel, while the images acquired using the line at $\delta = 17$ allowed visualisation of the volume of the ampoule around aerogel.¹²³ In addition, it was found that optically transparent and translucent samples correspond to different chemical shifts of the ^{129}Xe lines, thus indicating considerable differences in the pore structure of these samples. Shorter relaxation time T_2 points to smaller pore size in the translucent samples characterised by a lower concentration of ^{129}Xe . Two-dimensional NMR images of the periphery of aerogel revealed regions containing almost no xenon due to mechanical breakdown of pores.¹²³ The sensitivity of the chemical shift of adsorbed ^{129}Xe to the presence and concentration of co-adsorbates was used in diffusion studies of the adsorbed water in NiNaY zeolite at 100 °C.¹⁴⁶

The ^{131}Xe quadrupole nucleus with a spin of 3/2 can be more sensitive to the character and state of the surface of a material, despite a smaller gyromagnetic ratio and a lower natural isotope abundance compared to the ^{129}Xe nucleus. A study of liquid xenon in mesoporous aluminosilicate aerogels at 285 K (this temperature is close to the critical temperature, 289 K) showed that the chemical shift and especially the spin relaxation times of ^{131}Xe depend on the density of the aerogel.¹⁴⁷ In addition, ^{131}Xe in the regions outside of aerogel is characterised by a different chemical shift value and longer relaxation time T_1 , which allows selective suppression of the NMR signal from the environment. It was also shown¹⁴⁷ that the relaxation time T_1 of the ^{131}Xe isotope in the gel changes upon removal of the adsorbed water, whereas the relaxation times of ^{129}Xe remain unchanged. The results obtained demonstrated considerable promise of the use of quadrupole relaxation of the ^{131}Xe nuclei as a sensor in studies of the state of various surfaces and of the presence of non-paramagnetic substances on the internal surface of the pores.¹⁴⁷

3. Hyperpolarised gases

The potential of NMR imaging of hyperpolarised gases has been demonstrated using a number of phantom objects. For instance, NMR images of $^3\text{He}^*$ (3 atm) in a glass cell¹³⁴ and of $^{129}\text{Xe}^*$ in capillary tubes^{130, 131} or in nested glass tubes (with a spatial resolution of $\sim 0.1 \text{ mm}$)¹³⁰ have been reported. Hyperpolarised gas flow was also imaged.¹³¹ NMR images of a cylindrical aerogel sample revealed the presence of regions with characteristic millimetre-scale dimensions, which are hardly accessible to xenon.¹³⁰

Using chemical shift selective MRI of a sample of NaY zeolite powder in a porous glass tube, separate NMR images of xenon gas, xenon in NaY zeolite and xenon in porous glass were obtained.¹¹⁷ Separate NMR images of xenon in NaY and CaA zeolite granules were also acquired based on the difference in pore size and in the nature of the cation. All the experiments were carried out at a total gas mixture pressure of ~ 1 atm using a continuous flow of hyperpolarised xenon for continuous renewal of the spin polarisation within the sample and demonstrated the possibility of real-time investigations of the adsorption of xenon.¹¹⁷

Transport of xenon towards the inside of SiO₂ aerogels or spherical zeolite 13X granules was studied by acquiring separate NMR images of bulk phase xenon ($\delta = 130$) and xenon occluded in pores ($\delta = 25$).¹³³ When a continuous flow of the gas is used, the reduction of xenon polarisation by the RF pulses can be utilised to selectively observe the signal of the fresh, inflowing portion of gas. Therefore, by varying the repetition time of the pulse sequence one can obtain NMR images corresponding to different penetration depths of xenon in the porous sample. Experiments with aerogel at long pulse repetition times revealed a homogeneous distribution of hyperpolarised xenon over the sample. For zeolite, fast spin relaxation of xenon occluded in pores allowed acquisition of the Xe NMR signal only from a narrow near-surface region of the granules. The signal amplitude rapidly decayed towards the granule centres. Both samples exhibited obstructed penetration of xenon into the granules in the areas of close interparticle contact and near the walls of the sample container.¹³³

Long spin relaxation times of xenon and helium are convenient for diffusion studies² and provide the possibility of studying molecular displacements at times as long as several tens of seconds.¹⁴⁸ Diffusion coefficient measurements have been reported for ³He* in a glass cell¹²¹ ($D = 1.8 \text{ cm}^2 \text{ s}^{-1}$ at 1 atm) and in a glass cylinder,¹⁴⁹ as well as for ¹²⁹Xe* in a glass sphere¹²⁹ ($D = 0.057 \text{ cm}^2 \text{ s}^{-1}$ at 1.04 atm). Investigations of transport of hyperpolarised xenon towards the inside of a porous glass sample permitted the determination of the diffusion coefficient of adsorbed xenon ($D = 2.2 \times 10^{-8} \text{ cm}^2 \text{ s}^{-1}$ at 293 K) and the activation energy for diffusion ($4\text{--}5 \text{ kJ mol}^{-1}$).¹²⁷ A continuous-flow system was used in studies of ¹²⁹Xe* diffusion in narrow channels of nanoporous crystallites.¹⁴⁸ The temporal dependence of the NMR signal corresponded to a 'single-file' diffusion.

Using the cross-polarisation (CP) or spin polarisation induced nuclear Overhauser effect (SPINOE) techniques, the polarisation of xenon can be transferred to adjacent nuclei including the nuclei of the atoms of a solid surface.^{150–154} In particular, CP studies of the transfer of xenon polarisation to protons of polymer films¹⁵⁵ or to the surface of bulk polymer samples¹⁵⁶ have been reported. With a continuous flow system Seydoux and Pines¹⁵¹ studied the polarisation transfer from the ¹²⁹Xe* nuclei to the surface protons of aerosil. The CP technique is more efficient on less mobile atomic groups, whereas SPINOE works better with more mobile ones. The CP ¹H NMR spectrum exhibited a broad polarised line, while a much narrower signal was observed in the SPINOE experiment. By using the CP technique the proton polarisation thus obtained can be transferred to the ²⁹Si nuclei. In addition, direct SPINOE-induced polarisation transfer from the xenon nuclei to the ²⁹Si nuclei causes enhancement of the ²⁹Si NMR signal from the surface atoms by a factor of 20 to 30.

Navon *et al.*¹⁵⁰ also reported the nuclear polarisation transfer of ¹²⁹Xe* dissolved in benzene to the solvent protons. Due to the low efficiency of the cross-relaxation mechanism the maximum enhancement factor of the ¹H signal varied from 10% (for C₆H₆) to 50%–200% for a C₆D₆–C₆D₅H (3 : 1) mixture. The dynamics of changes in the 2D images of the ¹²⁹Xe* signal in the ampoule suggested that initially the dissolved xenon is accumulated in the bottom region of the ampoule rather than at the open upper end contacting the bulk gas phase. This is due to an increase in the fluid density upon the dissolution of xenon. The NMR images obtained using the signal from the solvent protons were in good agreement with those obtained by acquiring the ¹²⁹Xe signal. This demonstrates the possibility of indirectly mapping the spatial distribution of xenon and studying the properties of the medium through which xenon penetrates.

Most publications have been concerned with applications of hyperpolarised gases in biomedical studies and, first of all, in studies of pathologies of respiratory organs. Experiments on animal and human lungs are usually carried out with ³He* for which one can obtain a higher nuclear spin polarisation.¹²² In

addition, the polarisation can last over a long period of time due to very long relaxation times T_1 ($\sim 100 \text{ h}$ under normal conditions).¹⁵⁷

Hyperpolarised ³He was used for imaging rat lungs¹³⁴ and guinea pig lungs¹⁵⁷ *ex vivo*. In the latter case helium also penetrated into the myocardium (because of the use of a large volume of gas). Experiments with living guinea pigs^{158–160} showed that the chemical shift of ³He in their lungs is sensitive to the volume magnetic susceptibility of the surrounding tissues.¹⁶¹ This can be employed in studies of the microstructure of lungs and of various lung pathologies.

Helium was used in studies of rat lungs *in vivo*,¹⁶² human lung parenchyma,^{119, 160, 163–166} upper respiratory tract¹⁶⁴ and paranasal sinuses.¹⁶⁷ Experiments were carried out on healthy volunteers and patients with various lung diseases diagnosed using conventional methods.^{168, 169} The different abilities of helium and air to penetrate into partially blocked regions of internal organs have been pointed out.

The possibility of functional imaging of lungs by acquiring a set of 2D images of ³He* in different stages of the respiratory cycle with a temporal resolution of 50 ms has been demonstrated taking guinea pigs as examples.¹⁷⁰ Using fast imaging techniques (acquisition times 40–120 ms) allows real-time studies of the ventilation dynamics of human lungs during one respiratory cycle.¹³⁶

To optimise the NMR parameters, the diffusion coefficients and the T_2^* relaxation times of ³He* and ¹²⁹Xe* in lungs of a living guinea pig were measured.¹⁷¹ The relaxation time T_2^* of ³He* in human lungs was also determined.¹⁷² It was found that the diffusion coefficients of these gases in lungs are 3–10 times lower than in the trachea due to geometric restrictions on the molecular diffusion displacements and to different amounts of residual air.¹⁷¹ The T_2^* relaxation time in lungs is also shorter due to rather large local inhomogeneities of the magnetic field and the presence of the residual air.¹⁷²

Acceleration of the relaxation of ³He* in the presence of oxygen can be used for measuring the local partial pressure of O₂ as a function of time.¹⁷³ This was demonstrated taking measurements of the partial pressure of oxygen in a phantom object with the known oxygen concentration as an example. Analogous *in vivo* studies of ³He* in porcine and human lungs revealed a linear decrease in p_{O_2} with time upon breath holding. The error of measurements of p_{O_2} was $\sim 3\%$. The concentration of oxygen in lungs strongly depends on gas exchange, regional blood flow and oxygen uptake; therefore, this experiment offers new possibilities of studying lung work and diagnosing lung diseases.

The spin relaxation time T_1 of xenon gas is of the order of tens of minutes. This is much shorter compared to helium but sufficient for the use of xenon for NMR imaging of lungs. In addition, the T_1 and T_2 relaxation times of xenon are very sensitive to the environment and can be employed as the basis of image contrast agents.¹²² Xenon was used in, *e.g.*, the *in vitro* studies of forced ventilation of lungs on mice lungs (different stages of the filling of a lung were investigated),¹⁷⁴ lungs of a living mouse during unobstructed breathing¹⁷⁵ and lungs of a living rat.¹⁷⁶ Intensive research has also been carried out on volunteers; in particular, NMR images of lungs¹⁷⁷ and the oral cavity¹⁷⁸ have been obtained.

Guinea pig lungs were studied *in vivo* to compare the NMR images obtained using hyperpolarised xenon and helium.^{179, 180} Helium allows acquisition of high-quality images at higher spatial resolution.¹⁸⁰

At the same time, xenon also has some advantages over helium. It has high solubility in blood and various tissues and binds strongly to proteins. The solubility of xenon in blood and lipids is one and two orders of magnitude higher than that of helium, respectively.¹²² A study of the dynamics of changes in the NMR signal revealed rapid transport of xenon gas from lungs into the vascular system,¹⁸¹ which permits investigations of blood circulation in the organism and in various organs.¹⁷⁷ The spin

relaxation time T_1 of ^{129}Xe dissolved in blood strongly depends on the concentration of oxygen in blood due to the change in the interaction of xenon with hemoglobin ($T_1 = 4$ s in the absence of oxygen and 6.5–13.5 s in oxygen-saturated blood^{182, 183}). Taken together with good solubility of xenon in lipid-rich brain structures, this can be used as a promising technique for functional MRI, which is based on the variation of regional cerebral blood flow upon regional activation, and for investigations of the mechanisms of the action of anesthetics on living organisms.

In vivo experiments on rats showed that a fraction of the nuclear polarisation of $^{129}\text{Xe}^*$ survives transport from lungs to blood and then through myocardium to the brain.¹⁸⁴ Two-dimensional NMR images of xenon in brain tissue were obtained using the difference between the chemical shifts of xenon gas and xenon dissolved in tissues and blood. The signal from cerebellum was less intense than the signal from the cerebral hemispheres, which can be due to different blood flow velocities. Further experiments revealed four xenon resonances in the rat organism,¹⁸¹ which were attributed to bulk phase xenon gas and to xenon dissolved in blood, fat and tissues. Different chemical shifts of xenon in plasma and erythrocytes have been reported.¹⁸³ By combining the spatial resolution of the NMR images and spectral information it was possible to follow the transport of $^{129}\text{Xe}^*$ from rat lungs into lung parenchyma and pulmonary blood, and then with blood flow through heart ventricle into myocardium, brain and kidneys.¹⁸¹

Model estimations¹²⁸ showed that after intracarotid injection of a $^{129}\text{Xe}^*$ solution the peak concentration of Xe^* in the brain will be several times higher compared to Xe^* transport through lungs. Specific features of xenon delivery to tissues by intravenous injection of a xenon solution compared to xenon respiration have been documented.¹²² The potential and drawbacks of various biocompatible solvents for delivery of xenon to blood and tissue using xenon solution injection have been reported.¹⁸⁵ The spin relaxation times of xenon in various environments have also been measured.¹²²

Rat hindleg was imaged using intramuscular injection of xenon dissolved in saline.¹²⁸ Fresh human blood in an ampoule was imaged after addition of a xenon solution in an aqueous suspension of lipid vesicles.¹⁸⁵ Intrinsic exchange of xenon between erythrocytes and the plasma–saline mixture has been studied.¹⁸⁵ Intravenous injection of xenon dissolved in a 30% soya oil-in-water emulsion into the tail of a living rat with simultaneous acquisition of MR angiograms of the abdominal and pelvic veins was used¹⁸⁶ for visualisation of the vascular system (MR angiography²). This allowed selective imaging of relatively large veins and estimation of the velocity of blood flow through them. In contrast to proton MR angiography, the xenon-based technique does not require the elimination of the signal of immobile nuclei.

Compared to xenon, the solubility of helium in blood and biocompatible solvents is 10–100 times lower, which poses some problems. To overcome them, a suspension of hyperpolarised ^3He microbubbles in a biocompatible fluid (Hexabrix) was introduced into the caudal vein or the aorta of a living rat to provide visualisation of the venous and arterial system, respectively.¹⁸⁷ In the preliminary stage (prior to injection) the effective spin relaxation time T_1 of xenon in suspension was 42 s and partially reflected the loss of the signal due to rapid rise of bubbles out of the suspension. Hand-agitated suspension contained relatively large bubbles (mean bubble diameter was 31.8 μm and the standard deviation was 10.4 μm). A narrower size distribution centred at 8 μm , which can be achieved by modern techniques, seems to be more preferable. This would provide safe transport of bubbles through the pulmonary circulation and obviate the risk of embolism. The amount of suspension (7 ml or 25% of the total rat blood volume) can be substantially reduced due to an increase in both the concentration of bubbles and the polarisation of helium nuclei. A possible application of this approach is the quantitative assessment of blood circulation in myocardium.

VI. Magnetic resonance imaging of solids

The main problem of the MRI studies of solids is that the lines in the NMR spectra of solids are 3 to 5 orders of magnitude broader than those in the NMR spectra of liquids. For instance, the linewidth in the NMR spectrum of polyethylene depends on the properties of the material and varies between 20 and 60 kHz.¹⁸⁸ This imposes severe restrictions on the achievable spatial resolution. In addition, broad lines correspond to a short signal decay time, which substantially reduces the sensitivity. On the other hand, the decay time can be lengthened using various procedures for creating the spin echo signal in a solid material.¹⁸⁹ Molecular diffusion in solids is usually insignificant and has no effect on the spatial resolution of the technique.

From the standpoint of NMR, the so-called ‘soft’ solid materials such as polymers and elastomers occupy an intermediate position between liquids and ‘hard’ solid materials. That is, they are characterised by linewidths ranging from 100 to 3000 Hz and contain a large number of protons.¹⁸⁹ Therefore, ‘soft’ materials can sometimes be studied by the above-mentioned experimental methods. The spectral lines can be narrowed by increasing the mobility of macromolecules as a result of an increase in temperature or swelling of the material in a solvent.^{190, 191} For instance, heating of a polypropylene block to 330 K substantially improves the signal-to-noise ratio in the 2D NMR image.⁴ In the case of ‘rigid’ materials a high degree of orientational ordering and low concentration of the isotopes of the nuclei under study can substantially reduce the contribution of the homonuclear dipole–dipole coupling to the linewidth.¹⁸⁹

There is a number of methods for efficient eliminations of various types of interactions which contribute to the linewidths in the NMR spectra of solids.^{188, 189, 192, 193} For instance, the magic-angle spinning (MAS) technique is widely used to suppress the chemical shift anisotropy. In this case the imaging procedure requires synchronisation of the rotating (or pulsed) field gradients with the sample rotation. Magic-angle spin-lock allows averaging of anisotropic interactions without mechanical rotation of the sample.¹⁹⁴ Decoupling with composite pulses permits suppression of heteronuclear dipolar spin coupling while various multipulse techniques are used for suppression of homonuclear dipolar couplings and for line narrowing up to three orders of magnitude.^{195, 196} In particular, a signal dephased due to homonuclear dipole–dipole coupling can be rephased using the magic echo pulse sequence.^{188, 197} By combining the magic echo pulse sequence and the CPMG pulse sequence to eliminate the chemical shift effects the adamantane NMR line was narrowed from 13 kHz to 3–8 Hz.^{196, 198}

The so-called constant time imaging (CTI) techniques involve obtaining spatial information by phase encoding of the signal. Because of this, the linewidth does not impose limitations on the spatial resolution. For instance, the single point imaging (SPI) technique^{1, 199, 200} involves measurements of the FID amplitude at a single point 10–100 μs after application of the RF pulse, which allows studies of objects with short relaxation times T_2 , and T_2^* (gases, solid materials and samples with large internal magnetic field gradients). Such gradients are typical of, e.g., samples with numerous interfaces between phases with different magnetic susceptibilities (porous media, animal and plant tissues, etc.). In the SPI technique, the signal at the centre of the k -space ($k = 0$) is acquired at a zero external field gradient, so that diffusion causes no additional loss of the signal even in the studies of fluids and gases. Nevertheless, the signal-to-noise ratio decreases due to short relaxation times T_2 and T_2^* . SPI experiments with the phase encoding of the NMR signal instead of the frequency encoding elongate the image acquisition times.¹ In some instances the SPI method is employed in combination with fast imaging techniques (e.g., the turbo spin echo SPI technique).²⁰¹ This approach was used, in particular, for investigating heterogeneous samples including hardened cement. The SPRITE technique¹ is a

version of the SPI procedure, which also allows considerable reduction of the measuring time.^{202–206} It has been used in studies of various materials including cement, concrete, bone tissues, rigid polymers and gases with short spin relaxation times (including H_2).

Often, for short- T_2 materials acquiring the FIDs rather than echo signals provides a means for improving the sensitivity of the experimental technique. Therefore, in some instances the NMR images are reconstructed using a method similar to X-ray computerised tomography. The technique is based on recording the FID in the presence of a magnetic field gradient and multiple repetition of the experiment at different directions of the field gradient. The results obtained (1D projections) are then used for reconstruction of 2D or 3D NMR images from the projections using relevant software.¹⁹² Continuous-wave MRI can also offer some advantages over the pulsed techniques in studies of materials with submillisecond relaxation times T_2 .²⁰⁷

Broad-line effects on the spatial resolution can be eliminated using large-amplitude field gradients. NMR probes have been developed, which permit creation of pulsed field gradients up to $60\,000\text{ G cm}^{-1}$ (see Ref. 208). Finite inductance of gradient coils and the eddy currents induced in conducting materials cause the gradient switch on/off time to extend, thus shortening the minimum achievable echo time. In this situation one can use sinusoidal field gradients and a gradient coil incorporated into the resonant circuit.^{209–211} In this case, the RF pulses are applied at the instant when the gradient passes through zero. Using a doubly resonant coil, one can adjust the shape of the field gradient in such a way that it has an inflection point at zero, which permits an increase in the duration of the RF pulse, thus improving NMR image quality.^{211,212} Oscillating field gradients allow reduction of the echo time down to $\sim 100\text{ }\mu\text{s}$. For instance, a 3D image of a plastic LEGO[®] brick has been obtained (characteristic relaxation time T_2 of the material was $760\text{ }\mu\text{s}$).^{209,212}

A number of stray field imaging (STRAFI)¹ studies have been reported.^{213–217} The method involves placing the NMR probe in the region where the magnetic field amounts to *ca.* 40% of the maximum magnetic field value but the field gradient can exceed $10\,000\text{ G cm}^{-1}$. At such gradient amplitudes, even a short RF pulse affects nuclear spins only within a narrow slice of the sample. 1D STRAFI images are obtained by mechanically moving the sample along the field gradient direction through the sensitive slice. Stepwise rotation of the sample permits 2D and 3D NMR imaging. The method allows studies of samples with metallic inclusions and of paramagnetic materials.²¹⁸ Using an additional coil, one can vary the magnetic field, thus displacing the sensitive region within the limits of 1 cm without moving the sample.²¹⁹

Multiquantum NMR imaging involves creation of a coherence in the system of interacting spins (n th order coherence; $n > 1$).²²⁰ The evolution frequency of the multiquantum coherence is n times higher than the Larmor frequency of spin precession ($n = 1$) in the magnetic field. Because of this, at $n = 10–20$ the effective amplitude of the field gradients employed increases by an order of magnitude during acquisition of NMR images.²²¹

Using selective pulses for slice selection and chemical shift selective imaging also face some difficulties, since the pulse duration can exceed the signal decay time in solid materials.²²¹ Application of large field gradients permits slice selection with short RF pulses (several microseconds). Slice selection can also be achieved by spin-lock in the presence of a field gradient²¹⁰ and by selective saturation of the nuclear magnetisation outside the slice under study due to long relaxation times T_1 in solid materials. The above-mentioned line narrowing techniques allow the use of long pulses and pulse sequences for selection of a particular slice or spectral line.¹⁸⁹ Some other slice selection methods have been developed.^{222–224} Heteronuclear polarisation transfer²²⁵ between, *e.g.*, the ^1H and ^{13}C nuclei offers considerable promise for selection of a particular group of atomic nuclei in multi-component systems.

Short, large-amplitude RF pulses that are used in solid-state NMR studies require high RF power. This imposes limitations on the size of the sample (usually, the sample is no larger than 1 cm). Samples that can be as large as one likes (*e.g.*, the Earth) are studied using surface coils²²⁶ or a device which combines the RF coil and the magnetic field source. Local studies of the properties of large samples can be performed with a surface scanner ('NMR Mouse'), which is suitable for exploring almost any solid materials^{227,228} including metal-supported polymeric coatings, human skin and tendons, *etc.* Small size and weight make the device mobile. Because of this the spectrum of possible applications of the method is broadened and includes, in particular, studies of aircraft wings, auto-tyres reinforced with steel-wire cord, buildings, bridges and conveyor belts.¹⁰ The device comprises two permanent magnets and a surface coil which produce a static and an RF field in the near-surface layer of the sample. Inhomogeneity of the fields produced defines the size of the sensitive volume (characteristic dimensions are $4 \times 9\text{ mm}$ at a thickness of 0.5 to 1 mm). By varying the frequency of the alternating field the sensitive zone can be displaced over a distance of 0 to 5 mm from the surface. An additional gradient coil allows 1D spatially resolved NMR imaging within the field of view (15 mm) without mechanically moving the probe.²²⁹

An NMR image can be obtained using radiofrequency field gradients (B_1 -imaging technique) in combination with static magnetic field gradients or instead of them.¹⁹² The advantage of this approach is insensitivity to static magnetic field inhomogeneities typical of heterogeneous samples.

Feasibility of using MRI techniques to obtain information on solid materials (including real-time monitoring of technological processes) is of considerable interest in spite of technical problems and complexity of practical implementation. The major advantage of NMR imaging is the possibility of targeted variation of image contrast by choosing appropriate pulse sequences. It is this feature that allows one to collect information on the structure and state of the samples and processes occurring in them. This also holds for solids. Using theoretical and empirical relationships, one can estimate such characteristics of materials as the degree of homogeneity, the dynamics and degree of molecular ordering, chemical composition, molecular velocities and reaction rates, mechanical stress and deformations, degree of cross-linking of polymers, filler agglomerate distribution, ageing, temperature, viscosity, *etc.*, from the quantities measured experimentally (*e.g.*, relaxation times, chemical shifts, linewidth and lineshape). The most important procedures for creating image contrast in solids and methods of practical implementation have been well documented.^{230–232} Only a few examples are presented below.

NMR imaging of solids is most widely used in studies of polymers and elastomers (Figs 6 and 7). In particular, MRI experiments revealed the presence of inhomogeneously distributed spherical microvoids of different sizes in cross-linked poly-(isobutylene-*p*-methylstyrene-*p*-bromomethylstyrene) terpolymer.^{190,191} It was found that the concentration of microvoids correlates with the mechanical properties of the material. In particular, high concentrations of microvoids can cause early destruction of the material under mechanical stress.

The relaxation times are often used as the basis of image contrast. The T_2 and $T_{1\rho}$ values (see Ref. 1) are sensitive to the cross-linking density of polymers (the latter allows characterisation of the size of defects and the molecular dynamics of the polymer).²³³ The relaxation time T_2 nearly linearly decreases with an increase in the cross-link density, linearly increases with temperature and depends on the degree of tension of the sample.¹⁸⁸ This permitted studies of the local cross-link density in elastomers (including those during vulcanisation processes).^{10,188,234} Spatial inhomogeneity of cross-linking of the polymer chains in a composite sample of butadiene-styrene rubber was investigated by measuring the effective relaxation time T_1 .²³⁵ The degree of cross-linking and orientational ordering of macromolecules can be determined from measurements of

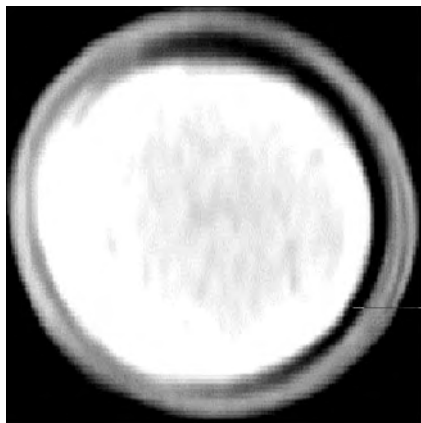


Figure 6. A 2D NMR image of the cross-section of a porous cylindrical alumina granule saturated with cyclohexane. The image was obtained using the spin echo technique. A sealing tape (bright ring around the granule) was wrapped around the granule.

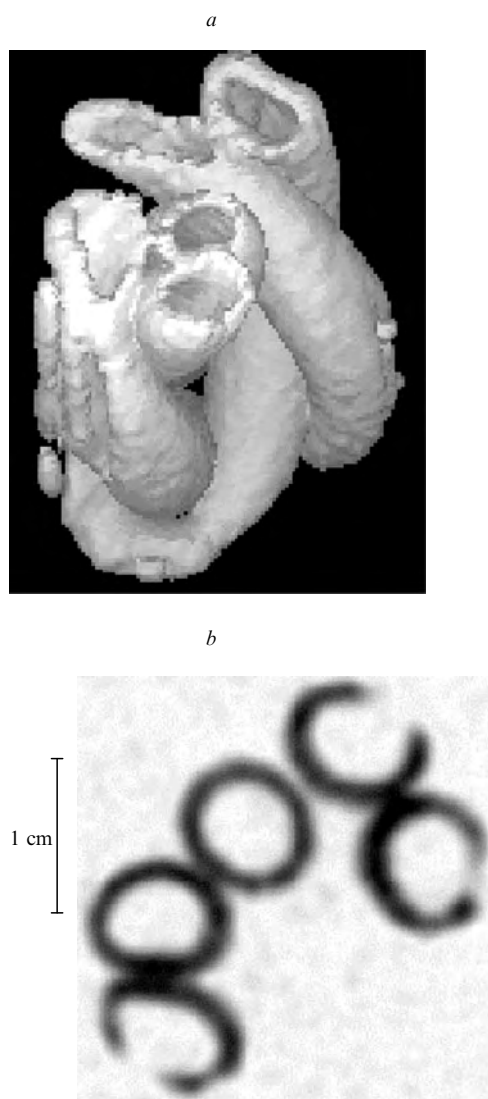


Figure 7. 3D surface rendering (a) and a horizontal section (b) of a polychlorovinyl tube tied in a bundle. The NMR images were obtained using the spin echo technique.

residual dipolar spin–spin coupling.^{236,237} Chemical shift anisotropy was used as the basis of image contrast in a study of the ordering of pre-stressed polytetrafluoroethylene²³⁸ and in monitoring the propagation of mechanical stress during crack growth in the material.¹⁸⁸ The density of cross-links between polymer chains can be determined *via* swelling of the materials in solvents.^{1,2}

The relaxation times T_2 and $T_{1\rho}$ are sensitive to slow molecular motions and suitable for studying changes in the mechanical properties of polymers and elastomers including vulcanisation and ageing.^{10,188} The results of real-time monitoring of vulcanisation of butadiene–styrene rubber without filler and with carbon black additive have been reported.^{10,11,188} Co-vulcanisation of composite materials has been studied.¹⁰ A study of oxidative ageing of butadiene–styrene and natural rubbers at elevated temperatures²³⁹ revealed the formation of a rigid ‘crust’ on the surface of the samples. The ‘crust’ was shown to thicken with time.^{10,188} It was separated from the unmodified material by a narrow region characterised by increased molecular mobility due to the polymer chain scission. The influence of external conditions and chemical composition of materials on the ageing and solvent transport in aged rubbers has been studied.²⁴⁰

Mechanical ageing can be due to crystallisation induced by mechanical stress or to additional cross-linking or scission of molecular chains upon an increase in temperature. Mechanical ageing has been studied taking samples cut from a tyre as examples.¹⁰ Inhomogeneous vulcanisation can induce early degradation of rubber items under the operating conditions. NMR images of swollen items reveal distinctions in the degree of vulcanisation between the damaged and normal regions.¹⁸⁸ NMR imaging also permits detection and studies of the properties of boundary regions at the interfaces between different types of rubbers upon vulcanisation.²⁴¹ A number of studies of rubber items characterised by the presence of an interface between the butadiene–styrene and natural rubbers have been carried out.

Knowledge of the distribution of mechanical stress and strain in polymeric and elastomeric items under the operating conditions is of great importance. NMR imaging provides a means for studying the changes in the molecular mobility and orientation of the molecular chains. For ‘soft’ materials this information can be obtained by directly measuring the molecular displacements.² In addition, the spin relaxation times, chemical shift anisotropy, quadrupole splittings and multiquantum coherence are sensitive to stress and deformation. The morphology of cold-drawn polycarbonate was studied^{188,242} using the effective relaxation time T_2 related to the local mobility of polymer chains as contrast agent. Measurements of the effective relaxation time T_1 permitted the determination of the mechanical stress distribution in a glass-supported tripropylene glycol diacrylate film 0.9 mm thick. It was also shown that the stress substantially increases as the distance from the film region under study to the support decreases.²³⁵ Crack growth in polymer samples was studied by inducing tensile stress and monitoring the morphology and mechanical stress near the tip of the growing crack.²⁴³

The fact that many spin interactions are anisotropic can be useful for studying the deformation and stress anisotropy. Quadrupole splittings in the ^2H NMR spectra are very sensitive to alignment of the molecular chains as a result of changes in the degree of averaging of anisotropic interactions. The samples can be deuterated either during the preparation of materials or by swelling in deuterated solvents or oligomers. The latter approach was used for studying mechanical stress in strained natural rubber.^{10,244} Creation of two-quantum coherence^{10,237} of single quadrupole nuclei or interacting nuclei with spin 1/2 also offers some advantages.

Studies of the properties of various materials under dynamic load conditions are of great value. In contrast to conventional techniques, MRI allows spatially resolved studies of the properties of various materials and, in particular, mapping the temperature distribution over the sample. For instance, the relaxation time T_1

of butadiene–styrene rubber exponentially decreases with an increase in temperature, while the relaxation time T_2 is proportional to the local temperature.^{10, 188, 245} An NMR probe was designed to carry out experiments under dynamic load conditions (compression or shear deformation) with frequencies ranging between 1 and 20 Hz. Experiments with a cylindrical sample at different load frequencies and different amounts of filler in the rubber revealed an increase in the temperature by 20 degrees and inhomogeneous temperature distribution over the cross-section of the sample.

Studies of polystyrene after bending strain or impact load^{188, 227} and acquisition of a 3D NMR image of extruded polycarbonate can serve as examples in the case of rigid materials.²⁴⁶ The study of polyethylene revealed nanometre-size transient regions between the amorphous and crystalline domains.²⁴¹ Spatial inhomogeneity of the distribution of crystalline and amorphous domains in polymeric materials was established by combining MRI data and spectral information obtained from ^{13}C NMR measurements.²⁴⁷ NMR imaging was also employed to study the damaged regions in low density polyethylene upon electrical breakdown and the dendritic microvoid structures created by electrical breakdown.²⁴¹ It was found that the breakdown zone is characterised by a decrease in the size of crystalline domains and by an increase in the size of amorphous domains as a

result of rapid local heating followed by cooling. ^1H and ^{27}Al NMR imaging was used to study solid propellants.¹⁸⁸

* * *

In conclusion mention may be made of a number of reviews, monographs and books concerning the problems considered in this review. They are concerned with basic MRI principles^{189, 248–250} and applications of the technique in various fields.^{251–260} Another group of references are devoted to MRI studies of porous materials^{252–254, 261} including fluid transport in porous media,^{262, 263} problems of application of NMR and MRI in chemical technology and catalysis,^{264–266} principles and examples of solid-state MRI applications^{192, 210, 256, 267, 268} and NMR studies of noble gases.²⁶⁹

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VII. Supplement

Table S.1 presents additional information on the MRI studies considered in this review.

Table S.1. Applications of NMR imaging techniques.

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
—	^1H	polypropylene block at 300 and 330 K	spin echo	2D	128×128 , a slice 5 mm thick	3.5 min	4
—	^1H	polymerisation of MMA + substituted peroxodisulfate (0.2%) in a mould at 60 °C	the same	2D	128×256 , a slice 4.5 mm thick	1 min	4
—	^1H	vulcanisation of a composite polymeric material reinforced with carbon fibre	"	2D	128×128 , a slice 5 mm thick	1 min	4
6.34	^1H	water or water + MnSO_4 in a cross-linked poly(methacrylic acid) gel	"	2D	a slice 2 mm thick	—	6
2.35	^1H	copolymerisation of methacrylamide with N,N' -methylenebisacrylamide + 10% ammonium persulfate + tetramethylethylenediamine at 25 and 35 °C	"	2D	—	—	7
4.7	^1H	epoxy resin reinforced with carbon fibres	"	2D	128×128 , a slice 1 mm thick	64 s	8
2	^1H , ^{19}F	methacrylic acid + benzoyl peroxide + N,N -dimethylaniline + 1,4-dibromotetrafluoroethylene	"	1D	256; 0.4 mm	5 s	12
2.9	^1H	photoinduced polymerisation of a resin containing methacrylic monomers	spin echo + STRAFI	1D, 3D	54 μm (1D); $128 \times 128 \times 128$, (100 μm) ³ (3D)	—	13
4.7	^1H	photoinduced polymerisation of hexamethylene dimethacrylate + benzyl dimethyl ketal	spin echo	2D	256×256 , (20 μm) ² , a slice 300 or 500 μm thick	—	14
—	^1H	1,6-hexanediol dimethacrylate + benzyl dimethyl ketal	the same	2D	256×128 or 256×256 ; from (11 μm) ² to $39 \times 78 \mu\text{m}$, a slice 300 μm to 1.7 mm thick	—	15
3	^1H	irradiated polymer gel	"	2D	128×128 or 256×256 (234 μm) ² or (195 μm) ² , a slice 1 mm thick	6.4 min or 6 h 49 min	16

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
0.2	¹ H	Fe(II) and Fe(III) ions in agar gel	spin echo with inversion – recovery	1D	512, a slice 0.11 mm thick	28 – 112 s	17
1.5	¹ H	irradiated polymer gel	spin echo	2D	144 × 256, (1.2 mm) ² , a slice 5 mm thick	4.5 min	19
1.5	¹ H	X-ray or electron-beam irradiation of acrylamide + bisacrylamide + gelatin + water – O ₂	the same	2D	256 × 256; (1.17 mm) ²	—	20
1.5	¹ H	X-ray irradiation of <i>N,N'</i> -methylene-bisacrylamide + <i>N</i> -vinylpyrrolidone + gelatin + water – O ₂	"	2D	256 × 256; from (1.9 mm) ² to (0.13 mm) ² , a slice 5 – 20 mm thick	—	21
2.3	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions + agarose + phosphate)	—	2D	a slice 2 mm thick	25.6 s	23
2	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions + agarose + orthophosphoric acid)	spin echo	2D	a slice 2 mm thick	12.8 s	24
2	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions + agarose + phosphate)	the same	3D	128 × 128 × 128; (250 μm) ³	51.2 s	25
2	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions + agarose + orthophosphoric acid)	spin or gradient echo	2D	a slice 2 mm thick	13 s (spin echo) or 2 s (gradient echo)	26
2	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions + orthophosphoric acid)	spin echo	1D	—	—	27
2	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Mn ions)	the same	1D	256; a slice 2 mm thick	100 ms	28,30
2.4	¹ H	B – Z reaction (oxidation of malonic acid by bromate ion + Ce, Ru or Fe ions)	spin or gradient echo	1D, 2D	a slice 2 mm thick or without slice selection	10 s (2D)	31
2.0	¹ H	aqueous sodium alginate solution + CaCl ₂	spin echo	1D, 2D	160 μm (1D); 256 × 256, (200 μm) ² , a slice 5 mm thick (2D)	40 s (1D); 21 min (2D)	34
—	¹ H	photolysis of <i>tert</i> -butyl methyl ketone in CCl ₄	—	2D	—	—	39
1.5, 2.4	¹ H, ¹³ C	dimethyl maleate in acetone or rat blood <i>in vivo</i>	gradient echo or spin echo	2D	64 × 128 or 256 × 256, 0.8 × 1.1 mm or (0.4 mm) ²	0.4 – 2 s	43
1.5	¹ H	rabbit or porcine brain, muscles, liver and kidney <i>ex vivo</i>	gradient echo	2D	256 × 256, (0.78 mm) ² , a slice 10 mm thick	26 s	45
0.5	¹ H	human brain tumour or human liver tumour	gradient echo	2D	256 × 128, 1.25 × 1.9 mm, a slice 4 mm thick	5 – 7 s	47
1.5	¹ H	agar gel	spin or gradient echo	2D	64 × 128, 4 × 2 mm, a slice 10 mm thick	15 s	49
4.7	¹ H	aqueous NaCl solution, agar, egg white, chicken muscles or cat brain <i>in vivo</i>	gradient echo	2D	128 × 128, (0.67 mm) ² , a slice 3 mm thick	—	52
2.35	¹ H	gelated starch suspension, agar gel, food sauce or aqueous gel based on organic hydrophilic polymer TX151	gradient echo (FLASH) technique	2D	256 × 64, (273 μm) ² or (312 μm) ² , a slice 5 mm thick	12.8 s	53
1.5	¹ H	human brain tumour during interstitial magnetic resonance-controlled laser-induced thermal therapy treatment	the same	2D	128 × 128, (1.8 mm) ² , a slice 5 mm thick	8 s	54

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
1.5	¹ H	rabbit brain <i>in vivo</i> during microwave radiation induced interstitial heating	gradient echo	2D	256 × 256, (0.31 mm) ² , a slice 5 mm thick	< 20 s	55
1.5	¹ H	porcine brain, muscles and liver <i>ex vivo</i>	the same	2D	128 × 128, (1.8 mm) ² , a slice 6 mm thick	1.3 s	56
1	¹ H	human peripheral muscle (<i>musculus gastrocnemius</i>)	"	2D	128 × 192, 2.2 × 1.47 mm, a slice 10 mm thick	—	57
1.5	¹ H	agar gel doped with CuSO ₄ , human leg muscles	"	2D	256 × 256, (0.86 mm) ² , a slice 10 mm thick	60 or 69 s	58
1.5	¹ H	agar gel	"	2D	256 × 256, (0.8 mm) ² , a slice 10 mm thick	1 min	59
1.5	¹ H	water, acetone, oil	"	2D	256 × 128, 0.63 × 1.26 mm, a slice 5 mm thick	18 s	60
4.7	¹ H	hind limb of a rat <i>in vivo</i>	FID	2D	32 × 32, (3 mm) ² , a slice 3 mm thick	2.5 min	61
3 (Ethylene glycol); 1.5 (liver)	¹ H	ethylene glycol in a double cylinder; porcine liver <i>in vitro</i>	gradient echo (EPI)	2D	32 × 32; (6.45 mm) ² (ethylene glycol); (5.16 mm) ²	10 s (ethylene glycol); 3 min (liver)	62
—	¹ H	agar gel or porcine muscle and fat tissues	gradient echo	2D	256 × 256, (0.78 mm) ²	—	63
1.5	¹ H	agar gel	the same	2D	256 × 256, (0.82 mm) ² , a slice 10 mm thick	26 s	64
1.5	¹ H	1.5% agar gel doped with CuSO ₄ ; turkey breast or pork	"	2D	256 × 256, (0.98 mm) ² , a slice 5 mm thick or 128 × 128, (1.2 mm) ² , a slice 10 mm thick	17 s	65
1.5	¹ H	gel or porcine liver <i>ex vivo</i>	"	2D	128 × 128, (1.97 mm) ²	0.8 s	66
0.15	¹ H	human peripheral muscle	"	—	—	—	67
1.5	¹ H	silicone gel or rabbit femor <i>in vivo</i>	"	2D	96 × 128	7–20 s	68
0.2	¹ H	agar gelatin or bull liver <i>ex vivo</i>	"	2D	128 × 128, (1.57 mm) ² , a slice 5 mm thick (gel); 256 × 256, (0.78 mm) ² , a slice 10 mm thick (liver)	4 s (gel); 13 s (liver)	69
1.5	¹ H	water; gel; porcine brain and fat tissues <i>in vitro</i> ; human brain	"	2D	180 × 256, 0.89 × 0.9 mm, a slice 4–5 mm thick	12 s	70
1.5	¹ H	rabbit femor <i>in vivo</i>	gradient echo	2D	256 × 128, 0.63 × 1.26 mm, a slice 3 mm thick	3.3 s	72
4.7	¹ H	agar gel	gradient echo (FLASH, PRESTO)	2D	64 × 60, (0.56 mm) ² , a slice 5 mm thick	144 ms (PRESTO)	73
1.89	³¹ P, ¹ H	inorganic phosphate solutions in three coaxial cylinders or water in two ampoules	spin echo	2D	128 × 128	—	74
7, 11.7	¹ H	DMSO, water or chloroform	FID	1D	170 μm	—	77
7, 11.7	¹ H	convection in DMSO, water or chloroform	stimulated echo	—	WSR	—	77
0.15	¹ H	human calf muscle	gradient echo	2D	128 × 128, (1.18 mm) ² , a slice 8 mm thick	—	80
1.5	¹ H	sheep dug and fat tissues <i>in vivo</i>	the same	2D	256 × 256, (0.78 mm) ² , a slice 5–7 mm thick	2.3 s	81
4.7	¹ H	agar gel	gradient echo (Snapshot FLASH)	2D	128 × 128, 0.4 × 0.8 mm, a slice 2 mm thick	2.1 s	82

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
1.5	¹ H	porcine muscle tissue, glandular tissue (sheep dug) or fat tissue	gradient echo (turboFLASH) with saturation – recovery	2D	256 × 256, (0.94 mm) ² , a slice 10 mm thick	3 s	83
1.5	¹ H	gel; bull muscles <i>in vitro</i> or rabbit muscles <i>in vivo</i>	gradient echo or spin echo	2D	192 × 256, 1.05 × 0.78 mm (gradient echo)	2 s (gradient echo), 112 s (spin echo)	84
1.5	¹ H	gel or bull muscles <i>in vitro</i>	gradient echo	2D	(1 mm) ² , a slice 5 mm thick	1.35 s	85
7.05	¹ H	water + CuSO ₄ in a tube or cylinder	spin echo	2D	256 × 128, (0.27 mm) ² , a slice 2 mm thick or 1024 × 64, 0.078 × 0.23 mm, a slice 0.4 mm thick	17 min or 2 min	86
2	¹ H	<i>cis</i> -polybutadiene block	gradient echo	2D	128 × 128, (0.3 mm) ² , a slice 4 mm thick	—	87
1.5	¹ H	polyacrylamide gel	—	2D	128 × 256, 1 × 2 mm, a slice 10 mm thick	3.5 min	88
1.5	¹ H	agar gel doped with black ink and sodium aluminosilicate particles; or rabbit brain <i>in vivo</i>	gradient echo (EPI)	2D	128 × 256, 3 × 1.5 mm, a slice 6 mm thick	150 ms	89
0.5	¹ H	human calf muscle	stimulated echo	1D	128, 1.97 mm, a slice 15 × 15 mm	51 s	90
1.5	¹ H	bull muscles <i>in vitro</i>	gradient echo	2D	128 × 256, 1.9 × 0.9 mm, a slice 5 mm thick	1.8 or 5 s	91
7	¹ H	CH ₂ Br ₂ in a nematic liquid crystal	spin echo	1D	—	—	92
2.35	² H	D ₂ O in a lyotropic liquid crystal	the same	—	WSR	—	94
0.5	¹ H	porcine liver <i>in vivo</i> or <i>ex vivo</i>	gradient echo (GRASS)	2D	a slice 3 mm thick	1.2 – 3.5 min	95
2.35	¹ H	rabbit liver <i>in vivo</i>	gradient echo	2D	256 × 192, 0.31 × 0.42 mm, a slice 4 mm thick	12 s	96
—	¹ H	electric current flowing through coaxial cylinders filled with salt – water phantom and water; electric current flowing through a plant stem	spin echo	2D	(60 μm) ² , a slice 2 or 3 mm thick	—	99
2	¹ H	electric current flowing through coaxial cylinders filled with salt – water phantom	the same	2D	128 × 128; (0.74 mm) ² , a slice 4 mm thick	—	100
2	¹ H	electric current flowing through a ping-pong ball filled with salt – water phantom	"	2D	(0.52 mm) ²	—	101
—	¹ H	electric current flowing through coaxial cylinders filled with salt – water phantom; electric current flowing through a human forearm	"	2D	(0.52 mm) ² , a slice 0.5 cm (cylinders) or 2 cm thick (forearm)	—	102
2.35	¹ H	electric current flowing through a fragment of chicken femor soaked with salt – water phantom	"	2D	256 × 256; (0.08 mm) ² , a slice 3 mm thick	18 min	103
4.7 (<i>in vivo</i>), 2.35 (<i>in vitro</i>)	¹ H	electric current flowing through a mice tumour <i>in vivo</i> or <i>in vitro</i>	"	2D	256 × 256; (0.12 mm) ² , a slice 2 mm thick	—	104
2.35	¹ H	electric current flowing during NaCl dissolution in a water + agar mixture; electric current flowing through a water + Ca(OH) ₂ + CO ₂ mixture	"	2D	256 × 256; (0.08 mm) ² , a slice 3 mm thick	—	105
2	¹ H	electric current flowing through coaxial cylinders filled with salt – water phantom	"	2D	128 × 128; (0.55 mm) ²	—	106

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
—	¹ H	electric current flowing through coaxial cylinders filled with salt – water phantom and water	spin echo	2D	128 × 128; (0.55 mm) ²	—	107
2	¹ H	electric current flowing through coaxial cylinders filled with doped water or mineral oil, electric current flowing through a rat body <i>ex vivo</i>	the same	2D	128 × 128; (0.55 mm) ² , a slice 5 mm thick (cylinders); 128 × 128; (0.8 mm) ² , a slice 5 mm thick (rat)	—	108
2.35	¹ H	electric current flowing through a rat brain <i>in vivo</i>	"	2D	256 × 256; (0.27 mm) ² , a slice 2 mm thick	—	109
2.35	¹ H	rat brain <i>in vivo</i>	RF-CDI + spin echo	2D	256 × 256, (275 μm) ² , a slice 2 mm thick	—	109
3	¹ H	electric current flowing through a copper conductor 60 μm in diameter placed in H ₂ O + NaCl + CuSO ₄ phantom solution	gradient echo	2D	256 × 256, (0.47 mm) ² or 64 × 64, (1.9 mm) ² , a slice 7 mm thick	—	110
3	¹ H	a copper conductor in an aqueous solution containing 0.75% NaCl + 5 mM CuSO ₄	gradient echo (EPI)	2D	64 × 64, (1.9 mm) ² , a slice 7 mm thick	—	110
1.4	¹ H	electric current flowing through a LiCl + H ₂ O or (CH ₃) ₄ NCl + D ₂ O solution	spin echo	—	WSR	—	111
2.4	¹ H	CH ₄ in a cylinder with partitions	SPRITE	1D	128 points, 700 μm	—	112
2.4	¹⁹ F	SF ₆ in a porous coral	SPRITE	3D	64 × 64 × 64, 2.5 mm	1.5 h	112
1.9	¹⁹ F	a SF ₆ –O ₂ (80 : 20 or 25 : 75) mixture in rat lungs	FID, PRI	3D	72 × 74 × 80, 529 μm	30.3 min	113
1.9	¹⁹ F	a C ₂ F ₆ –O ₂ (80 : 20) mixture in rat lungs	PRI	3D	46 × 46 × 54, 700 μm	4.3 h	114
7	¹⁹ F	C ₂ F ₆ (5 atm) in a ceramic composite	spin echo	2D	(100 μm) ² , a slice 0.5 mm thick	12 h	115
1.9	¹⁹ F	C ₂ F ₆ or C ₄ F ₈ in ceramics (Y-stabilised zirconia)	the same	3D	—	2 h	116
9.4	¹²⁹ Xe*	xenon in NaY and CaA zeolites and in porous glass	FID	2D	128 × 128, (156 μm) ² , a slice 4 mm thick	30 min	117
1.5	³ He*	helium in human lungs	gradient echo	2D	256 × 128, 2.1 × 4.1 mm, a slice 9 mm thick	20 s (a total of 8 slices)	119
2.35	³ He*	³ He (0.5 atm) in a glass cell	gradient echo (FLASH)	2D	32 × 64, 2.2 × 1.1 mm, a slice 2 cm thick	6.4 s	120
1.5	³ He*, ³ He	³ He* (1 atm) or a ³ He–O ₂ mixture (73 : 27, 3.6 atm) in a glass cell	gradient echo	2D	96 × 128, 5.2 × 3.9 mm, a slice 40 mm thick (³ He*), 64 × 64, (4.7 mm) ² , a slice 40 mm thick	13–20 s (³ He*)	121
—	¹²⁹ Xe*	gaseous Xe and Xe dissolved in perfluorinated solvent	the same	2D	—	—	122
9.4	¹²⁹ Xe	Xe (30 atm) with O ₂ additive in aerogel	chemical shift selective spin echo imaging	3D	(420 μm) ² , a slice 1 mm thick	—	123
1.5	¹²⁹ Xe	Xe (0.78 atm) + O ₂ (0.15 atm) in a glass sphere	FID after selective inversion	1D	1024 points, 0.5 mm (2 mm)	—	124
9.4	¹²⁹ Xe*	xenon in porous glass	gradient echo	1D	—	—	127
2.35	¹²⁹ Xe*	xenon in rat tissues <i>in vivo</i>	the same	2D	256 × 256, (1 mm) ² , a slice 10 mm thick	4.8 s	128
2, 7.05	¹²⁹ Xe*	Xe + N ₂ (10%) + Rb in a glass sphere at 790 or 896 Torr	FID	—	WSR	—	129
4.3	¹²⁹ Xe*	Xe (1–3 atm, 80% ¹²⁹ Xe) in nested tubes or in a capillary bunch	gradient echo (FLASH)	2D	128 × 64, 0.1 mm	—	130
4.3	¹²⁹ Xe*	Xe (1–3 atm, 80% ¹²⁹ Xe) in aerogel	the same	1D	0.1 mm	—	130

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
4.2	¹²⁹ Xe*	Xe (0.4 atm) + N ₂ (0.27 atm) + He at a total pressure of 4 atm in capillaries and in a tube	gradient echo	2D	256 × 128, 110 × 340 μm, a slice 5 mm thick	51 min	131
4.2	¹²⁹ Xe*	Xe (0.4 atm) + N ₂ (0.27 atm) + He at a total pressure of 4 atm; flow through a tube with a diaphragm or through polyurethane foam	dynamic NMR microimaging (PGSE)	2D in the <i>k</i> – <i>q</i> space	256 × 32, a slice 4 mm thick	—	131
4.3	¹²⁹ Xe*	Xe (0.5 atm) + N ₂ (0.5 atm) or Xe (3 atm) + N ₂ (1 atm) in SiO ₂ aerogel or in zeolite 13X	—	3D	250 × 250 × 100 μm (aerogel) 64 × 64 × 256, (100 μm) ³ (zeolite)	—	133
0.00206	³ He*	Rb + N ₂ (100 Torr) + ³ He (2.7 atm) in a glass cell or in rat lungs <i>ex vivo</i>	gradient echo	2D	128 × 128, (1 mm) ²	25 s	134
0.0031	³ He*	Rb (10–100 mg) + N ₂ (10–200 Torr) + ³ He (0.2–2.5 atm) in an ampoule with rectangular cross-section	FID	1D	—	—	135
1.5	³ He*	helium in human lungs	gradient echo (EPI)	2D	32 × 64, (6.25 mm) ² , a slice 10 mm thick	40.5 ms	136
0.0938	¹⁹ F	CF ₄ –O ₂ (80 : 20) mixture in dog lungs	PRI	3D	65 × 65 × 65, 0.5–1 cm	25 min	142
0.0938	¹⁹ F, ¹ H	perfluorinated solution and water in two-compartmental phantom	PRI	3D	65 × 65 × 65, 2–3 mm	—	142
2.35	³ He, ¹ H	helium in rat lungs	spin echo	2D	4.4 × 4.4 mm without slice selection (³ He), 128 × 64, 0.55 × 0.27 mm, a slice 5 mm thick (¹ H)	8 min (³ He)	143
14.1	¹³¹ Xe	liquid Xe in aluminosilicate aerogel at 285 K	chemical shift selective spin echo imaging	3D	128 × 32 × 32, 0.47 × 0.38 × 0.38 mm	3 h	147
11.75	¹²⁹ Xe*	Xe + He in tris(<i>o</i> -phenylenedioxy)-cyclophosphazene crystallites	broad-line NMR	—	WSR	—	148
1.9	³ He*	³ He (7 atm) in a cylinder	gradient echo	1D	0.8 mm	—	149
4.3	¹²⁹ Xe*, ¹ H*	xenon (80% ¹²⁹ Xe) at 1 atm dissolved in C ₆ H ₆ or C ₆ D ₆ –C ₆ D ₅ H (3 : 1) mixture	gradient echo (FLASH)	2D (¹²⁹ Xe), EPI 2D (¹ H)	128 × 64 (¹²⁹ Xe), 128 × 32 (¹ H)	24 ms (¹ H)	150
4.2	¹²⁹ Xe*	xenon in aerosil (or in modified aerosil), in CsI or in their mixture	—	—	WSR	—	151
2.0	³ He*	helium in guinea pig lungs <i>ex vivo</i>	gradient echo (GRASS)	2D, 3D	128 × 256, 0.56 × 0.28 mm, a slice 10 mm thick (2D); 128 × 256 × 32, 0.48 × 0.24 × 0.5 mm (3D)	1.41 s (2D)	157
2.0	³ He*	helium in guinea pig lungs <i>in vivo</i>	PRI	2D, 3D	(400 μm) ² (2D)	—	158
2.0	³ He*	the same	PRI	2D, 3D	128 × 128 × 128, (0.5 mm) ³	6.4 min (3D)	159
2.0	³ He*	"	FID, radial trajectories	2D	256 × 256, (188 μm) ²	24 s	160
1.5	³ He*	helium in human lungs	the same	2D	256 × 256, (1.3 mm) ²	—	160
2.0	³ He*	helium in guinea pig lungs <i>in vivo</i>	"	2D	512 × 512, (102 μm) ²	100 s	161
2.0	³ He*	helium in rat lungs <i>in vivo</i>	PRI	2D, 3D	128 × 128 × 128, (550 μm) ³	54 s	162
0.79	³ He*, ¹ H	helium in human lungs	gradient echo (FLASH)	2D	256 × 256, (1.2 mm) ² , a slice 3 mm thick	28 s	163
0.8	³ He*	helium in glass cells	the same	2D, 3D	256 × 256 × 32, 1 × 1 × 3 mm (3D)	3 min	164
0.8	³ He*, ¹ H	helium in human lungs or upper respiratory tract	"	2D	1–2 mm in-plane resolution, a slice 30 mm thick	14–28 s	164

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
1.5	³ He*, ¹ H	helium in human lungs	gradient echo	2D	128 × 256, 1.25 × 2.5 mm, a slice 20 or 6 mm thick	0.9 s	166
1.5	³ He*, ¹ H	helium in human paranasal sinuses	the same	2D	256 × 128, 0.9 × 1.9 mm, a slice 20 mm thick (He)	< 5 s (for 2 slices, He)	167
1.5	³ He*	helium in human lungs	gradient echo (FLASH)	3D	144 × 256 × 24, 2.4 × 1.4 × 7 mm	35 s	168
1.5	³ He*	the same	the same	3D	144 × 256 × 24, 2.4 × 1.4 × 7 mm	42 s	169
2.0	³ He*	helium in guinea pig lungs <i>in vivo</i>	PRI	2D	512 × 512, (73 μm) ² , a slice 16 mm thick	8 min	170
2.0	³ He*, ¹²⁹ Xe*	helium or Xe (82% ¹²⁹ Xe) in guinea pig lungs <i>in vivo</i>	FID, radial trajectories	2D	256 × 256, (190 μm) ² , a slice 5 mm thick (³ He); 128 × 128, (845 μm) ² (¹²⁹ Xe)	30 s	171
2.0	³ He*, ¹²⁹ Xe*	the same	the same	2D	256 × 256, (190 μm) ² , a slice 5 mm thick (³ He); 128 × 128, (840 μm) ² (¹²⁹ Xe)	60 s	172
1.5	³ He*	helium in human lungs	"	2D	256 × 256, (1.41 mm) ²	16 s	172
1.5	³ He*	helium in a silicon bag or in porcine lungs (<i>in vivo</i> or <i>ex vivo</i>) or in human lungs	gradient echo	2D	81 × 128, 4 × 2.5 mm, a slice 180 mm (<i>Homo sapiens</i>) or 120 mm thick	0.9 s	173
9.4	¹²⁹ Xe*	Xe (10 ¹⁹ cm ⁻³ , 70% ¹²⁹ Xe) in mice lungs <i>in vitro</i>	gradient echo (FLASH)	2D	128 × 128, (0.37 mm) ²	600 ms	174
9.4	¹²⁹ Xe*	xenon (70% ¹²⁹ Xe) in mice lungs <i>in vivo</i>	the same	2D	64 × 64, (0.39 mm) ² , a slice 2 mm	250 ms	175
4.7	¹²⁹ Xe*	xenon in rat lungs <i>in vivo</i>	"	2D	2.3 × 4.7 mm, a slice 15 mm thick	1.3 s	176
1.5	¹²⁹ Xe*	xenon (71% ¹²⁹ Xe) in human lungs	"	2D	64 × 128, (6.6 mm) ² , a slice 20 mm thick	12 s	177
1.5	¹²⁹ Xe*	xenon in the human oral cavity	gradient echo	2D	256 × 128, 1.6 × 3.1 mm, a slice 1 cm thick	—	178
2.0	³ He*, ¹²⁹ Xe*	helium or Xe in guinea pig lungs <i>in vivo</i>	FID, radial trajectories	2D	256 × 256, (188 μm) ² (³ He), 128 × 128, (847 μm) ² (¹²⁹ Xe)	4 s (³ He), 8 s (¹²⁹ Xe)	179
2.0	³ He*, ¹²⁹ Xe*	helium or Xe (82% ¹²⁹ Xe) in guinea pig lungs <i>in vivo</i>	the same	3D	128 × 32 × 128; 0.37 × 1.2 × 0.37 mm (³ He), 0.56 × 1.25 × 0.56 mm (¹²⁹ Xe)	—	180
2.0	¹²⁹ Xe*, ¹ H	xenon in rat lungs, blood and tissues <i>in vivo</i>	phase encoding, FID	1D, 2D	64 points, 1.8 mm (1D); 32 × 32, (1.9 mm) ² or (3.1 mm) ² (2D)	4 min (2D)	181
2.0	¹²⁹ Xe*, ¹ H	xenon in rat brain <i>in vivo</i>	chemical shift selective imaging	2D	32 × 32, (1.6 mm) ² , a slice 10 mm thick (Xe)	73 s	184
4.2	¹²⁹ Xe*	xenon (80% ¹²⁹ Xe) in human blood <i>in vitro</i>	spin echo (EPI)	2D	128 × 64	—	185
2.0	¹²⁹ Xe*	xenon (82% ¹²⁹ Xe) in rat blood <i>in vivo</i>	gradient echo (GRASS)	—	256 × 256 (256 × 128)	10 s	186
2.0	³ He*, ¹ H	xenon (80% ¹²⁹ Xe) in rat blood <i>in vivo</i>	gradient echo (time-of-flight angiography for ¹ H)	2D	256 × 256, (0.31 mm) ² (a slice 0.7 mm thick for ¹ H)	—	187
4.7	¹ H	vulcanised rubber impregnated with aluminium and sodium sulfate crystals, filled phenolaldehyde resin, or a 72-h <i>Manduca sexta</i> caterpillar	spin echo or PRI	—	180 FID, (35 μm) ² (PRI); 128 × 128, a slice 1 mm thick or without slice selection	2–17 h	192
0.5	¹⁹ F	a fluoroplastic cylinder	PRI	2D	1 mm	—	194
9.4	¹ H	hexamethylbenzene powder	magic echo	3D	64 × 64 × 64; (300 μm) ³	70 h	197

Table S.1 (continued).

Field /T	Nucleus	Object, process	Technique	Dimension	Spatial resolution characteristics ^a	Recording time	Ref.
2.35	¹ H	agar gel doped with Mn(II), mortar, concrete or polyethylene	SPRITE	2D	64 × 64, (1.25 mm) ² – (1.5 mm) ²	—	206
0.73	¹ H	plastic or rubber items	gradient echo with oscillating gradients	3D	64 × 64 × 64; (0.5 mm) ³	3 h 38 min	209
0.4	¹ H	various solid materials	spin echo	—	WSR	—	228
—	¹ H	a glass supported tripropylene glycol diacrylate film, butadiene–styrene rubber	magic echo or gradient echo	1D	350 μm	—	235
4.7	¹ H, ¹³ C	CHCl ₃ or 0.3 M CHCl ₃ in CDCl ₃ in an ampoule or between two coaxial cylinders	spin echo	1D	—	—	270
1.4	¹ H	water or agar gel in a tube	the same	—	WSR	—	271
7	¹ H	water in coaxial tubes	spin echo or stimulated echo	2D	64 × 64; (50 μm) ² , a slice 1.2 mm thick	—	272
9.4	¹ H	water or polydimethylsiloxane in a packed bead of silica granules	spin echo	—	WSR	—	273
1.5	¹ H	rabbit skeletal muscle or kidney cortex (<i>in vivo</i>)	gradient echo	2D	256 × 128, 0.63 × 1.26 mm, a slice 5 mm thick	7–18 s	274
1.5	¹ H	polyacrylamide gel or porcine liver <i>in vitro</i>	gradient echo or spin echo	2D	256 × 192, 0.78 × 1.05 mm, a slice 5 mm thick	—	275

Note: PRI is projection reconstructed imaging, WSR is without spatial resolution, FID is free induction decay, EPI is echo-planar imaging and FLASH is fast low-angle shot.

^a Listed are the image dimension (in pixels), spatial resolution and slice thickness.

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Institute of Problems of Chemical Physics of the Russian Academy of Sciences



This issue of the journal 'Russian Chemical Reviews' is fully composed of papers contributed by staff researchers of the Institute of Problems of Chemical Physics of the Russian Academy of Sciences (IPCP RAS), one of the leading research institutes of the Division of Chemistry and Materials Science of the RAS. In 1956, Academician N N Semenov, the former director of the Institute of Chemical Physics (ICP) of the USSR Academy of Sciences and a Nobel Prize Winner, and F I Dubovitsky, Corresponding Member of the USSR Academy of Sciences, set up an affiliated branch of ICP in the village of Chernogolovka (Noginsk Region near Moscow) with the primary goal to carry out large-scale research in combustion and explosion processes. In 1972, the affiliated branch was rearranged into a section of ICP and in 1991 the section was reorganised into the Chernogolovka Affiliation of ICP (presently, IPCP RAS).

The main lines of research pursued at IPCP RAS are as follows:

- general problems of chemical physics;
- structures and compositions of molecules and solids; kinetics and mechanisms of complex chemical reactions;
- physical chemistry of combustion and explosion;
- preparation and modification of polymers;
- biological processes and systems.

Noteworthy, all these studies have a common basis, *viz.*, study of kinetics and mechanisms of diverse chemical and biological conversions.

The Institute has at its disposal a unique experimental base: proving grounds; specialised reinforced premises for large-scale studies of fast processes; chemical, technological and microbiological pilot plants; a vivarium; cryogenic equipment; a multi-access analytical centre for experimental support of investigations in the framework of projects of the Russian Foundation for Basic Research (RFBR) and state-sponsored research programmes of the Russian Ministry for Industry, Science and Technology.

The computer centre of IPCP is equipped with the most up-to-date computing system RM 600 E60/E20 (Siemens, FRG) which is integrated into the computer network of the Chernogolovka Research Centre and provides facilities for other research institutes of the RAS residing in Chernogolovka as well as for Moscow State University (MSU), Moscow Institute for Physics and Technology (MIPT), Moscow Engineering and Physical Institute and many other research and educational institutions in Moscow, Kazan, Rostov-on-Don, Ivanovo and other cities. The establishment of a high-capacity computer centre at IPCP has made it possible to state new fundamental tasks:

- design of software tools for numerical simulation of development of hydrodynamic instability;
- development of an 'individual particles' technique for description of high-energy pulsed processes;
- study of phase transitions in organic crystals;
- quantum-chemical studies of mechanisms of chemical conversions in organic compounds.

Researchers at IPCP have developed new generations of software complexes based on the use of massively parallel technologies which allows one to reduce the computation time 10–20-fold and to carry out direct simulation of fire- and explosive-hazardous events at chemical and nuclear units.

The staff of the Institute consists of more than 800 researchers including 109 D.Sci. and 322 Ph.D's. A department of the MIPT is functioning successfully on the mode of IPCP. An affiliated branch of the Department of Chemistry of MSU was established in IPCP in 1995 owing to the joint efforts of IPCP RAS and the Department of Chemistry of MSU. The Moscow Regional Affiliation of MSU, which includes departments of chemistry, physics and geology, has been functioning at IPCP since 1997. The Institute provides degree research facilities to students of senior courses of MSU, MIPT and other higher educational establishments; postgraduate students prepare their doctoral theses on the

basis of the Institute. IPCP has three expert councils for Ph.D. and doctoral theses; the post-graduate courses offer research facilities in 16 scientific disciplines.

In recent years, the interest of talented young scientists in scientific research has increased considerably owing to the organisation in the Chernogolovka Research Centre of a continuous educational system: school–college–postgraduate courses. At present, 30 students of IPCP are carrying out diploma works and over 30 people are postgraduate students.

The Institute carries out research in the framework of various projects supported by the RFBR (about 100 research projects annually), the European Union (INTAS), the International Science and Technology Centre (ISTC) as well as in the framework of Federal purpose-oriented programmes and RF President's Grants for leading scientific schools and collaborates with more than 50 universities and institutions in Russia and abroad.

Such a broad range of research, which encompasses virtually all main areas of chemical physics, is reflected in the present structure of IPCP. The Institute has ten sections: combustion and explosion; kinetics of chemical and biological processes; kinetics and catalysis; extremal states of substances; polymers and composite materials; structures of substances; photochemistry; functional inorganic materials; chemical technology; mathematics. In-depth fundamental studies carried out at IPCP have provided results of fundamental importance in all these areas.

Methods for exact calculation of complex surfaces of potential energy and dynamics of elementary processes have been developed. The quantum theory of molecular rearrangements has been devised. The rate constants for the main elementary reactions occurring in gas, liquid and solid phases have been established both theoretically and experimentally. The mechanisms of action of metalloenzymes have been investigated. These data served as a basis for the construction of purely chemical systems for photocatalytic liberation of hydrogen and oxygen from water, oxidation of methane and catalytic reduction of hydrogen under mild conditions.

The mechanism of combustion of condensed compounds has been investigated and its general theory is developed. Some methods of control over combustion have been proposed. The regularities of heterogeneous and filtrational combustion have been analysed.

In-depth studies into various aggregate states of substances and chemical and phase conversions at high pressures and temperatures under intense shock and detonation waves have been carried out. The thermal properties of dense plasma characterised by strong interparticle interactions as well as thermodynamic and conducting properties of gaseous and liquid hydrogen under conditions of multiple shock-wave loading have been investigated. The ability of hydrogen, helium and xenon to pass to a highly conducting (metallic) state has been established. The transition of metals (particularly, of lithium and sodium) into dielectric states at high dynamic pressures has been detailed. The electrical resistance of fullerite C₆₀ under dynamic conditions has been measured for the first time. It has been established that the temperature dependence of resistance of shock-loaded fullerite is reversible and typical of semiconductors.

In-depth studies are carried out at IPCP within the framework of a general problem: molecular structure–solid structure–physical and chemical properties of materials. This resulted in the preparation and investigation of a vast variety of superconductors, metals, photochromic materials, superionics, materials with a broad range of useful mechanical, electrical and optical characteristics, nanomaterials and fullerenes.

Chemical modification of various classes of antitumour cytostatics by incorporation of fragments of iminoxyl radicals (bio-antioxidants) has resulted in the development of novel classes of drugs manifesting a broad range of antitumour activities as well as membrane protectors and antioxidants.

Adequate nitrosyl models of active [Fe–S] centres of non-heme proteins, a novel class of promising medicinal drugs, have

been obtained for the first time. Some new methods for the synthesis of these conjugates, which contain simultaneously two biochemical functional groups, *viz.*, the –NO group (radio- or chemosensitiser) and the –SR group (antibacterial and anti-inflammatory agents, enzyme inhibitors, antimetabolites), have been developed.

The Institute combines fundamental research with the solution of applied practical tasks and is actively engaged in the development and commercialisation of advanced technologies and processes. The German company 'Linde' has purchased the Institute's license for highly selective synthesis of higher linear α -alkenes based on controlled dimerisation and oligomerisation of ethylene and started the construction of several plants utilising this technology in Saudi Arabia. A process for pilot-plant production of poly- α -alkene bases for synthetic lubricants has been developed by IPCP in collaboration with the petrochemical company 'Petroleum Industry of Serbia'. This technology has served as the basis for the construction of the first plant in the Russian Federation for the production of synthetic motor oils in the town of Nizhnekamsk (Tatarstan).

The Russian–Chinese Joint Venture 'Sychuan Mianyang Lier' has been established for industrial realisation of a technology for preparation of pyridine-type pesticides developed by IPCP RAS in collaboration with the Chinese Academy of Physical Engineering. In 1997, the production of 3,6-dichloropicolinic acid and Lier (which represents an analogue of Lontrel) was set in operation at the Mianyang plant belonging to the Company.

In-depth studies of non-equilibrium filtration combustion processes have led to the development of environmentally safe technologies and equipment for processing industrial and domestic wastes and low-grade combustible fuels aimed at production of thermal and electric energy. Commercial plants for processing quenching oils (JSC 'Electrostaltazhsmash', Electrostal', Moscow Region) and household wastes (Lappeenranta, Finland) have been set up. The assembly of an incineration plant is near completion in Moscow.

Active engagement of IPCP RAS in the activities connected with commercialisation of its own achievements has led to the establishment, in 2001, with the assistance of the Academy of National Economy at the Government of RF and the British Council, of a new section, *viz.*, a Centre for commercialisation, which is aimed at performing technological audits, legal regulation and market research. The experts at the British Council render permanent support for the newly established Centre in organising training seminars on technological audits. This undertaking has received further support. At the end of 2002, it was decided to establish an Innovation-Technological Centre of the RAS on the basis of the Chernogolovka Research Centre in order to meet the need for qualified personnel for innovation spheres. The agreement on its establishment has been made between the Russian Academy of Sciences, MSU, the Government of the Moscow Region and the Academy of National Economy of the RF Government. One of the main provisions of this agreement is education of specialists and acquisition of professional skills and knowledge in the field of technological management, which includes commercialisation of new developments, estimation of commercial potentials of novel technologies, attraction of investments and advancement of novel technologies and scientific and technological products in the market.

The Institute takes an active part in international and domestic scientific-and-industrial exhibitions. In the past five years, IPCP researchers participated in 61 exhibitions, such as the International Industrial Fair in Hannover (FRG), Salon of Innovations, Novel Technologies and Inventions at Pittsburg (USA), and domestic exhibitions 'Khimekspo' and 'Ekspogorod'. Many of them won prizes at popular international exhibitions ('Innovations: Novel Materials and Chemical Products', 'Science and Scientific Instruments', 'Salon of Industrial Property 'Archimed') and the national exhibition 'Technologies from Russia'. The developments of the Institute were highly appraised

by the Jury of the 51st Salon 'Brussels: Eureka-2002' where they were awarded three gold, one silver and one bronze medals.

Every year, researchers of IPCP publish about 350 papers in domestic and foreign journals and make about 400 reports at national and international conferences. In the past five years, 34 monographs of IPCP researchers came out of such highly reputed publishing houses as Gordon and Breach, Elsevier, Springer, Kluwer Academic, Nauka, Khimiya, *etc.* The Institute publishes books of collected papers on diverse problems of chemical physics, physical chemistry, combustion and explosion, chemical kinetics, physics and chemistry of polymers. The Institute owns more than 60 patents for advanced developments and technologies; of those, 30 patents were granted in the last five years.

The Institute supports the organisation of numerous national and international scientific conferences and symposia devoted to combustion and explosion, chemistry and physicochemistry of oligomers, physical and chemical characteristics of elementary chemical processes, crystal chemistry and catalysis.

Several researchers of IPCP were awarded the honorary title 'Honoured Scientist of Russia'. Among other rewards granted to IPCP members in the new millennium are the Government Prize of RF for innovative activity, RF prizes for young scientists for outstanding achievements in science and technology and the European Academy prizes for young Russian scientists. In 2002, Academician V E Fortov was awarded a prestigious prize of the Max Planck Society for a series of experimental and theoretical investigations on the properties of various substances under extremal conditions.

The reviews published in this issue do not cover the whole range of investigations carried out at IPCP; many of the research subjects are intended for consideration by the physical community only.

As was mentioned previously, one of the most actively developed lines of research at IPCP is chemical physics of the formation and modification of polymers, namely, the kinetics of the formation and destruction of polymers, macromolecular design, interphase events occurring in polymers and composite materials; design and investigation of polymers and composite materials possessing unique optical, electrical and magnetic properties, structural theory of macromolecules and phase formation in polymeric materials; physical methods for studies of polymeric materials, *etc.* This line of research is detailed in the review by G V Korolev 'Current trends in investigations into the micro-heterogeneous mechanism of three-dimensional radical polymerisation' and the review by D P Kiryukhin and I M Barkalov 'Chain chemical reactions at low temperatures'.

Yet another important trend which combines different lines of research carried out at IPCP is related to the study of kinetics,

mechanisms and elementary acts of chemical reactions. Of particular interest is the study of short-lived intermediate species involved in these reactions. The review by E Ya Misochko, A V Akimov and I U Goldshleger 'Modern applications of matrix isolation technique to investigation of radical species generated in atom-molecular chemical reactions' describes one of the most efficient in contemporary chemical physics techniques for the study of transient products and its application to concrete systems. Special attention is given to the analysis of conditions for the stabilisation of radical intermediates generated in cryochemical reactions and combined applications of various spectroscopic techniques.

The fundamental line of research aimed at activation of hydrocarbons by transition-metal complexes is led by Academician A E Shilov. Some aspects of this problem have been considered in the review by V D Makhaev 'Structure of methane complexes according to the data of experimental and theoretical investigations', which is devoted to the analysis of relationships between the nature of the central metal atom and the ligands and coordination of methane within complexes with neutral atoms, ions and molecular fragments and the comparative study of structural regularities of methane and tetrahydroborate complexes.

The kinetics and mechanisms of thermal decomposition of high-energy compounds, their chemical stability and application safety have long been studied by F I Dubovitsky, Corresponding Member of RAS. The results of long-term exploratory works aimed at the synthesis of novel representatives of high-energy compounds of the triazine series and their analogues are presented in the review by A V Shastin, T I Godovikova and B L Korsunskii 'Nitro derivatives of 1,3,5-triazine: synthesis and properties'. This is the first attempt to systematise the published data on novel 1,3,5-triazine derivatives as high-energy and biologically active substances and reagents for organic synthesis. The ability of trinitromethyl groups of 1,3,5-triazine derivatives to undergo nucleophilic substitution presents unquestionable interest for the understanding of mechanisms of nucleophilic aromatic substitution in heterocyclic compounds.

These are only a few trends of research being carried out at IPCP. In one of the next issues of Russian Chemical Reviews we shall continue to get you acquainted with the results of our investigations. For more detailed information see our web-site (<http://www.icp.ac.ru>).

S M Aldoshin, Corresponding Member of the RAS
Director, IPCP

Current trends in investigations into the microheterogeneous mechanism of three-dimensional radical polymerisation

G V Korolev

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Abstract. Data on the kinetics and mechanism of the three-dimensional radical polymerisation of multifunctional vinyl monomers (oligomers) containing two (or more) double bonds are generalised and analysed. The history of this field of research is briefly outlined. The characteristic feature of the mechanism of three-dimensional radical polymerisation, *i.e.*, microheterogeneity, is considered. Special attention is focused on recent advances (last decade) in studies of three-dimensional radical polymerisation associated with the development of new techniques (fiber-optic techniques, information technologies, *etc.*). Consideration is given to methodological aspects of kinetic experiments in highly cross-linked reaction media in which three-dimensional radical polymerisation proceeds. The bibliography includes 223 references.

I. Introduction

In 1977, rigorous proof of the specific mechanism of radical polymerisation of multifunctional monomers (oligomers) was reported for the first time.¹ In the last 25 years, this mechanism found considerable supporting evidence. Presently, this mechanism is called microheterogeneous. The hypothesis about the microheterogeneous character of the formation of highly cross-linked polymer networks (three-dimensional polymerisation) was advanced long before 1977 and was rather clearly formulated by Howink as early as 1934.² Later on, this idea was developed by Kozlov,^{3,4} Galacher and Bertelheim,⁵ Korolev *et al.*,^{6,7} Notley,⁸ Bobalec *et al.*,⁹ and Dušek.¹⁰

First attempts to refine the model of microheterogeneous radical polymerisation were undertaken using the three-dimensional radical polymerisation (TRP) of phenol–formaldehyde resins as an example.^{3,4} In 1962, the knowledge of the mechanism of radical polymerisation was substantially improved due to the application of light scattering to the investigation of the nucleation and evolution of microheterogeneity (microgel particles) in

the course of the polymerisation of unsaturated esters.⁵ In the same year, an hypothesis was proposed about the formation of discrete microgel particles, which serve as autonomous microreactors in the course of the polymerisation of multifunctional methacrylic esters.⁶ In such autonomous microreactors, polymerisation proceeds much more rapidly than in the remaining bulk of the reaction system due to the local gel effect. In addition, important details of the TRP mechanism were revealed.⁸ In 1964, the microheterogeneous mechanism was postulated also for three-dimensional polyesterification of non-radical three-dimensional polymerisation processes.⁹ In 1970, the mechanism of TRP involving microheterogeneity was formulated on the basis of new experimental data.⁷ In 1971, microsineresis was observed¹⁰ in the course of formation of highly cross-linked macromolecular structures.

However, only long-term studies of model objects, *viz.*, oligoester acrylates (OEA) belonging to a new class of unsaturated oligomers whose chemical structures were varied in a desired mode,[†] with the use of original procedures[‡] culminated in 1977 with experimental evidence for the microheterogeneous mechanism of radical polymerisation. Hence, the above hypothesis not only became a proven concept but also was detailed. This provided a model suitable for quantitative calculations. The results of these calculations were reported in the study.¹¹

The present review surveys the most important stages of investigation into three-dimensional radical polymerisation of multifunctional oligomers, which is one of the most important fields of polymer science. Considerable progress made in this field recently in response to the requirements of modern technology is associated mainly with advances made due to the discovery of microheterogeneity as the main characteristic feature of the mechanism of TRP. Prospects of further progress are based on the possibilities of modern computer modelling and the discovery of new phenomena in the kinetics of radical polymerisation (living chains, kinetically active associates).

G V Korolev Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 515 54 20. Tel. (7-096) 522 10 89. E-mail: korolev@icp.ac.ru

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[†] The compounds were synthesised by A A Berlin and co-workers in the N N Semenov Institute of Chemical Physics of the Russian Academy of Sciences.

[‡] Procedures specially designed for kinetic, structural and physical measurements during TRP were developed by G V Korolev and co-workers in the N N Semenov Institute of Chemical Physics of the Russian Academy of Sciences.

II. Characteristic features of three-dimensional radical polymerisation

Three-dimensional radical polymerisation can involve many practically important classes of unsaturated multifunctional compounds, *viz.*, oligoester acrylates and maleates (for example, maleate–styrene resins), compositions based on allylic compounds, divinylbenzene and its derivatives. Oligoester acrylates are used as construction materials in the aircraft industry (as fiber glasses), paint-and-varnish materials and hermetics, stomatological materials (fillings, protection varnishes, materials for prosthetics) and modern liquid-crystalline systems. Since maleate–styrene resins contain a volatile toxic component (styrene), these polymers are of limited utility. Other classes of polyunsaturated compounds are of even more limited use. For example, divinylbenzene is used primarily in the synthesis of polymeric substrates for ion-exchange resins.

The TRP polymers are infusible and insoluble. These valuable properties are common to all polymers formed by any type of three-dimensional polymerisation, including non-radical polymers (for example, polycondensation of epoxide or phenol–formaldehyde resins). The advantages of TRP are both high polymerisation rates at rather low temperatures and the fact that various specific (associated with the chain nature of the process) highly efficient methods are available, which allow one to influence the TRP rate just in the course of radical polymerisation. These methods are: (1) the use of initiators (organic peroxides, azodinitriles, *etc.* at concentrations of 10^{-3} – 10^{-2} mol litre $^{-1}$), which enable one to reach very high TRP rates (10^{-2} – 10^{-3} mol litre $^{-1}$ s $^{-1}$) at moderate temperatures (300–350 K); (2) the use of inhibitors (stable free radicals, quinones, haloids, nitro compounds, *etc.* at concentrations of 10^{-4} – 10^{-2} mol litre $^{-1}$), which allow one to suppress TRP within a predetermined period of time τ (induction period) in order to prevent premature spontaneous polymerisation, particularly, in the course of technological processes; (3) the use of external sources of initiation (light or radiation), which enables one to start or terminate the TRP process at any temperatures (including below room temperature) at any instant of time and to control the TRP rate within any limits by decreasing or increasing the irradiation intensity. In the last-mentioned case, it is possible to reach high rates such that highly reactive monomers (for example, oligoester acrylates) are virtually instantaneously cured into thin films, which is of considerable importance, for instance, in solving the problem of freezing of liquid-crystalline structures.

Three-dimensional radical polymerisation can involve only unsaturated compounds (monomers, oligomers) whose molecules contain two or more double bonds. Only in this case does polymerisation afford linear chain structures (primary carbon chains) bearing one (if the starting monomer contains two multiple bonds per molecule) or more (if the number of multiple bonds is larger than two) double bonds that remain intact per unit (pendant vinyl groups), which serve as centres of branching and cross-linking of carbon chains to form a network. Further polymerisation of these vinyl groups gives rise to secondary structures (first branched structures and then three-dimensional networks) in which carbon chains are cross-linked to each other by cross-bonds, the starting molecules located between the vinyl groups (oligomeric blocks) serving as such cross-links. Generally, the latter are heteroatomic chains consisting of two or more carbon atoms and two or more heteroatoms (oxygen, nitrogen, sulfur, phosphorus, *etc.*).

Figure 1 shows successive stages of TRP exemplified by monomers containing two vinyl groups each. Apparently, the final structure is a macromolecular three-dimensional network. Hence, polymerisation of such polyfunctional compounds is called three-dimensional polymerisation. Network junctions are of the utmost importance as characteristics of highly cross-linked macromolecular structures, because it is the junction mobility that controls the relaxation properties of polymeric materials, which,

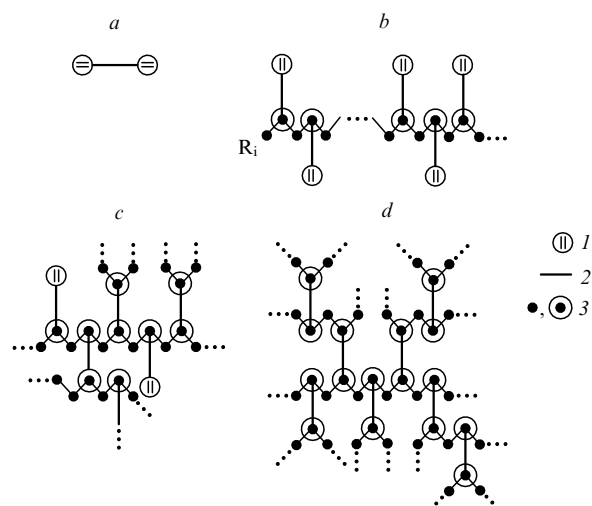


Figure 1. Successive stages of TRP of monomers containing two vinyl groups each; (a) the initial state, (b) primary (non-branched) polymer chain containing pendant double bonds, (c) fragment of the network with an incomplete structure (conversion < 1), (d) fragment of the final network (conversion is ~ 1); (1) vinyl groups, (2) oligomeric blocks, (3) secondary or tertiary carbon atoms containing substituents H or R, R_i is the radical of the initiator.

in turn, determine their main physical–mechanical characteristics. It can be seen that TRP gives rise to trifunctional junctions. Two or three interjunction chains per junction are very short rigid carbon chains $-\text{CH}_2-$, whereas the third heterochain (best suited for constructing a cross-linked structure) is longer and more flexible due to the presence of heteroatoms (in particular, oxygen). In the worst situation, this chain is also rigid, for example, in monomers of divinylbenzene, whose molecule contains the rigid aromatic $-\text{C}_6\text{H}_4-$ fragment and is devoid of heteroatoms.

The above-described topological feature is typical of polymer networks formed in TRP. Other types of polymerisation, for example, non-radical three-dimensional polymerisation (polycondensation) of compounds devoid of double bonds, afford products in which two short carbon chains are absent, because the latter can be generated only through the radical-initiated cleavage of multiple bonds. Catalytic hardening of diepoxides gives rise not to $-\text{CH}_2-$ but to $-\text{OCH}_2-$ heterochains, which, being also short, are much more flexible. Hence, macromolecular networks formed in the course of TRP, all other factors being the same, should be characterised by rigid structures and low relaxation ability. In certain cases, this is an advantage, whereas in other cases this is a drawback. Networks can be rather easily modified by copolymerisation with the use of comonomers, which contain only one double bond per molecule and are able to alternate under given conditions (copolymerisation constants for the monomers r_1 and r_2 are lower than unity). In this case, short interjunction carbon chains are elongated, but the volume concentration of the network junctions simultaneously decreases.

Three-dimensional radical polymerisation is a specific process. Thus, a homogeneous reaction system is transformed into a microheterogeneous system (microgel, nanodispersion) consisting of cross-linked polymer particles, which are rather weakly linked to each other by crossing chains, virtually from the very beginning of the polymerisation. These particles serve as autonomous microreactors in which further polymerisation proceeds. The particles remain discrete upon the completion of the polymerisation process. This is responsible for the specific morphology of TRP products as a nanodispersion of highly cross-linked particles (grains) separated by interlayers of a poorly cross-linked (defect) polymer (Fig. 2).

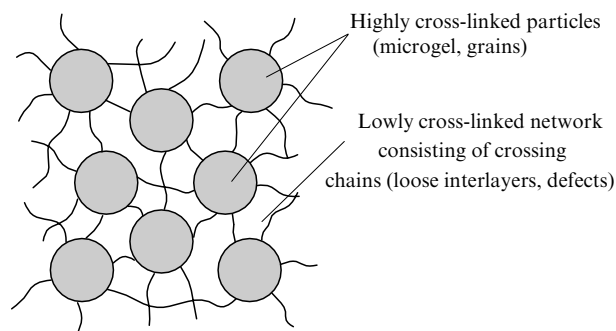


Figure 2. Morphology of TRP products as highly cross-linked particles separated by interlayers of a lowly cross-linked polymer.

The above-mentioned features complicate the TRP process. Therefore, the elucidation of the mechanism of TRP called for the development of a special methodology and new theoretical research in the field of radical polymerisation. As a result, TRP was classified as a special case of radical polymerisation, which could not be interpreted within the framework of the commonly accepted notions.

The basic research into the TRP mechanism was completed in 1977,¹ when the microheterogeneous model was proposed. These new concepts were experimentally supported by a series of systematic studies of the kinetics and mechanism of curing of oligoester acrylates. The latter proved to be very convenient model compounds for such studies, because the procedure for their synthesis enables one to vary the chemical composition and the length of oligomeric blocks over wide ranges in a desired fashion, while the terminal groups (methacryl or acryl), which are able to undergo polymerisation, remain intact.

Below are given the chemical formulae of several types of oligoester acrylates, which served as the basic compounds for revealing the fundamental features and mechanism of TRP.

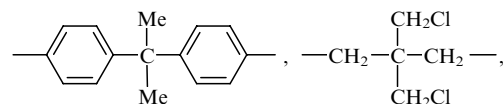
Oligoesters containing unsaturated terminal groups, which are able to undergo TRP, can be described by the general formula



where the substituents R^1 , R^2 and R^3 correspond to saturated dicarboxylic acids, polyols and unsaturated monocarboxylic acids, respectively; $n = 0, 1, 2, \dots$ (preferentially, $n \leq 2$). For oligomers of the first type, $\text{R}^2(\text{OH})_2$ is generally a diol $[(\text{CH}_2)_m(\text{OH})_2]$, $m = 1, \dots, 10$ and $\text{R}^3\text{CO}_2\text{H}$ is generally acrylic or methacrylic acid. Phthalic, adipic, sebacic, thiodivaleric and carbonic (used as COCl_2) acids can serve as $\text{R}^1(\text{CO}_2\text{H})_2$. In the case of carbonic acid, the oligoester fragment of molecule **1** includes not only ester groups $[-\text{C}(\text{O})\text{O}-]$ but also carbonate groups $[-\text{OC}(\text{O})\text{O}-]$ possessing specific properties. Hence, oligoester acrylates of this type are considered as a special class and are called oligocarbonate (meth)acrylates.¹² For this type of oligoester acrylates, the functionality in the TRP process (f) determined by the number of terminal groups (multiple bonds) in the molecule, which can be involved in polymerisation, is equal to two.

Oligoester acrylates of the second type described by formula **1** contain polyol $\text{R}^{2'}(\text{OH})_m$, where $m > 2$ (generally, glycerol with $m = 3$ or pentaerythritol, xylitol with $m > 3$) instead of diol $\text{R}^2(\text{OH})_2$. For such oligoester acrylates, the functionality in TRP is 3 (or larger). Correspondingly, the volume-averaged concentration of the macromolecular network junctions in the polymer increases (compared to oligoester acrylates of the first type).

Different reactions resulting in the introduction of various fragments, such as



the urethane groups, the symmetrical triazine ring, phosphorus-containing groups and metals, into compounds **1**,¹¹ give rise to oligoester acrylates of the third type.

III. Methodological basis of three-dimensional radical polymerisation

Beginning in 1960, systematic studies on the synthesis of various oligoester acrylates with variable structures were carried out by researchers under the supervision of A A Berlin. The results of these studies not only stimulated fundamental investigation but also gave impetus to the development of new (and also to the improvement of known) experimental techniques for studying the kinetics and mechanism of TRP (including structure–physical studies of polymerisates). The necessity of developing such techniques was dictated by the fact that conventional methods (gravimetry, dilatometry, molecular-mass distribution measurements, *etc.*) are inefficient in studies of TRP due to cross-linking of the reaction system in the early stages of polymerisation and the insolubility of the polymer formed.

Calorimetry,^{13–25} spectroscopy,^{13, 23, 26–34} densitometry¹³ and other kinetic methods^{13, 24, 35–57} proved to be most efficient in studies of the kinetics and mechanism of TRP as well as of the structure–physical features of highly cross-linked polymers.

1. Calorimetry

High-precision isothermal microcalorimetry using Calvet calorimeters finds wide application. Studies with the use of DSC non-isothermal calorimeters followed by complex mathematical treatment of experimental data give less reliable results. High heats of polymerisation ($\Delta H = 42–92 \text{ kJ mol}^{-1}$) are virtually independent of the conversion. Hence, only the velocity of heat evolution dQ/dt in the course of polymerisation can be continuously recorded with high accuracy by identifying this velocity with the polymerisation rate

$$W = -\frac{d[M]}{dt} \equiv \frac{dQ}{dt}.$$

The difference between the initial and running concentrations of the monomer $[M_0] - [M_t]$ is equal to the instantaneous quantity of liberated heat Q divided by ΔH of the monomer. In the case of copolymerisation, when

$$[M] = \sum_i M_i$$

and

$$\Delta H = \sum_i H_i,$$

the application of calorimetry to kinetic measurements is limited to azeotropic systems characterised by constant compositions of the monomer mixture and copolymer in the course of copolymerisation. For example, copolymerisation of the compound M_1 containing reactive styrene groups with the compound M_2 containing the methacryl groups in a molar ratio $[M_1]:[M_2] \simeq 1$ afforded a copolymer consisting of alternating units (because the copolymerisation constants correspond to the condition $r_1 \simeq r_2 < 1$), whose composition is independent of the conversion. In this case, the molar heat of copolymerisation can be calculated by averaging the heats of homopolymerisation of both monomers

$$\Delta H = 0.5(\Delta H_1 + \Delta H_2).$$

Then

$$[M] = [M_1] + [M_2] = \frac{2Q}{\Delta H_1 + \Delta H_2}$$

and

$$[M_1] = [M_2].$$

Most data on the TRP kinetics published in 1960–2003 were obtained by calorimetric methods.

Considerable progress has been made in the calorimetry of TRP, particularly in studies of photochemically initiated fast processes. The use of high-precision quick-response photocalorimeters, for example, a DSC-7 differential scanning calorimeter, Perkin-Elmer, Norwalk and CT,¹⁵ photocalorimeters¹⁵ equipped with a monochromatic photoaccessory, allows one to perform measurements in a second-scale range and, consequently, to record the kinetics of very fast TRP processes not only in the steady-state mode (during photoinitiation) but also in the post-effect mode (after termination of photoinitiation) at any stage of polymerisation (especially, at high conversions). Such a combination of steady- and non-steady-state kinetic measurements is necessary for estimating the rate constants of elementary stages of chain propagation and termination (k_p and k_t , respectively) as functions of the conversion (C). The results of such calculations are used as components of the database for macromolecular design.

It should be noted that the parameters $k_p = f(C)$ and $k_t = \varphi(C)$ for TRP (for oligoester acrylates) were experimentally measured for the first time in the 1960s.^{13, 24, 25}

2. IR spectroscopy

For kinetic studies of TRP, second in importance to calorimetry is the IR spectroscopic method of the determination of the instantaneous concentration of double bonds. In the Real-Time Infrared (RTIR) version, this method (1430, Perkin-Elmer, Norwalk and CR spectrometers) proved to be even faster than the photocalorimetric method. It enables one to solve the same problems of the stationary and non-stationary kinetics in an even shorter time. For example, the instantaneous concentrations of double bonds in acrylates were measured very rapidly (20 spectra per second)⁸ from the peak at 811 cm^{-1} .²⁶ The main source of errors in IR spectroscopy as applied to TRP is associated with the distortion of the spectral shape, which increases as the conversion increases due to cross-linking of the matrix. The latter is tantamount to a change in the calibration in the course of transformation. Generally, this problem can be solved to a greater or lesser extent on the basis of choosing spectral lines which show the least changes with increasing conversion.

3. Densitometry

Densitometric methods of kinetic measurements, particularly those on the basis of flotation and titration, proved to be convenient under the conditions of TRP. Densitometric methods are based on an increase in the density of polymerisation systems (from the density of the monomer up to that of the polymer) with increasing conversion. The difference between these values is 10%–20% of the density of the starting system. The density increases linearly with conversion. The deviations from linearity may appear only at high conversions in the case of very dense networks and high rates of TRP. Under these conditions, physical processes of structural relaxation may lag compared to the chemical addition reaction accompanying the contraction. Evidently, this complication is also inherent in dilatometry, which is based on measurements of the contraction of a polymerisation system in the course of TRP.²⁴

§In the plenary paper (*Photopolymerisation of functionalised oligomers*) presented at the International Conference on Chemistry and Physical Chemistry of Oligomers (September 9–14, 2002, Moscow–Chernogolovka), C Decker reported that this number could be increased to 50 spectra per second.

4. Other methods of kinetic measurements

Such methods as gravimetry, chemical analysis (determination of the concentration of double bonds),³⁵ dilatometry and some other techniques are employed with advantage and give excellent results in studies of radical polymerisation. However, substantial modifications of these methods were required to use them in the investigation of TRP. The first two methods deal with monomers isolated from reaction systems, and it is necessary to modify procedures for isolation, because conventional precipitation of the polymer cannot be performed due to cross-linking, while extraction may appear to be incomplete due to the presence of pendant double bonds. Hence, isolation should be preceded by the stage of de-cross-linking³⁶ (a very cumbersome and insufficiently selective process of destroying interchain cross-links, for example, by hydrolysis if cross-links contain ester or other bonds subjected to destruction by hydrolysis). The classical version of dilatometry is unsuitable for studies of TRP, because the system loses flowability in the early stages of polymerisation (at a conversion of less than 1%). Specially designed dilatometers are used, among which are long thin glass tubes (2–3 mm in diameter and 500–1000 mm in height), elastic dilatometers, etc. A very complicated differential dilatometric apparatus²⁴ equipped with two elastic cells and a high-precision detector of displacements proved to be most successful. This apparatus was used for performing the first non-stationary kinetic measurements of TRP processes and determining the dependences $k_p = f(C)$ and $k_t = \varphi(C)$.^{13, 25}

In recent years, specific methods in which the TRP process was monitored by indirect evidence associated with an increase in the viscosity, freezing of the molecular mobility of components of the reaction system, for example, of the unconsumed monomer (NMR spectroscopy^{37, 38}) or the addition of compounds, which are specially introduced as a molecular probe (fluorescence methods^{40–43}), have also gained acceptance. Compounds, which can undergo isomerisation in a TRP system, are also used as molecular probes.⁴⁴ If the activation volume in polymerisation is rather large, the isomerisation rate can serve as a measure of the free volume in the isomerisation system and, consequently, as an indirect characteristic of the conversion.

The use of isomerisable compounds, such as azobenzene and stilbene, as photochromic probes made it possible not only to observe an increase in the conversion in the course of TRP but also to judge the character of the free volume distribution in the system as well as to identify the microheterogeneous structure of the polymer network formed.⁴⁴

Methods based on light scattering are of particular importance in studies of the mechanism of TRP, because they allow one to observe the evolution of the structural microheterogeneity in the course of TRP.^{11, 45–53} The sizes of strongly branched macromolecules and microgels in the pre-gel state can be estimated with static and dynamic light scattering.^{20, 22, 54}

5. ESR method

Since free radicals $R^\bullet$ in cross-linked reaction media have long lifetimes (τ_R), the concentrations of $R^\bullet$ can be directly measured by ESR.^{11–13, 45, 50, 57–70} The use of ESR proved to be particularly efficient in the following fields of investigation: studies of the kinetics of accumulation^{11, 13, 45, 61, 62} and decay^{11–13, 45, 63} of free radicals and structure–physical studies.^{11, 45, 50, 65–70}

a. Studies of the kinetics of accumulation of free radicals in a non-stationary mode

In the case of the thermal decomposition of initiators (organic peroxides) in partially cured oligoester acrylates (30%–70% conversion), the temperatures of the process can be chosen in such a way that the kinetics of accumulation of $R^\bullet$ can be recorded by ESR over 10–20 min. For a non-stationary mode, this kinetics can be described by the following classical formula:

$$[R^\bullet] = \sqrt{\frac{W_i}{k_t}} \operatorname{th}(\sqrt{W_i k_t} t).$$

At short times

$$t \leq \frac{0.3}{\sqrt{W_i k_t}}$$

this formula is approximated by the equation

$$[R^*] \simeq W_i t,$$

at long times

$$t > \frac{1}{\sqrt{W_i k_t}}$$

this formula is approximated by the equation

$$[R^*] \simeq \sqrt{\frac{W_i}{k_t}},$$

which allows one to calculate W_i and k_t from the experimental data. The initiator and temperature can be chosen in such a way that once the stationary value of $[R^*]$ is attained, $[R^*]$ begins to slowly (at long times) decrease due to consumption of the initiator. Then, knowing the kinetics of this decrease, the rate constant of thermal decomposition of the initiator k_d can also be calculated. In this case, the efficiency of initiation can be estimated as

$$f = \frac{k_i}{k_d} = \frac{W_i}{[I]k_d},$$

where $[I]$ is the concentration of the initiator and k_i is the rate constant of initiation determined by the equation

$$W_i = k_i [I].$$

Therefore, this method enables one to determine k_i , k_d , k_t and f for TRP at high conversions and, correspondingly, to estimate the influence of cross-linking on chain initiation and termination. In the case of organic peroxides, k_t and f for oligoester acrylates decrease by factors of 10^6 – 10^7 and 25–50, respectively, as the conversion increases from 0% to 70%–90%. In the case of azonitriles as initiators, these values decrease by factors of 250–500.^{11, 13, 45, 61, 62}

b. Study of the kinetics of termination of accumulated free radicals

In studies of the kinetics of termination of accumulated (trapped) free radicals, photochemical or radiation initiation is used to prevent the undesirable thermal generation of R^* in the course of ESR measurements. Studies by ESR revealed important characteristic features. First, it was found that the kinetics of R^* death is described by the following complex equation:

$$[R^*] = f(t),$$

whose curve has bends at points $t_1, t_2, \dots, t_i$ ($i = 2-4$). In intervals between the bends, the kinetics are adequately described by the classical equation

$$-\frac{d[R^*]}{dt} = (k_t)_i [R^*]^2,$$

where $k_{t1} > k_{t2} > \dots > k_{ti}$. Second, the numerical value of k_{t1} correlates with the conversion and depends on the nature of the starting cross-linking monomer (oligomer). The factors controlling the flexibility of oligomeric blocks are of primary importance in these correlations. In a macromolecular network, the oligomeric blocks serve as interjunction chains, which link long carbon chains (*i.e.*, serve as interchain cross-links). The most important factors are the length of the oligomeric block and the presence of interatomic bonds characterised by low rotational barriers (for example, the replacement of the C–C groups by C–O–C leads to an increase in flexibility). Analysis of the termination kinetics of trapped R^* not only makes it possible to examine the mechanism of TRP but also enables one to obtain structure–physical information. Thus, bends in the $[R^*] = f(t)$ curves are indicative

of the microheterogeneity of a highly cross-linked polymeric matrix. The numerical values of k_{t1} serve as a measure of relaxation of a cross-linked structure at the molecular level.^{11–13, 45, 63}

c. Synchronic comparison of the $[R^*] = f_1(t)$ and $W = f_2(t)$ kinetic curves measured continuously

The polymerisation rate

$$W = f_2(t)$$

can be measured by any continuous method (preferentially, by high-precision kinetic calorimetry). Since

$$W = k_p [R^*] [M],$$

the current concentration of free radicals serving as chain carriers in the reaction system can be calculated from the instantaneous rate of TRP and the instantaneous concentration of the $[M]$ monomer according to the formula

$$[R^*]_2 = \frac{W}{k_p [M]}.$$

The concentration $[R^*]_2$ can be underestimated to any extent as compared to $[R^*]_1$ determined by ESR, because $[R^*]_2$ is the concentration of only those radicals, that are involved in chain propagation at a particular moment



If some radicals lose the ability to be involved in the reaction (for example, due to immobilisation in a highly cross-linked polymeric matrix), a synchronic comparison of the results of ESR measurements of $[R^*]_1$ with the results of calculations using kinetic data on $[R^*]_2$ makes it possible to determine the proportion of the radicals that lose activity

$$\gamma_R = \frac{[R^*]_1 - [R^*]_2}{[R^*]_1},$$

in a broad range of conversions and, consequently, to reveal the characteristic features of the changes in γ_R in the course of TRP. In the case of dimethacrylates, γ_R increases sharply once a certain (critical) conversion is attained. At moderate temperatures (20–70 °C), depending on the flexibility of the methacrylate molecules, this value varies from 10% (for very rigid molecules) to 50% (for very flexible molecules). The critical conversion increases as the temperature is raised.^{11, 13, 45}

d. Structure–physical studies by ESR

In studies of TRP products using paramagnetic probing with stable iminoxyl radicals externally introduced by vapour sorption,⁶⁵ two types of ESR spectra, *viz.*, narrow (2945.2–3024.8 A m^{−1}) and broad (5412.8–5651.6 A m^{−1}), are superimposed. This fact is interpreted as the manifestation of the microheterogeneity of TRP products. Thus, the narrow signal corresponds to defect microregions with a loose network (with a low concentration of junctions) and, correspondingly, with a high mobility of probe molecules (correlation time $\tau_c \ll 10^{-7}$ s), while the broad signal corresponds to microregions with low molecular mobility ($\tau_c \geq 10^{-7}$ s). When varying the temperature over a broad range (from −195 to +150 °C), the temperature range $\Delta T = T_2 - T_1$ (transition region) was found in which the intensity of the narrow signal increased at the expense of the intensity of the broad signal up to the complete disappearance of the latter at the upper limit ΔT (at T_2). Only the narrow signal was observed above T_2 . By contrast, only the broad signal was observed below T_1 . The state corresponding to the broad signal was interpreted as the glassy state, the state corresponding to the narrow signal was considered as the high-elasticity state, and ΔT was assigned to the α -transition region. Within the framework of this interpretation, the ratio between the intensities of the narrow (I_1) and broad (I_2) signals in the region of their superposition (ΔT)

characterises the ratio between the total microvolumes in the highly elastic and glassy states

$$\frac{I_1}{I_2} = \frac{\sum_{i=1}^m \Delta V_i}{\sum_{i=1}^n \Delta V_i},$$

where ΔV_i is the volume of the i th microregion, m , $(n - m)$ and n are the numbers of highly elastic and glassy microregions and their sum, respectively, and $\sum_{i=1}^n \Delta V_i$ is the total volume of the system.

Evidently, a smooth change in I_1/I_2 in a very broad range of ΔT (several tens degrees) can occur only if a microheterogeneous system consists of a large set of subsystems (microregions ΔV_i) including n different types of ΔV_i , each being characterised by its own (local) glass transition temperature T_{gi} , which successively changes in the series $\Delta V_1, \Delta V_2, \dots, \Delta V_n$. For example, $T_{g1} > T_{g2} > \dots > T_{gn}$. If n is rather large, a change in I_1/I_2 is smooth (without jumps). Apparently, the value of ΔT corresponds to the difference $T_{g1} - T_{gn}$ and, consequently, characterises the degree of microheterogeneity of TRP products (n is the number of subsystems ΔV_i , which differ by T_{gi} ; ΔV_i with higher degrees of cross-linking have higher local temperatures T_{gi}).

For oligoester acrylates,⁶⁵ ΔT values were estimated and their evolution in the course of TRP was traced. It was found that the degree of microheterogeneity characterised by the parameter ΔT increases with increasing conversion but only to a certain limit reached at $C \simeq 50\%$.

Other applications of ESR to structure–physical studies of TRP products, including radiation and diffusion probing, were described in the monographs^{11,45} and original publications.^{50,66–69}

A simple method was proposed for the identification of the structural heterogeneity of highly cross-linked methyl methacrylate–ethylene glycol dimethacrylate (EGDMA) copolymers.⁷⁰ The radicals accumulated in the polymer network were used to study the permeation of oxygen molecules by ESR. It was found that the permeability coefficient is maximum at the EGDMA concentration of ~ 70 mass %, which indicates that the porosity of the network increases with increasing concentration and reaches a maximum at the above-mentioned concentration of EGDMA.

This method can be considered as diffusion probing with oxygen molecules, which enables one to identify very small microheterogeneities.

6. NMR method

Nuclear magnetic resonance has proved to be an efficient method for studying chemical structures, molecular mobility and intermolecular interactions in high-molecular-weight compounds. However, this method is of limited use for studying TRP products because of their insolubility and non-fusibility. Of the other NMR techniques that are available, pulse NMR, broad-line NMR, and high-resolution cross-polarisation magic-angle spinning ¹³C NMR spectroscopic methods appeared to be the most efficient.^{37,38,43,45,59,71–73}

Studies of oligoester acrylates by pulse NMR demonstrated⁷¹ that the kinetics of the magnetisation decay includes at least two modes (fast and slow), whose contributions can be rather precisely separated due to a large difference in their relaxation times. Analysis of the kinetics of the magnetisation decay for a series of samples with different conversions led to the conclusion that a polymerisation system is microheterogeneous starting from low conversions up to completion of TRP.

Broad-line NMR spectroscopy is generally used for revealing the temperature dependence of the second moment of NMR lines in a broad temperature range. Analysis of this dependence allows one to judge the presence of relaxation transitions and to estimate

the corresponding activation energies. Investigation of a model series of oligoester acrylates with specified variations in the structure revealed fundamental characteristic features.^{45,72} High-resolution cross-polarisation magic-angle spinning ¹³C NMR spectroscopic studies of an analogous series of oligoester acrylates provided data on the configurations of the units in a polymer network and on the structural microheterogeneity manifested in broadening of spectral lines.

7. Physical-mechanical and thermomechanical methods

Upon deformation (ε) of TRP products in the mode of uniaxial compression with low rates ($\dot{\varepsilon} = 10^{-4} - 10^{-3} \text{ s}^{-1}$), profiles of deformation curves can be recorded in the range of $0 \leq \varepsilon \leq 0.5$ including the region of the transition from the Hook to the forced elastic deformation. Analysis of the profiles of deformation curves in this transition region allows one to draw justified conclusions about the structural features of highly cross-linked polymers, including their microheterogeneity. Thermomechanical curves $\varepsilon = f(T)$ in the region of the α transition are also suitable for an analogous analysis.

In the case of oligoester acrylates, physical-mechanical and thermomechanical measurements were carried out on a high-precision apparatus⁷⁴ specially designed for studying mini-samples ($\sim 0.1 \text{ g}$). These measurements were performed on a large number of various oligoester acrylates, including polymers, which can be synthesised only in small amounts and exclusively in laboratory conditions.

Physical-mechanical measurement in the dynamic mode have also been successfully employed in studies of the structures of TRP products. For this purpose, relaxation time spectra have been analysed. It was found that the degree of microheterogeneity of the structure correlates with the width of the spectra in a certain frequency region.⁷⁵

8. Application of pulsed radiation in non-stationary kinetic studies of three-dimensional radical polymerisation

A new promising method for determining the rate constants of elementary steps of the polymer chain growth is based on the use of pulsed coherent radiation (laser as a source) for photoinduced polymerisation followed by the analysis of molecular-mass distribution of the polymer formed (gel chromatography).^{76,77}

For TRP, this method can be used only in the early stages of polymerisation until the gel point is reached and the strongly branched polymer is still able to dissolve in chromatographic eluents.

Nevertheless, measurements of k_p even in this very limited conversion range ($C \leq 1\%$ in block polymerisation, $C \leq 10\%$ in solution) are of great importance, because they allow one to judge the effect of the degree of branching of growing polymer chains on their reactivity, which is one of the fundamental problems of TRP.

9. Complex techniques

Three-dimensional radical polymerisation involves a chemical transformation (radical polymerisation) and a series of competitive physical transformations (aggregation, microsineresis, *etc.*), which actively influence the chemical process. Hence, it is best to study TRP using complex techniques, which enable one to perform both kinetic measurements and follow the structural evolution in the course of polymerisation or reveal the structural features of the final polymeric products.^{11,15,20–23,34,35,39,43,45,48,50,53,54,66–69,78–86}

Advances in studies of the TRP mechanism and its main characteristic feature, *viz.*, microheterogeneity, are associated primarily with the development and use of a methodological complex, which involves more than ten kinetic and structure–physical methods.^{11,45,53} For example, in order for the structure–physical and kinetic information to be obtained directly in the course of polymerisation, the following combined approaches were developed: spectroturbidimetry in combination with calorimetry, the use of calorimeter–dielcometer, molecular labels and

IR spectroscopic monitoring of the kinetics of three-dimensional copolymerisation.^{48, 78–82} In some cases, not only known procedures were combined but also original techniques were developed. Among these methods are the detection of the local redistribution of an initiator using radiation probing in combination with diffusion probing with paramagnetic NO molecules.^{11, 45, 50, 66–69}

Studies of TRP by complex methods are being extensively developed.^{15, 20–23, 34, 35, 39, 43, 54, 83–86}

IV. Kinetic features of three-dimensional radical polymerisation

1. Characteristic features of polymerisation in a cross-linked polymerisation system at high conversion

All TRP processes follow the same scheme. The initial polymerisation rate W_0 is not constant even in a very narrow conversion range $0\% < C < 5\%$ and it increases virtually from the very beginning with increasing C . At a certain value of $C = C_{\max}$, the rate reaches maximum $W_{\max}$ followed by sharp autoretardation of TRP up to complete termination at $C = C_{\lim} < 100\%$. Apparently, both autoacceleration at the first stage of TRP at $0 < C \leq C_{\max}$ and autoretardation at the second stage at $C_{\max} < C \leq C_{\lim}$ should be interpreted within the framework of the diffusion kinetics. As the diffusion mobility of the reagents is frozen by the cross-linked structure formed in the reaction medium, first faster elementary steps (chain termination, k_t) and then slower elementary steps (propagation, k_p) become diffusion-controlled. Because of this, first autoacceleration takes place due to a decrease in effective k_t followed by autoretardation due to a decrease in effective k_p .

An analogy can be drawn with the well known gel effect, which takes place in usual linear bulk polymerisation of some monomers [for example, of methyl methacrylate (MMA)] and also gives rise to autoacceleration–autoretardation, because it has the same physical causes, *viz.*, freezing of diffusion mobility of the reagents to the level at which the elementary steps become diffusion-controlled, and their effective rate constants decrease as the diffusion hindrance increases. The only difference is the mechanism of freezing of diffusion mobility, which leads to substantial quantitative differences for TRP, both processes being qualitatively analogous.

In linear polymerisation, double bonds remain only in the monomers up to the end of the polymerisation process. Hence, the diffusion control over the processes involving monomer molecules (chain propagation) takes place only at very deep stages of polymerisation, when the polymer–monomer mixture begins to transform into the glassy state. In TRP, the starting molecules contain two or more double bonds. The addition of one of these bonds to the growing cross-linked network gives rise to pendant double bonds with substantially limited mobility. Hence, not only chain termination but also chain growth in TRP becomes diffusion-controlled even at low conversions. As a result, autoacceleration slows down. A comparison of autoacceleration for MMA and dimethacrylates (DMA) shows that the $W_{\max}/W_0$ ratio for MMA is 10–20 times larger than that for DMA, whereas dW/dC in the region characterised by the highest level of autoacceleration is 100–200 times larger than the corresponding value for DMA and dW/dC sharply increases with increasing conversion (for DMA, dW/dC is nearly constant throughout the autoacceleration region $0 < C < C_{\max}$).

The specific mechanism of freezing of the diffusion mobility in TRP is manifested also in specific kinetic features related to the correlation between the reactivity of the initial molecules and their physical (conformational) properties (length of the molecule, rotational barriers of the atomic groups). These characteristic features were analysed for a large number of TRP objects involving oligoester acrylates, because the method for their synthesis allows one to vary the molecular structure over a very wide range. It should be noted that only one particular parameter (for example, the length) can be varied, all other parameters (the

nature of the groups capable of undergoing polymerisation, the nature of the groups responsible for the internal rotation barriers and, finally, the flexibility) being unchanged. By contrast, the internal rotational barriers can be varied, all other parameters being constant. The reactivity of TRP monomers, which is characterised by the parameters W , $W_{\max}$, $C_{\max}$, and $C_{\lim}$ (where W is instantaneous polymerisation rate in the range $W_0 < W < W_{\max}$) at $T = \text{const}$, was found to increase with increasing length of oligomer blocks of the starting molecules and increasing flexibility, which is characterised by barriers to internal rotation provided that the nature of reaction centers (double bonds) is unaltered. The dependence of the above-mentioned physical (conformational) properties of the initial molecules on the reactivity becomes sharper with increasing conversion, the parameters $W_{\max}$, $C_{\max}$ and, particularly, $C_{\lim}$, being most sensitive.

The kinetic features of TRP are illustrated in Figs 3–7. The reactivity is expressed in terms of the reduced rate $W/[M]$ ($[M]$ is the instantaneous concentration of the monomer, which was measured using a specially designed high-speed kinetic calorimeter (Fig. 3) and a high-precision DAK-1-1 kinetic Calvet calorimeter (Figs 4–7)). The parameters associated with the nature of the monomers (oligomers), *viz.*, the length of the chain linking the terminal methacryl groups (oligomeric block) and internal rotation barriers of the atomic groups of the oligomeric block, control the mobility of cross-linking chains of macromolecular networks formed in the course of TRP. It is these oligomeric blocks that become one of three cross-linking chains with trifunctional junctions once both methacryl groups of dimethacrylate are involved in the reaction. Since two other cross-linking carbon chains are very short and rigid, it is the third chain that provides junction relaxation controlling the molecular mobility of a highly cross-linked reaction medium. Curves 1, 2, 4 and 5 in Fig. 3 correspond to analogous (with the same set of rotation barriers) DMA with successively increasing length of the oligomeric block. The reactivity sharply increases in the same order, particularly, at deep stages of transformation, so that the maximum conversion for DMA with the shortest oligomeric block $C_{\lim} \rightarrow 40\%$ (curve 1), whereas autoretardation in the case of DMA with rather long chains (curves 4 and 5) virtually disappears and $C_{\lim} \rightarrow 100\%$. Curves 3 and 4 correspond to DMA, which have

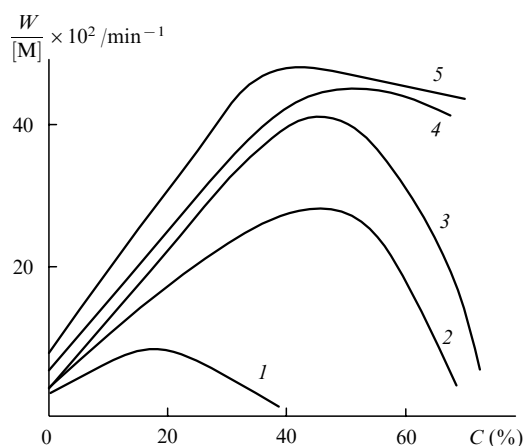


Figure 3. Kinetics of polymerisation of related molecules of different length (1, 2, 4, 5) and internal rotational barriers of molecules of comparable length (2, 3). $T = 70^\circ\text{C}$, benzoyl peroxide (1 mass %) as the initiator.

The following reagents were subjected to TRP: $M-(\text{CH}_2)_n-M$, $n = 4$ (BM; curve 1), $n = 10$ (DM; curve 2); $M(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2M$ (TGM-3; curve 3); $M[(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{O}(\text{C})-Z-\text{C}(\text{O})\text{O}]_n(\text{CH}_2)_2$. $\text{O}(\text{CH}_2)_2M$, $n = 1$ (decandiol dimethacrylate orthophthalate, DMP-1; curve 4), $n = 2$ (DMP-2; curve 5). Here and in Figs 4–7, M is the $\text{CH}_2 = \text{C}(\text{CH}_3)\text{C}(\text{O})\text{O}$ group and Z is the fragment of orthophthalate.

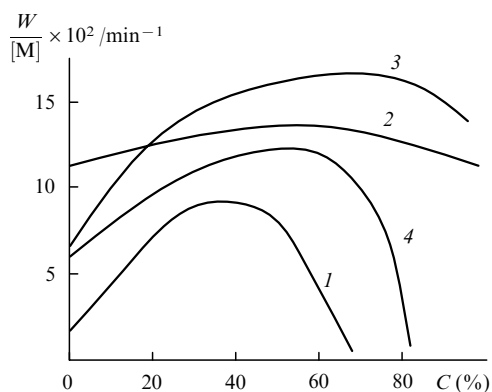


Figure 4. Kinetics of copolymerisation of the molecules of different types; (1) homopolymerisation of TGM-3, (2) homopolymerisation of DMP-8, (3) copolymerisation of TGM-3 and DMP-8 in a mass ratio of 1:1; (4) homopolymerisation of GMP-9 $M(CH_2CH_2O)_3(O)C-Z-C(O).(OCH_2CH_2)_3M$ serving as a model of a copolymerisation system with respect to the number of double bonds. $T = 50^\circ C$, dicyclohexyl peroxycarbonate (CPC) as the initiator, $[CPC] = 1$ mass %.

oligomeric blocks of similar lengths but differ by the set of internal rotational barriers. In decanediol dimethacrylate (DM, curve 2), only two ester groups are rather weakly hindered. In triethyleneglycol dimethacrylate (TGM-3, curve 3), not only rotations of the ester groups but also those of the ether bonds are weakly hindered and, as a result, the reactivity in the later stages of TRP increases.

Figure 4 shows the data on the dependence of TRP on non-trivial factors, which are also associated with the physical properties of the reaction medium. It appeared that the reactivities of binary systems of dimethacrylates of different length are not intermediate between the reactivities of each component but are higher than both of them (!) (*cf.* curves 1, 2 and 3). Curve 4 corresponds to dimethacrylate, which was specially chosen in such a way that the length of its oligomeric block was equal to the average length in the binary system (the nominal volume concentrations of the junctions of the macromolecular network, which were equal to the concentration of the double bonds in the starting mixture, were also equalised). As can be seen from curve 4, in this case the reactivity has an intermediate value and the unusual effect typical of mixtures of molecules of different length disappears.

The influence of external factors, which are not associated with the nature of the starting oligomers, *viz.*, dilution of the reaction mixture with inert solvents, addition of inhibitors and surfactants, is illustrated in Figs 5–7. It can be seen that good solvents (from the viewpoint of thermodynamic affinity) enhance the reactivity, whereas bad solvents (heptane) decrease the reactivity. Apparently, it is associated with the fact that the chain growth is diffusion-controlled even in the early stages of polymerisation due to microheterogeneity. Hence, good solvents hinder microheterogenisation of the reaction mixture, whereas bad solvents facilitate chain aggregation and, consequently, increase microheterogenisation.

Figure 6a presents the kinetic dependences reflecting the influence of a rather strong inhibitor (X), *viz.*, benzoquinone, for which the rate constant of the linear chain termination is ~ 4 times as large as that of chain growth. Due to this difference in the rate constants, X is completely consumed in the early stages of TRP. The concentration of X was varied, the concentration of the initiator for each [X] being chosen so that the reactivity in the initial stages of TRP remained the same (see curves 1–3 at $C < 20\%$). A considerable increase in the difference in the reactivity as C increases cannot be explained without considering the microheterogeneous character of TRP. Actually, the microheterogenisation in the presence of X proceeds in such a way that the higher is the concentration of X, the larger is the number of

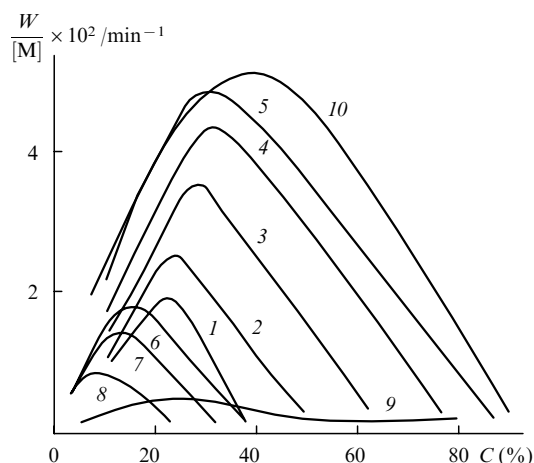


Figure 5. Effect of inert solvents on the kinetics of TRP using TGM-3 as an example.

The concentration of TGM-3 in a solution (vol.%): 100 (1), 80 (2), 60 (3), 50 (4), 40 (5), 90 (6), 80 (7), 70 (8), 30 (9), 40 (10). $T = 40^\circ C$, $[CPC] = 2.6 \times 10^{-3}$ mol litre $^{-1}$; the solvent: (2–5) benzene, (6–9) heptane, (10) acetonitrile.

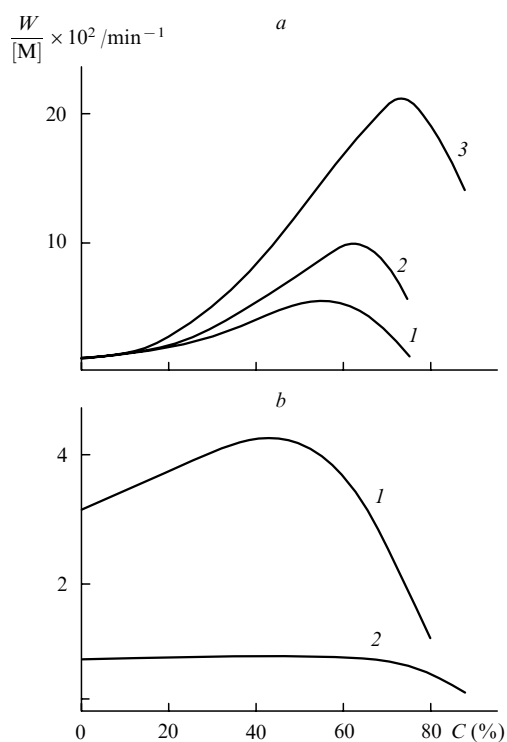


Figure 6. Effect of the structural defects, which are generated upon termination of growing polymer chains by inhibitors, on the kinetics of TRP.

(a) polymerisation of GMP-9 at a fixed molar ratio initiator (CPC)/inhibitor (benzoquinone) = 1:1; increasing absolute concentrations of the initiator and inhibitor (mass %): (1) 2, (2) 4, (3) 6; $T = 35^\circ C$; (b) polymerisation of TGM-3 in the presence of inhibitors (trinitrotoluene, TNT), which act throughout the TRP process; $T = 60^\circ C$, dinitrile of azoisobutyric acid (AIBN) as the initiator, $[AIBN] = 0.02$ mol litre $^{-1}$; $[TNT] = 5 \times 10^{-3}$ (1), 3×10^{-2} mol litre $^{-1}$ (2).

autonomous microreactors (N) simultaneously acting in the reaction system^{11,45}

$$N_{\text{lim}} = \frac{(k_X[X])^2}{(f-1)k_p^2[M]_0}$$

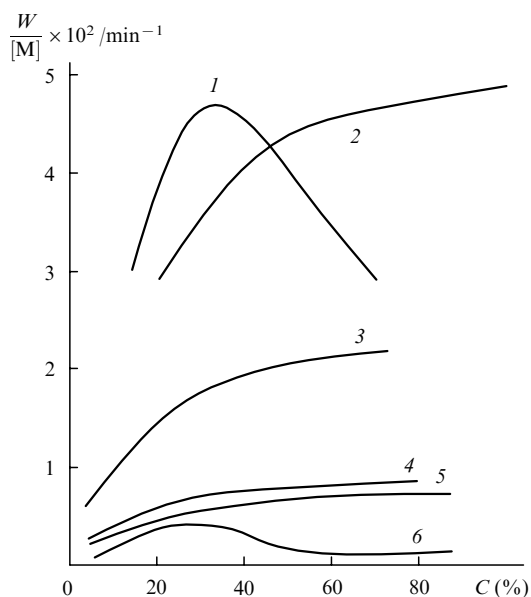


Figure 7. Kinetics of polymerisation of TGM-3 in a solution containing stabilising additives.

Additives: (1–3) acetonitrile, 40% TGM-3; (4–6) heptane, 30% TGM-3; $T = 40^\circ\text{C}$, $[\text{CPC}] = 2.6 \times 10^{-3} \text{ mol litre}^{-1}$. The additive and its concentration (mass %): (1, 6) without an additive; (2) colloxylin, 0.1; (3) linoleic acid, 0.2; (4) polyisoprene, 0.4; (5) surfactant, 0.5.

This is consistent with the arrangement of curves 1–3. Thus, the higher is the concentration $[X]$, the higher is the reactivity.

The dependences shown in Fig. 6*b* illustrate the influence of the inhibitors of another type with rather low constants k_X ($k_X < k_p$), which act throughout the process rather than only at the initial stages of TRP. In this case, quadratic chain termination $R + R$ controlled by diffusion due to large sizes of R (macro-radicals, some of which are already bound to the network) is changed for linear chain termination $R + X$ involving small (mobile) molecules X , the latter process being diffusion-controlled to a much lesser extent. Hence, at a particular concentration of X (curve 2), the kinetics typical of TRP (autoacceleration–maximum–autoretardation) are transformed in such a way that the stage of autoacceleration completely disappears and the stage of autoretardation is shifted to very high C .

The results of experiments on the suppression of microheterogenisation by adding surfactants are presented in Fig. 7. These compounds prevent aggregation, which is the initial stage of the formation of microheterogeneous (microgel) particles. Besides, within the framework of the microheterogeneous mechanism, autoretardation at deep stages of TRP is also interpreted as being a result of aggregation of microgel particles.^{11,45} Three types of surfactants were used and the autoretardation stage was completely suppressed in all cases.

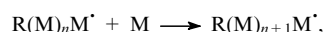
Therefore, the kinetic characteristic features at the later stages of TRP are determined by the conformational properties of the starting multifunctional monomers (oligomers), such as the length of the molecule and internal rotational barriers, and the reaction medium (diluent, surfactants, additives of inhibitors), which influence the aggregation of polymer chains and microgel particles as well as the length of primary polymer chains (inhibitors with $k_X > k_p$) and the character of chain termination (inhibitors with $k_X < k_p$). In the initial stages of TRP (initial rate W_0), the reactivity of the system at $C \rightarrow 0$ (non-cross-linked system) depends on other factors.

2. Early stages of three-dimensional radical polymerisation

At a very low conversion ($C < 5\%$), the reactivity of oligomers characterised by W_0 depends, generally, on the viscosity of the reaction system. The higher is the viscosity, the larger is

W_0 .^{11,13,45,87,88} As in the case of the reactivity at a high conversion, the physical properties (those, which control the level of intermolecular interactions in the reaction system) of the starting oligomers rather than their conformational properties have a dominant role, *i.e.*, the presence of centres of strong intermolecular interactions, which can form hydrogen dipole–dipole and other labile bonds, is of importance. Cooperative hydrocarbon groups characterised by very weak dispersion interactions can also serve as such centres [for example, the methylene groups $-(\text{CH}_2)_n-$ at $n > 4$ are involved in intermolecular interactions with the energy $E > 17 \text{ kJ mol}^{-1}$ comparable to the energy of hydrogen bonds and the phenyl groups are involved in intermolecular interactions with $E = 29–33.5 \text{ kJ mol}^{-1}$]. Generally, it is the ability of starting oligomers to form intermolecular interactions that controls the viscosity of the reaction system at low conversions. The viscosity exerts a trivial effect on W_0 , *viz.*, chain termination in the TRP process is diffusion-controlled even at $C \rightarrow 0$, and the diffusion depends on the viscosity. The higher is the viscosity, the lower is the effective constant k_t and, consequently, the larger is W_0 . A correlation between W_0 and the viscosity was found for a large number of compounds involved in TRP.

However, an anomalous reactivity was sometimes observed in the early stages of TRP.^{11,45,89,90} In some cases, for example, the rate constant of chain growth (measured by a non-stationary kinetic method in the region of $C < 5\%$) sharply decreases in the presence of very small additives of inert compounds, including the polymer formed. In other cases, the viscosity has an anomalous effect on W_0 , and W_0 increases rather than decreases as the viscosity decreases (for example, upon dilution with an inert solvent).⁹¹ These anomalies provide evidence in favour of the existence of yet another specific feature of TRP processes associated with the involvement of polyfunctional molecules, which differ from usual monomers by a rather large size. These molecules are prone to the formation of associates. The lifetime (τ) of labile associates, particularly, if molecules contain centres of strong intermolecular interactions (generally, several centres, taking into account the large size of the molecules), often reaches $\tau_{ph} \approx 3 \times 10^{-3} \text{ s}$, which is comparable to the characteristic time of the chain propagation ($\tau_{ch} \leq 10^{-4} \text{ s}$; the indices *ph* and *ch* denote ‘physical’ and ‘chemical’, respectively). Evidently, if $\tau_{ph} > \tau_{ch}$ and the degree of association of the starting oligomers is rather high, the chain growth takes place in an associated reaction medium. In this case, the packing (mutual orientation) of the molecules in the associate (if it is regular and characterised by the correlation time $\tau_0 > \tau_{ch}$) can be either favourable or unfavourable for growth



because all reactions of the addition of free radicals at the double bonds are sterically strictly controlled (as evidenced by very low steric factors $10^{-3}–10^{-5} \ll 1$). An anomalous change in W_0 is due to the presence of associates with either a favourable molecular packing (associate-plus) or an unfavourable molecular packing (W_0 increases with dilution; associate-minus). Recently, using polymerisation of specially chosen model compounds, which can form associates of both types (plus and minus), not only the existence of such associates and their effect on the kinetics of polymerisation processes have been proved but also the quantitative model of polymer chain growth in regular associates has been proposed.^{92–102} The average length of sequences of molecules oriented in a like manner in the absence of perturbing agents (several tens of molecules can be involved in such a sequence) were calculated from the kinetic data on the influence of small additives of comonomers incorporated into the associate as agents interrupting the above sequence.

Recently, processes for the formation of associates in a medium containing groups capable of being involved in strong intermolecular interactions (acrylates and methacrylates) were examined by molecular mechanics and molecular dynamics.^{101–104} These methods are based on the fundamental laws of

physics. Hence, the results of calculations by these methods are as convincing as the results of direct experiments and one can say about computer experiments. This is all the more important because the interpretation of the kinetic anomalies^{92–95} was made possible based on the hypothesis of the existence of associates with a regular molecular packing (*i.e.*, molecules oriented in a particular way) in a medium of acrylates and methacrylates undergoing polymerisation. In other words, this hypothesis assumes the existence of associates with a pronounced long-range order. However, direct experimental methods for the detection of such associates, *i.e.*, methods necessary for verification of the correctness of this hypothesis, are lacking. In this case, the results of computer simulation (experiment) are evidently of great importance. Let us consider these results in more detail.

The kinetic anomalies,^{89–106} which are presumably related to the formation of associates, are particularly pronounced in the polymerisation of higher alkyl acrylates (HAA) and higher alkyl methacrylates (HAM),^{92–95,100} which can be considered as models of monomers (oligomers) containing centres of strong intermolecular interactions. In the case of HAA, the kinetic anomalies are interpreted by postulating the formation of associates in which the mutual orientation of the molecules is favourable for chain growth (precursor). In the case of HAM, the formation of associates with the orientation of the molecules unfavourable for chain growth is postulated (anti-precursor). The correctness of these hypotheses was strongly supported by the results of experiments^{93,95,100} on the influence of small additives (one molecule per 100 molecules of the main monomer) on the rate of polymerisation of comonomers possessing the same ability to undergo polymerisation *via* double bonds (the acryl group for HAA and the methacryl group for HAM) but containing alkyl substituents of different length. A very strong negative effect of such additives in the case of HAA was interpreted by assuming that the comonomer molecules are readily incorporated into the pre-associate but simultaneously disturb the positional (or) orientational order due to the difference in the size of alkyl fragments. As a result, due to an unfavourable orientation of the double bonds, the molecules of additives terminate the polymer chain growth developed within the precursor. Based on these concepts, the computational apparatus was devised, which made it possible to evaluate the average number of molecules in the precursor (this number increases from 10 to 40 as n in the alkyl fragment $-(CH_2)_n-$ increases from 4 to 12) and the ratio between the rate constants of the chain growth within and outside the associate (from 50 to 200 in the same range of changes in n). The most probable reason for an increase in these parameters is the increase in the energy of intermolecular interactions in the homological series of HAA due to cooperation of weak dispersion interactions in alkyl fragments to form a centre of strong intermolecular interactions and, correspondingly, an enhancement of stability of the precursor.

The positive effect of very small additives of related comonomers observed in the case of HAM was interpreted as an effect of degradation (or a decrease in stability) of anti-precursors by molecules incorporated into the associates with a different positional or orientational packing.

The correctness of these hypotheses was confirmed by computer simulation,^{101–104} as evidenced by the following results. It was demonstrated that higher alkyl acrylates and alkyl methacrylates, starting from butyl esters, can form regular associates, in which the ester molecules (or their hydrocarbon fragments, ester groups and double bonds) are mutually positionally and orientationally ordered (Fig. 8). These regular associates were related to kinetically active associates, whose existence was postulated in the interpretation of the kinetic anomalies occurring in HAA and HAM polymerisation.

The double bonds in the HAA and HAM molecules are ordered both within associates and with respect to the double bonds of the adjacent associates. The order of the double bonds within the associates is virtually identical to that in associates of

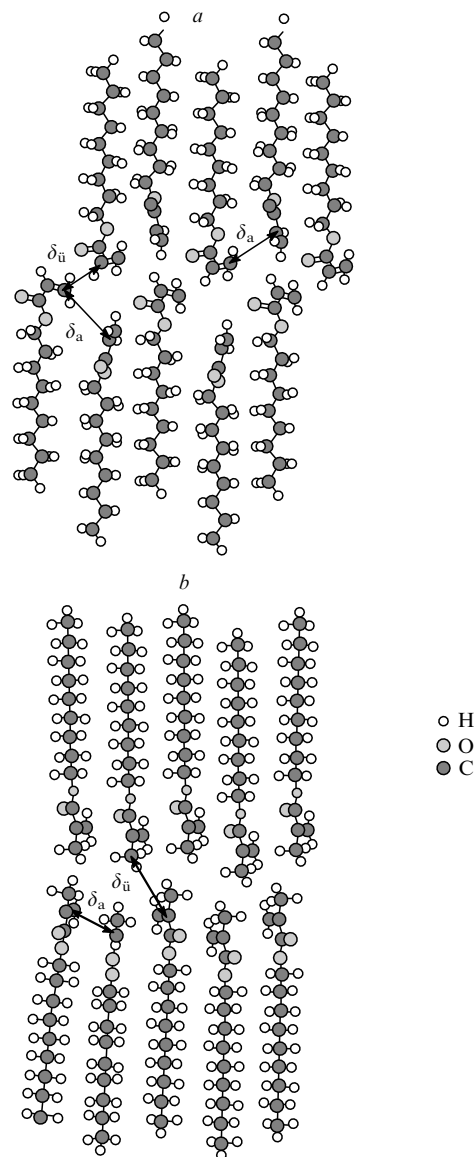


Figure 8. Monomolecular sectional view of the medium layer of a regular associate of NA (a) and NMA (b) in polymerisation of HAA and HAM.

nonyl acrylate (NA), nonyl methacrylate (NMA) and other alkyl acrylates and alkyl methacrylates (see Fig. 8), whereas the inter-associate order of the double bonds in alkyl acrylates and alkyl methacrylates, including NA and NMA, is substantially different (Table 1).

It is believed that it is these characteristic features of the interassociate order of the double bonds of associated molecules that are favourable for polymerisation of NA and other higher alkyl acrylates and, by contrast, are unfavourable for polymerisation of NMA and other higher alkyl methacrylates. Apparently, these factors control the addition of polymeric radicals at the double bonds of the monomers. It was found that the incorporation of additive molecules into associates not only changes the positional order of the double bonds in the sites of localisation of the additive molecules by increasing the distance between the carbon atoms at the double bonds to 0.6–0.9 nm but also changes the molecular dynamics of all other associates. Molecular dynamics simulation of the thermal motion of molecules in regular associates of HAA and HAM showed that the inclusion of the molecules of BA or ethylhexyl acrylate (EHA) [BMA or ethylhexyl methacrylate (EHMA)] into regular NA (NMA) associates leads to their destabilisation (Fig. 9) by shifting

Table 1. Average distances between the carbon atoms at double bonds (δ) and the angle characterising the mutual orientation of the double bonds (θ) in the adjacent molecules in associates of alkyl (meth)acrylates (δ_a , θ_a) and between associates (δ_m , θ_m).

Associates	δ_a /nm	θ_a /deg	δ_m /nm	θ_m /deg
n-Alkyl acrylates				
BA	0.352	3	0.392	81
NA	0.343	1	0.365	88
DcA	0.340	1	0.358	89
CA	0.403	0	0.379	92
n-Alkyl methacrylates				
BMA	0.348	3	0.675	177
NMA	0.378	1	0.684	183
DcMA	0.358	1	0.624	182
CMA	0.392	1	0.648	182

Note. The distances δ and the angle θ in the models were determined with an accuracy of ± 0.001 nm and $\pm 2^\circ$, respectively; BA is butyl acrylate, DcA is decyl acrylate, CA is cetyl acrylate, BMA is butyl methacrylate, DcMA is decyl methacrylate, CMA is cetyl methacrylate.

the dissociate $\rightleftharpoons$ associate equilibrium toward the non-associated monomers. For n-alkyl acrylates, this should lead to a decrease in the concentration of precursors and to a corresponding decrease in the polymerisation rate. In the case of HAM, the inclusion of the above-mentioned molecules should decrease the concentration of anti-precursors and increase the polymerisation rate.

The results of computer simulation of fluoroalkyl (meth)acrylates also confirmed the existence of rather stable structures influencing the kinetics of polymerisation processes.

The hypothesis,¹⁰⁵ which was proposed in the 1950s after the discovery of the kinetic anomalies in polymerisation of the monomers crystallised in the phase transition region, was then extended to the high-temperature region far from the phase transition due to the discovery of new kinetic anomalies.^{89–91,106} Its computational apparatus was devised on the basis of experiments on specially chosen model monomers and their mixture.^{93–95,100} This hypothesis can be considered to be reliable as applied to TRP.

In conclusion, let us note the brave attempt¹⁰⁷ to represent the associated structure of a reaction medium as pseudopolymer chains with a limited lifetime τ_{ph} (blinking chains), whose units are linked *via* intermolecular interactions. For example, these chains can appear upon binding of alcohol molecules to form linear associates through hydrogen bonds.^{108–110} It is assumed that the behaviour of blinking chains is somewhat analogous to

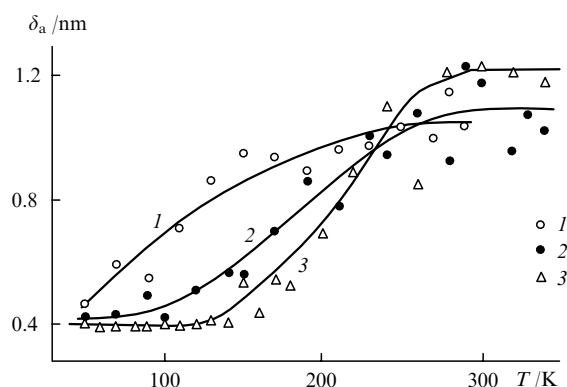


Figure 9. Temperature dependence of the distances between the double bonds (δ_a) in associates.
(1) BA, (2) NA + BA, (3) NA.

that of usual macromolecules formed by covalent bonds. Hence, these chains can be described using the concepts and approaches developed in the physics of polymers, including scaling approaches. For chemical reactions proceeding in such a pseudo-polymer medium, the relations were found in which the reaction order and other parameters reflect the characteristic features associated with the polymer statistics rather than with the laws of chemical kinetics.

V. Three-dimensional radical polymerisation as a tool of macromolecular design

In recent years, researchers involved in different fields of fundamental science (chemists, physicists, mathematicians), specialists in computer simulation and engineers have focussed their efforts on the macromolecular design, *viz.*, the chemical construction of macromolecules and the target synthesis of macromolecules with predicted structures and properties. In the area of highly cross-linked polymers formed by TRP, the macromolecular design is based on data from fundamental science, which made it possible to reveal the characteristic features of the kinetics and mechanism of TRP, whose distinguishing feature is the microheterogeneity. To use these data as an efficient tool of macromolecular design, it is necessary to transform them into mathematical (computer) models of TRP. Such models of TRP can be divided into two groups.

The first group of models developed in the period from 1977 to 1983 is based on the maximum simplified concepts.^{1,11,45} Microgel particles acting as autonomous microreactors are approximated by spheres of the average radius r . It is assumed that the polymerisation process is localised in the peripheral layer of this sphere (with the thickness h , which remains unchanged with conversion). The calculated estimates showed that the number of microreactors remains virtually constant in the course of the polymerisation, so that the conversion increases due to an increase in r . When r reaches the value at which the spheres come into contact with each other, their loose peripheral layers acting as efficient reactors partially overlap with each other and their cores, which consist of highly cross-linked polymers with the maximum conversion (and, hence, which cannot interpenetrate), are packed to form a tetragonal or (which is less probable) hexagonal structure. In this stage, the polymerisation process is localised (reaction zone) in cavities of the structure composed of spheres (more precisely, in the inner near-surface layer of these cavities with the thickness h). It is assumed that at a rather high conversion, these cavities are spherical (of the average radius r'). Evidently, r' decreases in the course of further transformation. Within the framework of this model (percolation model), the rate constants of all elementary steps (initiation, propagation, termination) do not vary with conversion, because the conditions in the reaction zone (in loose near-surface layers above the dense highly cross-linked polymer) remain unchanged during polymerisation and only the total volume of the reaction zone changes (first it increases until the spheres come into contact with each other and then decreases). Correspondingly, the overall (experimentally observed) reduced polymerisation rate $W/[M]$ first increases (autoacceleration) and then decreases (autoretardation). In this case, both stages can be described by the following simple mathematical expressions:

autoacceleration

$$W = W_0 \left(1 - \frac{C}{C_{lim}}\right) + W_r (4\pi N)^{1/3} h \left(\frac{3C}{C_{lim}}\right)^{2/3}, \quad (1)$$

where W_0 and W_r are the polymerisation rates in the starting reaction mixture and spherical layers with the thickness h , respectively, C is the instantaneous conversion, C_{lim} is the limiting conversion, N is the concentration of spherical microreactors (microgel particles, grains);

autoretardation

$$W = W_0 \left(1 - \frac{C}{C_{\text{lim}}}\right) + W_r (4\pi N)^{1/3} h^{2/3} \left(1 - \frac{C}{C_{\text{lim}}}\right)^{2/3}. \quad (2)$$

The region between autoacceleration and autoretardation cannot be described by such simple expressions.

The number of microreactors (microgel particles) formed in the reaction system reaches a constant value N_{lim} in the early stages of TRP (at $C < 1\%$). This parameter depends on both the kinetic parameters and reaction conditions.

In the absence of inhibitors,

$$N_{\text{lim}} = \frac{W_i k_t}{(f-1)k_p^2 [M]_0}, \quad (3)$$

where W_i is the initiation rate, f is the functionality and $[M]_0$ is the initial concentration of the monomer.

In the presence of the inhibitor X

$$N_{\text{lim}} = \frac{(k_X [X])^2}{(f-1)k_p^2 [M]_0}, \quad (4)$$

where k_X is the rate constant for the trapping of radicals as chain carriers.

Equations (1)–(4) indicate the manner in which the morphology of the polymer can be controlled. For example, a coarse-grained structure can be transformed into a fine-grained structure by increasing W_i or (and) adding additives X. The main advantage of this model is that it accounts for the microheterogeneous character of TRP.

Another group of mathematical (predominantly, computer) models deals with more complex equations.^{111–120} Generally, it is assumed that k_p and k_t depend on the conversion. The character of the dependences is established on the basis of the corresponding concepts of molecular physics. Some of the physical constants remain unknown and serve as fitting parameters in the further comparison of the results of calculations with experimental data. From the applied viewpoint, this semiempirical theory has certain advantages. Thus, the above-mentioned equations are suitable for planning macromolecular design (but they are of limited use due to the empirical origin of the parameters). In the best-developed model, the rate constants of elementary steps are described by the following equations:¹¹⁸

$$k_p = \frac{k_{p0}}{1 + \exp[A_p(1/v - 1/v_{cp})]},$$

$$k_t = \frac{k_{t0}}{1 + \{R_d k_p [M]/k_{t0} + \exp[-A_t(1/v - 1/v_t)]\}^{-1}}.$$

Here, k_{p0} is the true kinetic rate constant, *i.e.*, k_p in the absence of diffusion control; A is the parameter determining how fast the diffusion-controlled kinetic constant decreases with increasing diffusion hindrance; v is the average partial free volume of the system; v_{cp} is the critical free volume for the chain propagation reaction determined as the value of v at which $k_p = (1/2)k_{p0}$; $R_d k_p [M]$ is the component accounting for the contribution of the reaction-diffusion mechanism; $[M]$ is the instantaneous concentration of double bonds and R_d is the parameter characterising the reaction diffusion.

To calculate the partial free volume at a particular conversion, it is necessary to know the following six characteristics of the material: the densities of the monomer and polymer (ρ_m and ρ_p , respectively), their glass transition temperatures (T_{gm} and T_{gp} , respectively) and the differences between the expansion coefficients in the high-elasticity and glassy states (α_m and α_p).

The parameter R_d was evaluated¹²¹ from the results of non-stationary experiments (post effect) as follows:

$$R_d = \frac{k_t}{k_p [M]}.$$

VI. Critical conversion in three-dimensional polymerisation

The theory of polymer-network formation is one of the most important lines of investigation into the TRP mechanism. This theory has been developed in the studies of Dušek and co-workers,^{10, 115, 122–143} Kloosterboer,^{144–146} Boots and co-workers,^{113, 145–147} Macosko and co-workers,^{148–152} Lee and co-workers,^{153–156} Hamielec and co-workers,^{157–163} Chomppf and co-workers¹⁶⁴ and Okay and co-workers.^{114, 165–170} The results of these studies were generalised and analysed in the reviews.^{120, 170, 171}

Some concepts of the theory of network formation are based on the Flory–Stockmayer model of polymerisation processes (for example, of stepwise reactions). Attempts to apply these concepts to TRP-type chain polymerisation processes were based on doubtful assumptions and rough approximations. Recently, it has been demonstrated^{172–178} that calculations of the critical conversion α_c (gel point) for TRP with the use of the Flory–Stockmayer equations gave incorrect results even if these equations were specially adapted to this process. The equations, which work well for polycondensation (stepwise process), differ substantially from those derived in the studies^{172–178} specially for TRP (chain process). Expressions relating α_c to the kinetic parameters of TRP stages (initiation, propagation, quadratic and linear chain termination and chain transfer) were deduced in the studies.^{172–178} The problem was solved by the moments method followed by the generalisation of the numerical solutions in the form of equations. The starting model was based on the scheme of radical polymerisation including stationary-state conditions as the only assumption.

The critical conversion α_c in the formation of cross-linked polymers, which characterises the transition of the system from the flowable state to the state with the equilibrium modulus of elasticity, is an important parameter of the system both from the technological and theoretical standpoints.^{179, 180} The formation of an insoluble gel in technological processes complicates the preparation of polymers. By contrast, the relation between the critical conversion, on the one hand, and the structural and kinetic parameters of the process, on the other hand, enables one to prepare cross-linked polymers with required physical-mechanical characteristics. Theoretically, the gel point determines the fluidity threshold in the polymer system formed and, hence, it is important to reveal the dependence of this value on the kinetics of the process and structural characteristics of the product.

The problem of the determination of the critical conversion was solved by Flory and Stockmayer¹⁸¹ for polycondensation reactions of the type



which give rise to bonds between the functional groups A and B. The reactions can either be accompanied by elimination of by-products or proceed without the formation of the latter, groups A and B being either different or identical. If the number of functional groups per molecule of the starting reagents is larger than two, branched and cross-linked polymers can be generated. At a particular degree of conversion, higher-order (starting from the second) moments of the molecular-mass distribution of macromolecules approach infinity. This degree of conversion is called critical. The experimental critical conversions are determined from the results of viscosimetric measurements (the viscosity approaches infinity) or relaxation measurements (the appearance of the equilibrium modulus of elasticity). In recent years, the determination of the gel point on the basis of the frequency dependence of the relaxation modulus have gained wide acceptance.¹⁸² It is believed that the critical conversion corresponds to the equality of $G'(\omega)$ and $G''(\omega)$.

The critical conversion and the structure of the network depend on the character of the functional-group distribution for

the starting reagents,¹⁸³ which can be expressed in terms of the average ($\bar{f}_n$) and weighted average ($\bar{f}_w$) functionalities^{179, 183}

$$\bar{f}_n = \frac{\sum_i im_i}{\sum_i m_i}, \quad \bar{f}_w = \frac{\sum_i i^2 m_i}{\sum_i im_i}$$

where m_i are the concentrations of the starting reagents bearing i functional groups.

For polycondensation with related functional groups, it was found that

$$\alpha_c(\bar{f}_w - 1) = 1. \quad (6)$$

In the case of functional groups of different nature

$$\alpha_c^2 r (\bar{f}_{aw} - 1)(\bar{f}_{bw} - 1) = 1, \quad (7)$$

where r is the ratio between the concentrations of the interacting functional groups,

$$r = \frac{\sum_i im_{ai}}{\sum_j m_{bj}} < 1,$$

the indices a and b correspond to different types of functional groups.

The cross-linking of polymer chains is a special case. Generally, the critical conditions are expressed as follows:

$$\alpha_c(\bar{P}_w - 1) = 1, \quad (8)$$

where $\bar{P}_w$ is the weighted average degree of polymerisation of macromolecules subjected to cross-linking. It is implicitly assumed that the cross-linking can involve any unit of the polymer chain.

Equations (6)–(8) were derived by both the statistical method and kinetic calculations.^{179, 180} These equations were also supported by the experimental data. The prerequisite to their applicability is the absence of intramolecular reactions.

The three-dimensional polymerisation, which can be represented by the scheme



(M is the monomer, R_i is the active chain, the index i denotes the number of units in the chain), is generally described by Eqn (8), in which the critical branching proposed by Flory and Stockmayer^{181, 184} is used as α_c . The relation between α_c and the conversion was established by solving the kinetic equations of the consumption of the functional groups of monomers.¹⁸⁵ Hence, calculations were based on probabilistic considerations, which are of limited usefulness in the case of polymerisation.^{179, 180} The procedure for kinetic calculations of the gel point was developed in the studies.^{1, 11, 45, 180, 186–189}

In the studies,^{186–188} the gel point was calculated assuming

$$\frac{dN}{dt} = 0.$$

Evidently, these calculations should overestimate values, because, as in polycondensation, the second moments of the molecular-mass distribution (and, consequently, the functional-group distribution) approach infinity at lower conversions than the 'zero' concentration of polymer chains.^{179–181}

The correct requirement for the infinity of the second moment of the molecular-mass distribution was used in the studies.^{1, 11, 45, 180, 189} The following equations were derived:

$$\alpha_c = \frac{(k_t W_i)^{1/2}}{(n-1)k_p[M]_0}$$

and

$$\alpha_c = \frac{\{(k_t + k_t^1)[R] + k_m[M]\}^2}{k_p[M]\{(3k_t + k_t^1)[R] + 2k_m[M]\}}.$$

In these cases, the chain length was determined from the following kinetic parameters of the polymerisation process: the initiation rates W_i ; the rate constant of chain propagation (k_p), the rate constants of chain termination by disproportionation (k_t^1) and recombination (k_t) and the rate constant of chain transfer to the monomer (k_m); the functionality of the monomer (n). It should be noted that in the latter case, the conversion with respect to the monomer rather than with respect to the functional groups was considered as the degree of conversion. Besides, it was noted that the equations in the above-given form can be deduced only for special conditions.

The above-mentioned equations were not confirmed experimentally. However, their validity was not questioned by researchers, because it is known that these conditions are not realised in the case of three-dimensional polymerisation.^{1, 11, 45, 179, 180} Thus, intramolecular cyclisation proceeds rather vigorously due to fast chain growth by the radical mechanism and because of a low concentration of the chains in the early stages of TRP.^{179, 190} It is believed that repeated cross-linking within the same pair of chains (formation of multiple junctions and ladder macromolecular structures) also decreases the effective concentration of interchain cross-links thus increasing the critical conversion. Hence, the radical polymerisation can be considered as a typical microheterogeneous process.^{1, 11, 20, 45, 117, 168}

At the same time, polymerisation and polycondensation are radically different from the kinetic viewpoint.¹⁷⁹ A comparison of Eqns (5) and (9) shows that two functional groups are consumed in the course of the former reaction, whereas only one group is consumed in the latter case (in this reaction, the concentration of active centres remains unchanged). Hence, one functional group per monomer molecule is sufficient to prepare a polymer chain by polymerisation. In the polycondensation reaction of a monofunctional monomer, the chain is terminated. This fact casts doubt on whether the approaches, which were developed for studying polycondensation, can be extended to an investigation of polymerisation processes.

The study of living three-dimensional radical polymerisation demonstrated¹⁹¹ that Eqn (8) is not fulfilled in this case as well,¹⁹² although cyclisation is of little importance and the microheterogeneous character of the process is not manifested.^{192, 193}

This fact served as the basis for stating the problem, whose solution revealed the critical conditions (gel point) for TRP. The analysis carried out in a number of studies^{172–178} demonstrated that the critical conversion is related to the kinetic conditions of polymerisation in a complex way. Depending on the ratio between the rates of initiation and termination of a material chain, the gel point is determined by only one of the following parameters: (1) initiation rate, (2) termination rate. The former situation takes place if chain branching can occur, *i.e.*, at a high concentration of a multifunctional monomer, the process being substantially influenced by the kinetics of accumulation of active centres. In the latter case, the length of the material chain is of importance, because the number of pendant functional groups (probable branching points) per polymer chain is a controlling factor at a low concentration of the multifunctional monomer. However, the weighted average functionality of the starting monomer mixture is, on the whole, the governing factor.

The results of the solution of this problem are given in Table 2 in the form of equations for α_c in different processes. The criteria conditions limit the field of application of each equation. It should be emphasised that these equations are not analytical but were derived by generalising numerical solutions.

It is evident that the equations listed in Table 2 differ from all solutions obtained with the use of the Flory–Stockmayer theory. As mentioned above, an experimental comparison is hampered by side processes of the formation of small rings, which have a strong effect on α_c (shift toward higher values). However, under partic-

Table 2. Equations for critical conversion α_c .

Process	Φ_{22} small	Φ_{22} large	Criteria conditions
Living polymerisation, instantaneous initiation	$\frac{\alpha_c^2 \Phi_{22}}{I_0} \approx 1$	$\frac{\alpha_c^2 \Phi_{22}}{I_0} \approx 1$	$\frac{k_i}{k_p} > \sqrt{I_0 \Phi_{22}}$
The same + chain transfer	$\alpha_c \approx \frac{1}{2} \frac{k_X X_0}{k_p \Phi_{22}}$	$\frac{\alpha_c^2 \Phi_{22}}{I_0} \approx 1$	$\Phi_{22} > \frac{(k_X X_0)^2}{k_p^2 I_0}$
Living polymerisation, slow initiation	$\frac{\alpha_c^2 \Phi_{22} k_p}{W_i} \approx 1$	$\frac{\alpha_c^3 \Phi_{22}^2 k_p}{W_i} \approx 1$	$\frac{k_i}{k_p} > \sqrt{I_0 \Phi_{22}}$
The same + chain transfer	$\alpha_c \approx \frac{1}{2} \frac{k_X X_0}{k_p \Phi_{22}}$	$\frac{\alpha_c^3 \Phi_{22}^2 k_p}{W_i} \approx 1$	$\Phi_{22} > \frac{(k_X X_0)^3}{k_p^2 k_i I_0}$
Slow initiation, chain termination by recombination	$\alpha_c \approx 0.33 \frac{\sqrt{k_i W_i}}{k_p \Phi_{22}}$	$\frac{\alpha_c^3 \Phi_{22}^2}{W_i} \approx 1$	$\Phi_{22} > \frac{\sqrt{k_i^3 W_i}}{k_p^2}$
Slow initiation, linear chain termination	$\alpha_c \approx \frac{1}{2} \frac{k_{tY} Y_0}{k_p \Phi_{22}(0)}$	—	—
Replacement effect, chain termination through disproportionation	$\alpha_c = \frac{\sqrt{k_i W_i}}{k_{p2} \Phi_{22}}$	—	$\frac{k_{p1} \Phi_{22}}{\sqrt{k_i W_i}} < \frac{k_t}{k_{p2}}$

Note. Φ_{22} is the second moment of the functionality distribution for the starting reaction mixture (at $t = 0$); $\Phi_{22} \equiv \Phi_{22}(0) = \sum i(i-1)m_i$, where m_i is the initial concentration of i functional monomers (oligomers); W_i is the initiation rate; I_0 , Y_0 and X_0 are the initial concentrations of the initiator, inhibitor and agent of chain transfer, respectively; k_i , k_p , k_t , k_{tY} and k_X are the rate constants of initiation, propagation, quadratic and linear termination and transfer of the chain, respectively; k_{p1} and k_{p2} are the rate constants of propagation for free and pendant double bonds in the processes in which the reactivities of the starting molecules containing two double bonds change after the one of these double bond has reacted; $\varepsilon = k_{p2}/k_{p1}$.

ular conditions (for example, if the probability of cyclisation is low), it is nevertheless reasonable to perform such a comparison.

The results obtained with the use of these equations and equations based on the Flory–Stockmayer theory were compared with the results of experiments performed under conditions in which internal cyclisation is suppressed.^{176, 178} Two examples of such a minimisation are considered below.

Inhibited polymerisation of dimethacrylates. Radical polymerisation of triethyleneglycol dimethacrylate initiated by dicyclohexyl peroxydicarbonate in the presence of large amounts of inhibitors (benzoquinone or TNT) was carried out in cylindrical evacuated sealed tubes (250 mm in height and 3–3.5 mm in diameter). The conversion was detected from the contraction (shift of the meniscus was followed with an accuracy of 0.1 mm; the total shift at the instant of gel formation in the inhibition range under examination was 3–10 mm). The gel point was detected from the loss of flowability. A comparison with other methods showed that this approach gives a rather accurate estimate of the critical conversion.¹⁹²

In the region of the longest lengths of growing polymer chains (at the smallest parameters $k_{tY} Y$), there is a large discrepancy (several orders of magnitude) between the calculated and experimental critical conversions, but then these values converge as the chain length decreases ($k_{tY} Y$ increases), and the best agreement is attained with the use of the equation

$$\alpha_c = \frac{1}{2} \frac{k_{tY} Y_0}{k_p \Phi_{22}(0)}, \quad (10)$$

where k_{tY} is the rate constant of linear chain termination involving molecules of this inhibitor, Y_0 is the starting concentration of the inhibitor (at $t = 0$).

Calculations were also carried out with the use of the Flory–Stockmayer formula

$$\alpha_c = \frac{1}{\rho(\bar{P}_w - 1)}, \quad (11)$$

where ρ is the molar fraction of the cross-linking agent, $\bar{P}_w$ is the weighted average degree of polymerisation of primary polymer chains, *i.e.*, chains which can be generated in the absence of a cross-linking agent at the instant corresponding to the gel point. This value was determined by gel permeation chromatography at degrees of conversion lower than α_c followed by extrapolation to zero conversion.

Since the experimental values of α_c are overestimated primarily due to cyclisation¹⁷⁹ (interchain cross-linking of pendant double bonds), it is believed that the probability of cyclisation decreases as the length of the growing polymer chain decreases and $k_{tY} Y$ increases. Hence, a comparison with the experiment at the largest values of $k_{tY} Y$ demonstrated that Eqn (10) is most precise. At the same time, this result indicates that the above-described calculations gave the correct estimate of the critical conversion not only in the range of parameters where Eqn (10) is valid, but also in the range where all relations presented in Table 2 are true.

This is all the more important because the discrepancy between the experimental and calculated values of α_c is often¹⁹⁴ considered as a test for estimating the percentage of cyclic structures in polymer networks, α_c being calculated with the use of the Flory–Stockmayer formula (8). Evidently, the use of the relations presented in Table 2 enables one to eliminate erroneous conclusions.

The experimental and calculated values of α_c for the inhibited polymerisation of triethyleneglycol dimethacrylate are given in Table 3.

Table 3. Experimental and calculated α_c for inhibited polymerisation of triethyleneglycol dimethacrylate (the molar initiator : inhibitor ratio is 2, dicyclohexyl peroxydicarbonate as the initiator).

Concentration of inhibitor /mol litre ⁻¹	$k_{tY} Y_0$ /s ⁻¹	Experiment	Calculations by Eqn (11)	Calculations by Eqn (10)
Trinitrotoluene as an inhibitor ^a				
0.05	5	~0.01	3.6×10^{-3}	8.9×10^{-4}
0.1	10	0.06	7.2×10^{-3}	1.8×10^{-3}
0.2	20	0.08	1.4×10^{-2}	3.6×10^{-3}
0.5	50	0.11	3.6×10^{-2}	9.0×10^{-3}
Benzoquinone as an inhibitor ^b				
0.005 (4) ^c	10	0.065	7.2×10^{-3}	1.8×10^{-3}
0.005 (2) ^c	10	0.055	7.2×10^{-3}	1.8×10^{-3}
0.005 (1) ^c	10	0.045	7.2×10^{-3}	1.8×10^{-3}
0.01	20	0.085	1.4×10^{-2}	3.6×10^{-3}
0.05	100	0.125	7.2×10^{-2}	1.8×10^{-2}
0.01	200	0.135	1.4×10^{-1}	3.6×10^{-2}
0.03	600	0.16	4.3×10^{-1}	7.2×10^{-2}
0.05	1000	0.19	7.2×10^{-1}	1.8×10^{-1}

^a $k_{tY} \approx 10^2$ litre mol⁻¹ s⁻¹. ^b $k_{tY} \approx 2 \times 10^3$ litre mol⁻¹ s⁻¹, $k_p \approx 350$ litre mol⁻¹ s⁻¹ (see Ref. 204), $[M]_0 \approx 4$ mol litre⁻¹, $\Phi_{22}(0) \sim 8$ mol litre⁻¹. ^c The kinetics of polymerisation were recorded by high-precision calorimetry; initiation rates $10^7 W_i$ (mol litre⁻¹ s⁻¹) are given in parentheses.

Copolymerisation of divinylbenzene with styrene. It was expected¹⁹⁵ that the probability of cyclisation would decrease to a negligibly small value and the polymer network would have an ideal structure with decreasing concentration of divinylbenzene (*m*-DVB) used as a polyfunctional agent in the initial comonomer mixture. Verification of this conclusion was searched for in the agreement between the calculated [according to Eqn (11)] and experimental values of α_c .

The criteria condition for estimating α_c at chosen kinetic constants dictates the choice of the equation

$$\alpha_c \approx 0.33 \frac{\sqrt{k_t W_i}}{k_p \Phi_{22}}, \quad (12)$$

which was used in calculations. The results are given in Table 4.

Table 4. Experimental and calculated α_c for copolymerisation of *m*-DVB with styrene.

[<i>m</i> -DVB] (mol.%)	$10^3 \bar{P}_w$	$\Phi_{22}(0)$	Experi- ment	Calcula- tions by Eqn (11)	Calcula- tions by Eqn (12)
1	1.19	0.154	0.215	0.0425	0.032
0.5	0.79	0.077	0.333	0.133	0.065
0.25	0.74	0.039	0.488	0.271	0.128
0.17	0.67	0.026	0.549	0.435	0.192

Note. Block copolymerisation initiated by AIBN (4×10^{-2} mol litre⁻¹) at 60 °C, $W_i = 4 \times 10^{-7}$ mol litre⁻¹ s⁻¹, $k_p = 200$ litre mol⁻¹ s⁻¹, $k_t = 10^7$ litre mol⁻¹ s⁻¹, $\Phi_{22} = 15.4$ mol litre⁻¹ for pure *m*-DVB.

Analysis of the data in Table 4 casts doubt on the conclusion¹⁹⁵ that an ideal network is attained at low concentrations of *m*-DVB (the last row in the table). The conclusion about the attainment of an ideal-network state upon copolymerisation of dimethacrylates with monomethacrylates¹⁹⁶ is also in doubt. In this case, agreement between the experimental values of α_c and those calculated by Eqn (11) was observed at an even lower concentration (0.03 mol.%) of the bifunctional component (dimethacrylate). Calculations according to Eqn (12) gave lower α_c in this case as well. Consequently, contrary to the conclusions drawn in the study,¹⁹⁶ the contribution of cyclic structures is rather high. This contribution is also essential, if the length of primary chains can be decreased by several orders of magnitude due to an extensive chain transfer in the course of the polymerisation process,¹⁹⁶ although there is a tendency for cyclisation to be suppressed. For example, the ratio of the experimental critical conversion in the polymerisation of dimethacrylates to the calculated value decreases from 100 (at $\bar{P}_w = 1000$ in the absence of a chain transfer agent) to 13 ($\bar{P}_w = 142$) and then to 7–8 ($\bar{P}_w = 64$) in the presence of highly efficient chain transfer agents (dodecanethiols). In the case of diallylic monomers, which serve as active chain transfer agents, this ratio decreases to 5.2–5.5 at the smallest values $\bar{P}_w = 39$ –49. This tendency is manifested not only upon a decrease in the chain length but also upon an increase in its rigidity.¹⁹⁷

In the case of the above-considered inhibited polymerisation of dimethacrylates (see Table 3), the agreement between the calculated and experimental values of α_c is observed at $\bar{P}_w$ of less than 10. Apparently, this is the main reason for the fact that the contribution of cyclisation is close to zero, *i.e.*, an ideal structure of the network is attained.

VII. Living three-dimensional radical polymerisation as a tool of macromolecular design

The discovery of living radical polymerisation (in the 1980s), reliable evidence for its occurrence in particular polymerisation

processes obtained in 1993 and subsequent rapid progress in studies in this field of polymer science led to the development of a new tool of macromolecular design, *viz.*, living TRP.[†] It appeared that living chain TRP radically changes the kinetic characteristic features, mechanism and structure (both topological and morphological) of the polymer formed. Correspondingly, the properties of the polymer material (physical-mechanical, sorption, thermomechanical, *etc.*) are sharply changed due to the transformation of the detailed mechanism of polymer chain growth, *viz.*, the instantaneous chain growth of macromolecules (taking place in the case of usual TRP) is transformed into a slow stepwise process. The term 'instantaneous' is used in reference to processes satisfying the condition $\tau \ll t$ (where τ is the interval from the onset of the growing chain to its death due to quadratic or linear termination, t is the polymerisation time). The term 'slow' is taken to mean that the process meets the condition $\tau \geq t$. As a result of this transformation, the main factor responsible for the appearance of microheterogeneity is eliminated. Since it is the microheterogeneity that determines the main specific features of TRP, elimination (even partial) of the above factor leads to radical changes. From this viewpoint, living TRP as a tool of macromolecular design is considerably superior to usual TRP in efficiency.

Using dimethacrylates and their copolymers as examples,^{198–200} it was established that the transformation of usual TRP into living TRP leads to a sharp change in the properties, *viz.*, the molecular mobility increases and, correspondingly, the properties controlled by molecular mobility change. The modulus of elasticity decreases (both in the glassy and high-elasticity states at $T > T_g$). The glass transition temperature decreases by 20–40 °C. The rate of diffusion of the solvents and their equilibrium sorption increase. The temperature dependence of the rate constant of the quadratic termination of free radicals stabilised in a polymer matrix follows an alternative law (the character of the function changes); in this case, the radicals are generated by irradiation of the polymer with γ radiation (⁶⁰Co source) within the framework of the special techniques used in structure–physical investigation called radiation probing.⁴⁵

The properties of the polymerisates prepared in the living chain and usual modes (according to the results of a studies^{198–200}) are given in Table 5. Polymerisates of the typical reagent of TRP, *viz.*, triethyleneglycol dimethacrylate (TGM-3), with the conversion $C = 0.80 \pm 0.02$ were prepared in the presence of AIBN as the initiator at 90 °C. To perform the living chain polymerisation, CuBr₂ and tetramethylthiuram disulfide were added to the initiator. The latter new agent of living radical polymerisation proposed in the study²⁰⁰ provides a virtually complete transformation of usual TRP into the living chain mode at a particular component ratio.

In addition, Table 5 gives the characteristics of highly cross-linked macromolecular structures formed upon copolymerisation of triethyleneglycol dimethacrylate (TGM-3) with styrene (copolymerisation constants $r_1 \approx r_2 \approx 0.5$, equimolar mixtures, alternation of the units) in the presence of initiators (peroxides) at 125 °C. A benzoyl peroxide–2,2',6,6'-tetramethylpiperidin-1-oxyl system (nearly equimolar ratio) was used as the agent of living TRP. This system, which has been intended only for reaction mixtures containing no less than 50 mol.% of styrene, was used with advantage.¹⁹¹

Living TRP is an efficient tool of macromolecular design for preparing highly cross-linked macromolecular structures with high molecular mobility (which are used, for example, in gel chromatography or for the preparation of materials with enhanced relaxation). Apparently, these changes in the properties are associated with either the absence or low concentration of high cross-linked regions ('grains') in living cross-linked polymers.

[†]The history of this discovery, the stages of development, analysis of the state-of-the-art of this scientific field and prospects in this area of investigation have been surveyed in the review.¹⁹¹

Table 5. Characteristics of usual and living TRP using homo- and copolymerisation as examples.

Parameter	Homopolymerisation		Copolymerisation	
	usual ^a	living ^b	usual ^c	living ^c
E /MPa	2122	1328	$\frac{1652}{1314}$	$\frac{1486}{403}$
σ ($\varepsilon = 10\%$) /MPa	104	58.9	$\frac{77.1}{52.3}$	$\frac{62.8}{17.0}$
W_g (%) during one hour	1.24×10^{-3}	0.42	$\frac{0.14}{1.38}$	$\frac{0.22}{2.00}$
S (%)	< 1	16.5	$\frac{15}{35}$	$\frac{38}{46}$
T_g /°C			$\frac{138}{-}$	$\frac{96}{-}$
$E_g(T > T_g)$ /MPa			$\frac{43.6}{-}$	$\frac{10.7}{-}$

Note. Physical-mechanical tests were carried out in the mode of uniaxial compression at 25 °C (glassy state) with a deformation rate $\dot{\varepsilon} = 10^{-4} \text{ s}^{-1}$; E is the modulus of elasticity, σ is stress on deformation $\varepsilon = 10\%$; W_g and S are the diffusion rate and sorption of benzene vapour, respectively, at 25 °C for 24 h. Free radicals (methacryl) were generated in polymer matrices with the initial conversion $C \simeq 80\%$ under the action of ^{60}Co γ radiation (dose was 2 Mrad).

The temperature dependence of the rate constant of recombination: ^a linear; ^b non-linear; ^c parameters at $C = 0.85 \pm 0.02$ and $C = 0.78 \pm 0.02$ are given above and below the bar, respectively.

This new tool has gained acceptance only recently,^{192, 193, 198–202} because both theoretical and, in particular, experimental bases of living TRP are not sufficiently advanced. Although living radical polymerisation has been studied extensively, only $\sim 3\%$ of more than 400 studies published up to the year 2000 inclusive were devoted to living TRP.

Problems associated with living chain TRP are due, primarily, to two factors. First, information on the behaviour of agents of living radical polymerisation under conditions of highly cross-linked reaction media is scarce. It can be assumed that the diffusion hindrance and specific phenomena, such as microsyneresis and microredistribution of components of initiating systems, influence elementary steps of reversible trapping of radicals serving as chain carriers, which is the essence of the mechanism of living radical polymerisation. Second, (meth)acrylates are most commonly used in TRP, whereas the action of many agents of living radical polymerisation is limited to styrene, its derivatives and styrene-containing reaction mixtures. Hence, there is a need to search for new agents or adapt the available agents to conditions of TRP. The problem is that most of agents suitable for TRP of (meth)acrylates contain copper, iron, cobalt and other variable valence metal halides as basic components, which are insoluble or poorly soluble in cross-linked reaction media.

Living TRP was examined in the study.²⁰³ Using polyethylenglycol dimethacrylates as examples, it was demonstrated that the methyl α -bromophenylacetate–Cu(I)Br–1,1,4,7,10,10-hexamethyltriethylenetetramine system can serve as an efficient agent of living TRP of methacrylates starting with 70 °C. A comparison of the kinetic characteristic features of polymerisation, the critical conversions (gel points), molecular-mass characteristics of sol fractions and the kinetics of accumulation of stabilised radicals serving as chain carriers for usual and living TRP demonstrated that autoacceleration–maximum rate–autoretardation kinetic curves typical of usual TRP are transformed into curves with a maximum rate at small conversion ($C \rightarrow 0$) if the living-chain mode is used. Subsequently, the rate decreases more rapidly than

one would expect (assuming the first-order reaction with respect to the monomer), *i.e.*, the process shows evidence of autoretardation. The characteristic kinetic evidence for the living chain mode, *viz.*, the linear time dependence of $\ln([M]_0/[M])$ ($[M]_0$ and $[M]$ are the initial and instantaneous concentrations of the monomer, respectively), is true only up to the conversion $C \simeq 40\%$. This gives grounds to assume that the later stages of TRP ($C > 40\%$) proceed in the usual fashion (due to the influence of a highly cross-linked macromolecular structure of the reaction medium). In living chain polymerisation, the critical conversion was shifted from $< 1\%$ to $\geq 5\%$, which is consistent with other experimental data¹⁹⁸ and the new theory of gel formation.^{172–178} Analysis of TRP by gel chromatography showed that a sol fraction in the course of usual TRP consists of a pure monomer in all stages of the polymerisation process starting with $C \rightarrow 0$ and up to $C > 50\%$, which is consistent with the microheterogeneous mechanism of TRP (see Section II). On going to the living chain mechanism, M_n of the sol fraction linearly increases with conversion (the characteristic feature of living radical polymerisation¹⁹¹) to a critical value and then slightly decreases in the range $10\% \leq C \leq 40\%$ (from $M_n = 8000$ as a maximum at $C = 10\%$ to $M_n = 6000$ at $C = 40\%$). In the above-mentioned C region, the M_w/M_n ratio remains equal to ~ 2.5 .

Presumably, the data from ESR measurements can be used for obtaining quantitative estimates. However, this was not done in the study.²⁰³ It was found that the kinetics of accumulation of the free methacryl radicals $[R'] = f(t)$, where t is the polymerisation time, is described by curves with a maximum $[R']_{\max}$ attained at $C \simeq 50\%$ both for usual and living TRP. When the temperature changes from 70 to 90 °C, $[R']_{\max}$ decreases by a factor of 3.5 and by more than an order of magnitude in the case of usual and living TRP, respectively. However, quantitative estimates are of most interest. These estimates can be made by comparing the data on the reduced polymerisation rates

$$\frac{W}{[M]} \equiv W',$$

where $[M]$ is the instantaneous concentration of the monomer with $[R']$ at the same t . Actually, taking into account that

$$W = k_p[R'] [M],$$

the instantaneous rate constant of chain propagation can be represented as follows:

$$k_p = \frac{W'}{[R']},$$

where $[R']$ is the concentration of radicals as chain carriers which can add molecules M . The concentration of the $[R']_{\Sigma}$ radicals measured by ESR includes not only $[R']$ but also the dead methacryl radicals immobilisation in a highly cross-linked structure in microregions with frozen mobilities of both R' and M .^{11, 13, 63} Hence, it can be written that

$$k_p \geq \frac{W'}{[R']_{\Sigma}},$$

i.e., using $[R']_{\Sigma}$ measured by ESR instead of the unknown concentration $[R']$, the lower limit can be estimated as

$$k_p \equiv k'_p \quad \left(k_p \geq k'_p = \frac{W'}{[R']_{\Sigma}} \right).$$

The k'_p constants thus estimated from the published experimental data²⁰³ are given below. In the case of usual TRP performed at 70 °C, k'_p decreases from 9800 to 380 litre $\text{mol}^{-1} \text{ s}^{-1}$ in the range of $55\% \leq C \leq 75\%$. In the case of living TRP at the same temperature and in the same C range, k'_p is in the range of 60–70 litre $\text{mol}^{-1} \text{ s}^{-1}$. If the data obtained in the study²⁰³ are considered to be reliable, this result is unexpected. It is known²⁵ that in the course of usual TRP, k_p decreases (see Ref. 204) from 300–500 at $C \rightarrow 0$ to < 10 litre $\text{mol}^{-1} \text{ s}^{-1}$ at

$C > 50\%$. Since $k_p > k'_p$, $k_p > 9800$ (!?) at $C = 55\%$. For living polymerisation at 70°C , $k'_p = 60-70$ ($k_p > 60-70$) seems to be normal as related to the results of the study,²⁵ because the molecular mobility of a cross-linked macromolecular medium increases in going from TRP to living chain polymerisation. However, the results of the study²⁰³ of living TRP at higher temperatures also gave unexpected results. At $C \geq 50\%$, k'_p is in the range of 250–500 at 80°C ($k_p > 250-500$, which is inconsistent with the prediction) as the conversion increases to the limiting values. At 90°C , $k'_p = 1500-3000$ (!!).

To summarise, studies of living TRP are at their infancy.¹⁷²⁻¹⁷⁷ Hence, the use of TRP as an efficient tool of macromolecular design of highly cross-linked polymer structures can only hold promise for the (hopefully close) future.

VIII. Conclusion

In the late 1950s–early 1960s, TRP attracted considerable attention due to the development of a new class of unsaturated polyester resins, *viz.*, polyester acrylates, which were later called oligoester acrylates. Extensive systematic studies on the basis of a large number of oligoester acrylates in combination with the development of new experimental techniques enabled researchers first to reveal the main kinetic features of TRP and then to discover its main distinguishing feature, *viz.*, microheterogeneity. Later on, the presence of microheterogeneity was repeatedly confirmed by both experiments and calculations. These results were generalised in the monograph.¹¹ In more recent studies of TRP, new original procedures were developed^{45, 49-51} for the investigation of the microheterogeneity and these procedures were applied to molecular design. These studies were surveyed in the monograph.⁴⁵

Beginning in 1990s, interest in TRP has quickened all over the world resulting in a more than tenfold increase in the number of publications. This is associated with the development of new technological approaches, for example, in rapidly progressing materials science (construction of materials for information storage, biomaterials, fiber-optic coatings, *etc.*). It is TRP that has proved to be best suited for solving new technological problems owing to its distinguishing features, among which are the possibilities of performing reactions in the superfast mode at any (including low) temperatures, control of the process by initiation (including easily controlled sources of photochemical initiation), *etc.* Besides, the discovery of living radical polymerisation has opened up new opportunities for macromolecular design.

The following modern trends in studies of TRP should be noted. Fundamental studies of the kinetics and mechanism of TRP are carried out with the use of new experimental possibilities associated with the development of reliable fast-acting efficient methods for kinetic studies, such as fast-response calorimetry, spectroscopy, *etc.* It should be noted that no radically new data on the kinetic characteristics and mechanism of TRP have been obtained since 1977.^{1, 11} Both the correlations between the kinetics and conformational properties of the starting multifunctional monomers and microheterogeneity as the principal features of TRP, which have been described and discussed earlier in the study¹ and monographs,^{11, 13} were confirmed in many studies of a large number of materials with the use of modern techniques. Three-dimensional radical polymerisation was investigated primarily using two classes of monomers, *viz.*, divinylbenzene and its derivatives (including copolymerisation with styrene), on the one hand, and multifunctional (di-, tri-, tetra-) methacrylates and acrylates, on the other hand. The quantitative identification of cyclisation and a decrease in the reactivity of the pendant vinyl group in the course of TRP are major achievements of studies of the first group of compounds (divinylbenzene).^{151, 168, 169, 194}

In studies of compounds belonging to the second group (acrylates and methacrylates), considerable efforts have recently focused on the examination of superfast modes of TRP under

conditions of photochemical initiation. It was found that at high photoinitiation rates, the initiating radicals R_i serve as main partners in the quadratic chain termination $R + R_i \rightarrow$ death reactions (where R_i is a radical of small size due to which it is highly mobile in a cross-linked medium; R is a polymeric low-mobile chain carrier). This fact radically changes the TRP process. Thus, autoacceleration disappears and the reaction rate order with respect to initiation decreases from 0.5 (normal) to ~ 0 (anomaly).

It should be noted that considerable efforts in the studies of both groups of compounds have been directed to computer simulation of TRP.¹¹¹⁻¹²⁰ This direction of investigation is progressing rapidly, which is of great importance for extending the possibilities of macromolecular design.

Of special note are the development of procedures for performing living radical polymerisation involving both the adaptation of the known agents of living TRP to complex conditions of cross-linked media and the construction of new agents specially designed for TRP. Prominence is given to detailed studies of the kinetics and mechanism of living TRP.

Applied studies are carried out primarily in the field of materials science. These studies are aimed at using cross-linked polymers for producing materials for microelectronics and information storage systems, polymers for paint-and-varnish coatings, films and packings, biomaterials, materials for aspherical lenses, polymeric carriers for control drug delivery, fiber-optic coatings, ultraviolet curable adhesives, dental materials, abrasive-resistant coatings, polymeric hosts for luminophores and liquid-crystalline structures. The properties of TRP products and fields of application of these products were considered in the studies.²⁰⁵⁻²²²

Problems of three-dimensional radical copolymerisation are beyond the scope of the present review and will be surveyed in the future.

In conclusion, it should be noted once again that there are two radically different approaches to the interpretation of the dependence of the reduced polymerisation rate on the conversion within the framework of the microheterogeneous mechanism (microheterogeneous model) of TRP. One approach is based on the assumption that elementary steps of TRP (chain initiation, propagation and termination) are diffusion-controlled. Hence, their effective rate constants depend on the conversion and they change in the course of polymerisation. The functions $k = f(C)$ depend on the choice of a physical model for the diffusion control of elementary steps (according to Smolukhovskii, within the framework of the free volume theory or on the basis of the reaction-diffusion model). This approach does not explicitly take into consideration the microheterogeneity of the reaction medium and does not radically differ from the known theories for the gel effect developed for linear polymerisation of usual (monofunctional) vinyl monomers in high-viscous media.²²³ The trivial kinetic features of TRP (autocatalysis in the early stages, auto-retardation at high conversions, the dependence of $W/[M]$ on the initiation rate at fixed C) and the results of non-stationary kinetic measurements of elementary (actually, effective) rate constants of chain growth and termination are in satisfactory agreement with the results obtained with the use of models relying on the correlation between the diffusion-controlled rate constants and the state of the reaction medium determined by the conversion.

However, TRP involves unusual processes and phenomena (which are discussed in the present review and have been described and analysed in detail in the monograph⁴⁵), which cannot be interpreted on the basis of homogeneous models with the constants $k = f(C)$. This gave impetus to the development of the microheterogeneous model of TRP. The simplest version of this model involves two types of local microreactors in which polymerisation processes occur, *viz.*, microreactors with a high-viscous reaction medium (peripheral layers of microgel particles) and microreactors with a reaction medium consisting of the virtually pure starting monomer (oligomers). Because of this, the microheterogeneous model deals with only $(k)_0 = f(C = 0)$ and

$(k)_g = f(C = C_g)$, where the index g denotes the gel, instead of the rate constants $k = f(C)$ changing continuously in the course of TRP (homogeneous model). Hence, the rate constants of the elementary stages of TRP (chain initiation, propagation and termination), $(k)_0$ and $(k)_g$, in the case of the microheterogeneous model are independent of the depth of polymerisation. The occurrence of autoacceleration in the early stages and autodeceleration in the later stages of TRP (interpreted within the framework of the homogeneous model as a result of the dependence of k on the conversion) is associated first with an increase (at conversions lower than the critical value) and then with a decrease (at conversions higher than the critical value) of the total volume of microreactors of the first type (microgel particles).

Apparently, both models (homogeneous and microheterogeneous) are limiting cases of TRP. In actuality, the microheterogeneity of TRP is most pronounced for oligomers with short and(or) rigid oligomeric blocks in polymerisation with low (no higher than 10^{-7} mol litre $^{-1}$ s $^{-1}$) initiation rates. For oligomers with long and(or) flexible oligomeric blocks or upon polymerisation with very high initiation rates (higher than 10^{-6} – 10^{-5} mol litre $^{-1}$ s $^{-1}$), the microheterogeneity is less pronounced. In recent experiments on living chain TRP, sources of the appearance of microheterogeneity in copolymerisation with the specially chosen comonomers as well as in polymerisation under conditions leading to the formation of very short chains (inhibition, chain transfer, catalytic chain transfer) were eliminated to an extent that the homogeneous model of radical polymerisation became quite suitable.

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Chain chemical reactions at low temperatures

D P Kiryukhin, I M Barkalov

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Abstract. The review generalises results of studies on chain cryochemical polymerisation and copolymerisation, oxidation, chlorination and hydrobromination of saturated hydrocarbons and alkenes in the crystalline and glassy state. Chain chemical reactions that occur at liquid helium temperature with a measurable, temperature-independent rate are considered; high-intensity autowave modes of low-temperature reactions in solid phase are discussed. The bibliography includes 111 references.

I. Introduction

Chain chemical reactions were discovered and their study was started at the beginning of the 20th century. The term ‘chain reaction’ appeared in 1913 when Bodenstein was studying the reaction of hydrogen with chlorine. The application of the chain reaction theory turned out to be exceptionally fruitful for understanding the kinetics and mechanisms of many processes, including natural ones. Chain processes that had originally been discovered in the gas phase were later observed in liquid and solid phases. A fundamental contribution to the development of the quantitative theory of chain processes was made by Academician N N Semenov and his disciples, and also by Professor S Hinshelwood (Semenov and Hinshelwood were awarded the Nobel prize in chemistry for these works in 1956). Chain reactions were classified into the following basic types: non-branched, branched and degenerate branched; furthermore, the following steps of a chain process were distinguished: chain initiation, chain growth, chain branching and chain termination. The history of the creation and development of the theory of chain reactions is described in detail in the monograph by Emanuel *et al.*¹

Until recently, the obstacles to studies on chemical reactions at low and ultralow temperatures (4.2–77 K) were the traditional theory of the chemical reaction mechanism. The requirement that an activation barrier has to be overcome in each elementary event postulated by this theory precludes any noticeable chemical transformations in the vicinity of absolute zero temperature. The

thousand-year experience of the mankind showed that cooling prevents any complex chemical transformations.

The classical picture of the elementary event of a chemical reaction is based on the following postulates: (1) the activation energy barrier is necessary to be overcome in order to start a reaction between reactants; (2) the reactants get the energy they need to overcome the activation barrier from intermolecular interactions; (3) the time required for the reactants to accumulate this energy (the characteristic time of an elementary event) is determined by the temperature of the environment. It is easy to show that these postulates totally exclude the possibility for a chain chemical reaction to occur near absolute zero. However, a considerable fraction of matter in the Universe exists in the cold of the cosmic space. It is hard to believe that this matter has been scattering since the Big Bang without undergoing any chemical evolution.

The natural chemical transformations in solids only become noticeable on a geological time scale; they also involve liquid and gas phases, mechanical destruction, as well as high pressures and temperatures. The combustion of solid fuels, explosions and sintering processes were always considered as reactions occurring at interfaces between a solid and a gas or liquid. It should be noted that it is most thermodynamically favourable to perform the majority of important industrial processes, *e.g.*, synthesis of ammonia from nitrogen and hydrogen, at the lowest possible temperatures. Low-temperature synthesis is also preferable because, for complex chemical processes, only those of the possible transformation channels ‘survive’ which have the lowest activation energy.

In the 1930s, polymerisation of crystalline monomers was reported.^{2–4} It was found, for example, that transparent trioxane undergoes polymerisation in the presence of formaldehyde vapour to give polyoxymethylene fibres oriented along one of the crystallographic axes. The formation of polymers was observed^{3,4} upon freezing of acetaldehyde (m.p. 150 K). This was a step to the low-temperature synthesis. It was found that chain reactions can occur in solid matter even at low temperatures, although this is forbidden.

The concept that chain chemical reactions are impossible near absolute zero was discarded after a low-temperature threshold of the rate of a chemical reaction had been revealed experimentally in studies on the polymerisation mechanism of solid formaldehyde at 4–100 K.^{5–7} Subsequently, the low-temperature reaction rate threshold was found to exist for many chain and non-chain chemical processes.⁸ It was found that certain chemical reactions can occur with a measurable temperature-independent rate at

D P Kiryukhin, I M Barkalov Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 515 54 20. Tel. (7-096) 522 32 46. E-mail: kir@icp.ac.ru (D P Kiryukhin). Tel. (7-096) 522 19 73. E-mail: barkalov@icp.ac.ru (I M Barkalov)

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liquid helium temperature. Just after the low-temperature reaction rate threshold had been discovered, it was suggested that the mechanism of this phenomenon could be interpreted within the framework of the molecular tunnelling concept. Later, this idea was developed with intramolecular oscillations taken into account.^{8–12}

The scope of studies on chain cryochemical reactions expanded considerably after the discovery of transformations in autowave modes that occur upon local brittle destruction of solid samples subjected to radiolysis or photolysis at 4.2–77 K.^{13–15} When a sufficiently extended sample undergoes local brittle destruction, a chemical reaction starts on the newly formed surface. The temperature or density gradients that appear during the reaction create stresses that favour subsequent layer-by-layer destruction of the solid sample. Owing to this positive feedback, an autowave of the chemical transformation spreads along the sample, *i.e.*, a kind of mechanoenergetic chain is realised.^{13–15} The autowave mode is observed for many reactions (chlorination of hydrocarbons, hydrobromination of alkenes, polymerisation) in the temperature range 4–77 K. This concept allowed us to put forward new ideas regarding the mechanisms of the ‘cold’ chemical evolution of matter in the Universe.¹⁵

In the present work, we generalise experimental data of studies on chain cryochemical processes that have led to the discovery of the low-temperature threshold of the chemical reaction rate and also the autowave and self-oscillating modes of low-temperature transformations. Consideration of general trends of the evolution in this field of chemistry is certainly interesting; however, our review pays the most attention to studies performed over the last years.

II. Chain reactions in crystals

1. Polymerisation of solid formaldehyde

In the 1960s, studies on the solid-phase polymerisation were developed intensely. However, most of these studies were phenomenological, and the theoretical conclusions and hypotheses were rather speculative than based on experimental results. Initially, it was assumed¹⁶ that the strict orientation of monomer molecules in the crystal can predefine the regularity of chains of the macromolecules formed, and hence the ‘precursors’ of reactants in the crystal will favour the realisation of unusually fast chemical transformation mechanisms. As early as in 1960, N N Semenov proposed the energy chain mechanism for the solid-phase polymerisation.¹⁶ The idea was that the energy evolved in each elementary event of the polymer chain growth does not dissipate as heat, but is consumed for overcoming the activation barrier in the next event. A variant of such collective interaction is the exciton movement along the chain of monomer molecules in the crystal. In this case, the polymer chain growth will occur at a rate equal to the exciton propagation rate.¹⁷

The reader can find vast experimental data collected to date in a number of reviews.^{18–22} Let us outline the main conclusions of studies carried out during that period. When a polymer is formed, the mean distances between the fragments of the monomer crystal lattice change (*i.e.*, the intermolecular distances are replaced by the lengths of chemical bonds). Two extreme cases are possible: (1) the monomer crystal structure defines the structure of the resulting polymer (diacetylene derivatives, trioxane); (2) the polymer is formed as a separate phase in extended defects of the crystal lattice, which leads to subsequent destruction of the monomer crystal (acrylamide). In addition, many intermediate cases exist.

It is hard to imagine that the decay of the growing macroradicals can occur by recombination or disproportionation in a crystal where the translational movement is quite limited. The previously developed ideas of ‘polychronous kinetics’ were found to be also applicable when considering the polymerisation in a crystal.^{23,24} As the polymer chain grows in a solid, the access of the monomer to the active site is hampered and kinetic inhibition of

the process occurs; this is called polymer chain ‘freezing’ (the opposite process is called ‘revival’).

The main results of studies on the radiation-induced polymerisation of solid formaldehyde at 5–150 K were described by Kiryukhin.²⁵ The dependences of the formaldehyde polymerisation rate (m.p. 155 K) and the radiation-chemical yield of the polymer [$G(-M)$] on temperature were studied in the temperature range 4.2–140 K. It was found that these dependences become weaker as the temperature is decreased, and are no more observed in the range 5–20 K (Fig. 1). Even at 5–20 K, polymerisation occurs with high radiation-chemical yield $G(-M) = 1000$ which is typical of chain processes.[†] This is the first experimental proof of the existence of long polymeric chains formed upon conversions in the vicinity of absolute zero temperature (~ 1000 monomer units at 4.2 K). The non-steady-state process kinetics was studied and the elementary polymerisation rate constants were determined. In the temperature range 80–140 K, the time required for the chain to lengthen by one unit increases with a decrease in temperature according to the Arrhenius law, with an activation energy of ~ 10 kJ mol⁻¹, and no longer depends on temperature upon deeper cooling, *i.e.*, a low-temperature threshold of the chain chemical reaction is observed.⁷ The formaldehyde polymerisation is a typical chemical reaction: a number of planar triangular molecules of the monomer are transformed to a long $-CH_2-O-CH_2-O-$ chain; obviously, the formation of chemical bonds in the macromolecules being formed should increase considerably the density of the compound.

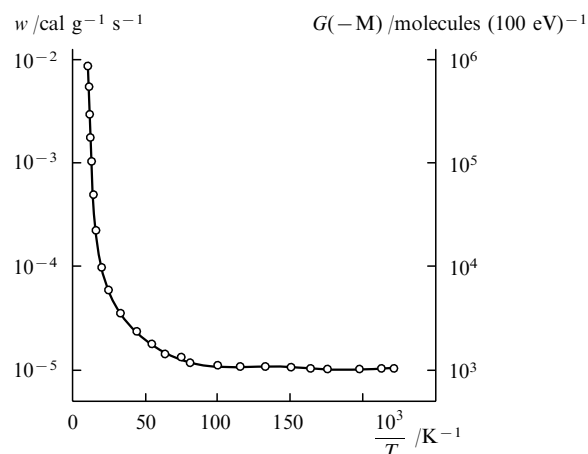


Figure 1. Temperature dependences of the rate (w) and radiation-chemical yield [$G(-M)$] of formaldehyde polymerisation under γ -irradiation.²⁵

Studies of low-temperature photoinitiated solid-phase formaldehyde polymerisation were also carried out. It was reported^{26,27} that a polymeric phase was formed in crystalline and amorphous formaldehyde containing an additive of β -naphthol as a result of photoinitiation at temperatures above 20 K. Low-temperature transformations in amorphous formaldehyde–chlorine mixtures were studied.^{28–30} Photolysis of chlorine under these conditions was carried out by an excimer laser ($\lambda = 308$ nm) or an arc mercury lamp ($\lambda = 365$ nm). In the temperature range 10–77 K, the formation of oligomers containing 5–7 monomeric units was observed. At temperatures above 90 K, the chain length increased twofold. These values are much lower than those of the polymer formed upon radiolysis of crystalline formaldehyde (chain length 10^3 – 10^6); this is probably due to the molecular disorder in the amorphous compound.

[†] The radiation-chemical yield of active sites (g) that initiate polymerisation is usually 1 (per 100 eV of absorbed energy); in this case, $G(-M)$ equals the kinetic length (ν) of the polymeric chains: $\nu = G(-M)/g = 1000$.

Polymerisation of crystalline acetaldehyde (the nearest homologue of formaldehyde) and glyoxal (the simplest dialdehyde) occurs with much lower rates; at $T < 77$ K, no long polymeric chains are formed from these monomers.^{25,31} Subsequent search for cryochemical chain reactions involved two-component polycrystalline systems.^{32–37}

2. Solid-phase hydrobromination and chlorination of ethylene

The photochemical hydrobromination of alkenes at temperatures above 77 K has been reported in detail.^{32,33} A detailed study of the kinetics and mechanism of radiation hydrobromination of ethylene in the temperature range 4.2–90 K revealed long kinetic transformation chains in the low-temperature range ($\nu \approx 300$ chain units at 20 K).^{34,35} This process is yet another example of a low-temperature rate threshold of a chain chemical reaction. The elementary events of chain growth in hydrobromination and deuterobromination were compared in the following systems: C_2H_4-HBr , C_2H_4-DBr , C_2D_4-HBr and C_2D_4-DBr . This made it possible to determine more precisely the chain growth mechanism in the hydrobromination of ethylene at ultralow temperatures. It was found that it is the approach of heavy species (including intermolecular oscillations) rather than the tunnelling transfer of the hydrogen atom that limits the rate of the low-temperature chain growth.

A method to obtain reactive cryocrystals was reported; the activation-free growth of chains ~ 300 units long at 17–45 K was studied for ethylene photochlorination as an example.³⁶ The role of the spatial packing of reactants in solid-phase chain chemical reactions at ultralow temperatures was considered by Misochko.³⁷ Three limiting cases were discussed: (1) growth of one-dimensional chains along a specific direction in a mixed crystal with alternating arrangement of reactants; (2) chain growth in a random binary mixture of reactants; (3) chain growth with long-range migration of 'hot' atoms. In the first case, where the products formed in the reaction gradually replace the reactants in the lattice sites without any considerable displacement of the neighbouring molecules, chains up to ~ 300 units long can grow. In the second case, the mean chain length is determined by the number of molecules in the first coordination sphere which are accessible to any reactive species. The chain growth ends in the stabilisation of radicals; the mean chain length is 3–7 units. If chain growth involves 'hot' atoms, the latter can migrate to a far distance from the cage and thus increase the efficient number of sites that separate successive chain units.

Thus, data on the radiation-induced formaldehyde polymerisation and ethylene hydrobromination and on the ethylene photochlorination in crystalline state have shown that chain processes can occur at temperatures near absolute zero. These experiments promoted theoretical studies aimed at the development of the concept of the elementary event of a chemical reaction in a solid.^{8,12,36–41}

3. Low-temperature oxidation

Studies on the gas-phase and liquid-phase oxidation of various compounds have contributed markedly to the development of the chain reaction theory.¹ In particular, the possibility, in principle, of radiation-induced oxidation of sulfur dioxide with molecular oxygen under low temperature conditions (at 77 K and in the post-radiation effect mode, *i.e.*, upon heating of a pre-radiated system) was shown experimentally.⁴² The radiation-induced oxidation of SO_2 is of interest in the context of decontamination of gaseous industrial exhausts and the possibility of obtaining sulfuric acid. Therefore, it is important to evaluate the efficiency of the non-traditional environmentally safe method for the SO_3 synthesis at low temperatures where undesirable admixtures can be frozen-out. Studies of the low-temperature oxidation of sulfur dioxide showed that the basic process occurs by a chain mechanism during γ -irradiation at 77 K; the initial radiation-chemical yield is 30. The optimum starting molar ratio $SO_2:O_2$ which

provides the maximum conversion of sulfur dioxide is 1 : 4. In the post-radiation mode, the conversion is no greater than 1%.

4. Low-temperature radiation-induced conversions of hydrogen cyanide and cyanogen bromide

Hydrogen cyanide (prussic acid) is a compound that is rather common in the outer space: HCN molecules have been detected in comets, in protoplanet formations, in giant clouds of interstellar dust and in other galactical structures. In principle, the HCN molecule may be regarded as the basis of pre-biological chemical evolution, since hydrogen cyanide is a precursor of purines, pyrimidines and amino acids.^{43–47} Stahler⁴⁸ suggested that the chain length of azapolyene macromolecules formed upon HCN polymerisation may be used as a kind of clock to determine the age of interstellar clouds. Other astrophysical aspects of the chemical conversions of hydrogen cyanide are also being developed intensely.^{49,50}

It seemed interesting to study the chemical behaviour of this simple molecule under conditions that are close to those in outer space (low temperatures and radiation) and the role it plays in the 'cold' chemical evolution of the Universe. Below we present the results of experiments carried out in a number of studies.^{51–54}

Cooling of liquid HCN to 77 K converts it to the crystalline state. On heating of hydrogen cyanide cooled to 77 K, a 'crystal-crystal' phase transition occurs (248 K) followed by melting (260 K). The heat of melting of HCN is 8.4 ± 0.4 kJ mol⁻¹.

When solid HCN undergoes radiolysis (with doses of 1–800 kGy) at 77 K, the active sites of radical and radical ion nature are stabilised in the crystal.⁵⁴ On subsequent heating of the system, a brown polymer ($-HC=N-)_n$, which contains conjugated double bonds, and crystals of the tetramer (1,2-diaminomaleonitrile) are formed in the solid phase. At low temperatures, the polymerisation rates of crystalline HCN are low, and chain polymerisation at 77 K under γ -radiation is not observed. A polymer is formed at temperatures near the melting point of the monomer.

The ESR spectrum of the polymer represents a singlet typical of polyconjugated systems. Within the framework of the suggested radical transformation scheme,⁵⁴ the brown colour of the polymer may be explained by the formation of the $-HC=N-HC=N-$ conjugation chain. The formation of needle-like crystals of 1,2-diaminomaleonitrile (tetramer of hydrogen cyanide) may be⁵³ due to the formation of an intermediate biradical, *viz.*, aminocyanocarbene; dimerisation of the latter results in the tetramer. The fact that 1,2-diaminomaleonitrile is formed under conditions that are close to those in outer space (low temperatures and radiation) seems very important to us, since this compound may play a key role in pre-biological organic synthesis because its hydrolysis directly gives an amino acid.

Crystalline cyanogen bromide does not contain $N\cdots H$ hydrogen bonds typical of crystalline HCN. It was of interest to compare the ability of this compound and hydrogen cyanide to undergo cryopolymerisation. Polymerisation of BrCN following radiolysis at 77 K occurs upon unfreezing in the temperature range 220–230 K and near the monomer melting point (324 K).⁵⁵ The heats of melting of BrCN (11.6 kJ mol⁻¹) and of polymerisation (86.0 ± 2.0 kJ mol⁻¹) have been determined. The dependence of the polymer yield from cyanogen bromide on the pre-irradiation dose has an unusual shape with an extremum. At doses in the range 0–900 kGy, the polymer yield increases monotonically to reach a maximum value of $\sim 9\%$ at 900 kGy. A subsequent increase in the irradiation dose decreases the yield to $\sim 4\%$ at 1200 kGy; at higher doses, the yield remains nearly constant up to a dose of 2000 kGy. It is assumed⁵⁵ that the suppression of the polymerisation of cyanogen bromide at high pre-irradiation doses results from the progressive degradation of the matrix structure. Such radiation-induced degradation may increase rather strongly the molecular mobility near the monomer melting point. As a result, the rate of polymer chain termination may increase, which would result in degeneration of the chain

process and hence decrease the polymer yield. Thus, the absence of intermolecular chains with strong N...H hydrogen bonds in crystalline cyanogen bromide predetermines a difference in the dynamics of the cryopolymerisation of BrCN and HCN and decreases the radiation resistance of BrCN.

5. Cryopolymerisation of ketene

Work on the mechanism of cryochemical chain reactions involved studies on the radiation-induced polymerisation of carbonyl-containing compounds (formaldehyde, acetaldehyde, glyoxal, *etc.*).²⁵ Ketene ($\text{H}_2\text{C}=\text{C}=\text{O}$) is of considerable interest for studying the features of the low-temperature polymerisation of such compounds. Since the ketene molecule contains cumulated hetero-chain double bonds, its linear polymerisation may occur by three different pathways to give a polyketone, a polyacetal or a polyester.

Polyketones are formed in the presence of cationic catalysts (*e.g.*, AlBr_3) at -60°C ,⁵⁶ whereas polyesters and polyacetals are formed with anionic catalysts (AlEt_3).⁵⁷ Radical initiators do not cause ketene polymerisation.

In addition to soluble linear macromolecules, polymerisation can give insoluble cross-linked structures, since each ketene molecule contains two double bonds.

On cooling to 77 K, ketene is completely converted to the crystalline state. When such a sample is heated, the calorimetric curve displays only an endothermic peak, which corresponds to the melting of crystalline ketene at 140 K (Fig. 2, curve 1). The heat of melting of ketene determined from calorimetric measurements is $4.0 \pm 0.4 \text{ kJ mol}^{-1}$.

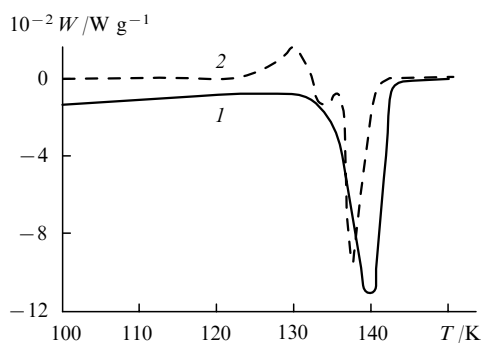


Figure 2. Calorimetric curves of ketene unfreezing;²⁵ (1) non-irradiated sample; (2) sample exposed to γ -irradiation with a dose of 300 kGy (here and in Figs 4 and 5, W is the heat evolution rate).

Heating of crystalline ketene pre- γ -irradiated at 77 K results in the solid-phase polymerisation of the monomer, which starts near the melting point and occurs near the melting point, as well. An increase in the pre-irradiation dose decreases the measured temperature of the beginning of polymerisation. For example, at a dose of 300 kGy, the temperature of the beginning of the reaction is about 30 K lower than the melting point of the monomer (Fig. 2, curve 2). The polymer yield increases with an increase in the pre-irradiation dose and reaches 17% at a dose of 350 kGy.

The thermal effect of ketene polymerisation in this reaction mode as determined from the comparison of the gravimetric yield of the polymer with data from calorimetric measurements is $18.1 \pm 1.8 \text{ kJ mol}^{-1}$. The resulting polymer is yellow; on heating to room temperature, it gradually turns dark-orange. It is partially soluble in ethyl methyl ketone. The ratio between the soluble and insoluble polymer fractions depends on the time of exposure of the sample at room temperature. For example, the solubility of the polymer obtained after pre-irradiation of the monomer with a dose of 350 kGy is 85%. If a sealed tube containing this polymer and non-consumed monomer is kept for 20–30 min at $\sim 20^\circ\text{C}$,

the soluble polymer fraction decreases to 60%. Hence, post-polymerisation of ketene gives a partially cross-linked polymer; this polymer undergoes additional structuring at room temperature in the presence of the monomer, and the proportion of the cross-linked fraction in it increases. This indicates that the polymer retains double bonds which are involved in cross-linking of the macromolecules.

Analysis of the IR spectra of the polymer (the ratio of the band intensities characterising the $\text{C}=\text{C}$ and $\text{C}=\text{O}$ bonds in the regions of 1600 and 1720 cm^{-1} , respectively) suggests that ketene polymerisation mainly involves cleavage of the $\text{C}=\text{O}$ bonds.

The preferential cleavage of $\text{C}=\text{O}$ bonds during the post-radiation polymerisation of ketene is additionally evidenced by the measured thermal effect of the reaction, which is 18 kJ mol^{-1} . This is close to the thermal effect of polymerisation⁵⁸ occurring with the cleavage of $\text{C}=\text{O}$ double bonds [the experimentally determined heat of polymerisation of acetaldehyde is 10.5 kJ mol^{-1} and that of glyoxal is 21.0 kJ mol^{-1} (see Ref. 25)]. The thermal effects of polymerisation involving the cleavage of $\text{C}=\text{C}$ bonds are much higher, *viz.*, about $50\text{--}80 \text{ kJ mol}^{-1}$.

The cross-linking of the polymer on its storage at room temperature probably occurs through $\text{C}=\text{O}$ bonds, since the IR band intensities corresponding to the stretching vibrations of these bonds decrease during this process.

Thus, the low-temperature post-radiation polymerisation of crystalline ketene mainly involves the cleavage of $\text{C}=\text{O}$ bonds to give a polyester. The retention of $\text{C}=\text{O}$ bonds enables the cross-linking of the polymer.

6. Carbon suboxide

Unusual features were observed in the low-temperature polymerisation of carbon suboxide (tricarbon dioxide) C_3O_2 (m.p. 160 K).^{59,60} Calorimetric measurements showed that no radiation-induced polymerisation of solid C_3O_2 with measurable yields in the temperature range 77–160 K could be detected. Similarly, no polymerisation of the monomer was observed in the radiolysis of liquid carbon suboxide. However, it was found that heating of C_3O_2 samples which have been exposed to preliminary γ -irradiation at 77 K resulted in efficient post-polymerisation. The calorimetric curve of unfreezing of samples pre-exposed to radiolysis shows that the heat evolution due to the polymerisation of C_3O_2 is observed starting from the melting point of the monomer. In the temperature range 180–260 K, polymerisation occurs with a very low rate; its rate increases significantly upon subsequent heating, reaches a maximum and then decreases as the monomer is consumed. Probably, radiolysis of crystalline carbon suboxide at 77 K and subsequent heating produce oligomeric active sites (containing 3–5 monomer units); the probability of their decay is low both in the solid and liquid phases. It is these sites that are responsible for the efficient liquid-phase post-radiation polymerisation of C_3O_2 . The chain growth in this reaction occurs by the cationic mechanism.^{25,60}

Yet another interesting feature of the post-polymerisation of carbon suboxide is the auto-acceleration of the process at constant temperature. The post-polymerisation of C_3O_2 was studied calorimetrically (Fig. 3) at 297 K .⁵⁹ At this temperature, the process rate first increases with time, *i.e.*, auto-acceleration of the reaction is observed, and then decreases to zero because the monomer is exhausted. This phenomenon is unusual because the number of active sites 'preformed' during preliminary irradiation can only decrease. Probably, the most likely reason for the auto-acceleration is branching of the chain reaction in an elementary event of monomer addition. Without specifying the particular branching mechanism, let us note that the specific features of the electron structure of the C_3O_2 molecule allow us to speak of both physical and energetic branching. Anyway, the issue of the auto-acceleration mechanism remains open as yet.

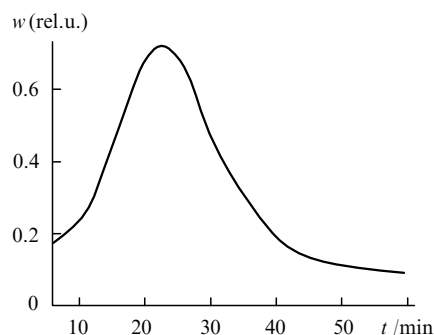


Figure 3. Variation of the post-polymerisation rate (w) of C_3O_2 at 297 K with time; the pre-irradiation dose is 10 kGy.⁵⁹

7. Cryocopolymerisation of dienes and α -alkenes with sulfur dioxide

Certain dienes, such as butadiene, isoprene and 2,3-dimethylbutadiene, efficiently copolymerise with sulfur dioxide to give copolymers with the 1:1 composition.⁶¹ Two main mechanisms of the formation of alternating copolymers are possible in such two-component systems. One of them is based on the assumption that two monomers are added sequentially. The alternation of monomer units is due to the considerably higher rate constants of the cross-growth of chains in comparison with the addition constants for each of the monomers. The other mechanism assumes that the copolymer is formed by the mutual addition of binary charge-transfer complexes, which are formed upon mixing of the monomers. The results of studies on the alternating copolymerisation were reported by Golubev⁶² for a broad range of such systems.

A specific feature of alternating copolymerisation is that copolymers with the 1:1 composition are formed, no matter what the composition of the original monomer mixture. However, the reaction has specific features at low temperatures, which not always comply with the common concept of liquid-phase processes. In fact, solid-phase chemical transformations and copolymerisation in particular depend considerably on the complex phase state of the solid reactant mixture, and are sometimes determined by this composition.²² As a rule, radiolysis of solid organic mixtures at 77 K results only in the accumulation of stabilised active sites, which are released from the traps upon subsequent heating of the system in the absence of irradiation and initiate the chain chemical transformations. When the system melts, all the growing active sites usually decay, and the polymerisation processes stop. Thus, both phase transitions and chain copolymerisation occur in the temperature range from 77 K to the melting point region of the multicomponent system.²¹

Experimental results obtained by Kichigina *et al.*⁶³ indicate that the phase composition of an isoprene- SO_2 system affects both the copolymer composition and the dynamics of post-radiation copolymerisation. On sufficiently rapid cooling of a liquid solution of these monomers to 77 K, the system vitrifies; however, it can also be obtained in polycrystalline state upon 'annealing'. The eutectic mixture formed in the system is not equimolar. If isoprene is copolymerised with SO_2 in the post-radiation effect mode at these low temperatures and with an excess of one of the monomers, the isoprene and SO_2 molecules are incorporated in the chain not in strict sequence but with violated alternation of units in the copolymer, as deduced from the results of elemental analysis and the heats of polymerisation.

The processes of post-radiation copolymerisation of a number of dienes and alkenes (ethylene, but-1-ene, cyclopentene, hex-1-ene, oct-1-ene, *etc.*) with sulfur dioxide, occurring both on heating of samples irradiated at 77 K and spontaneously (upon mutual dissolution of the compounds) were compared.⁶⁴ It was concluded that the possibility of the formation of donor-acceptor complexes of SO_2 with a monomer is not a sufficient condition, as it is

necessary that the structure and composition of the resulting complex favour subsequent polymerisation. A vivid example is provided by comparison of the following two-component systems: cyclopentene- SO_2 and cyclohexene- SO_2 . Spontaneous polymerisation is only observed in mixtures of cyclopentene with SO_2 ; neither spontaneous nor radiation-induced polymerisation is observed in the case of cyclohexene.

8. Quenched high-pressure phases

The radiation-induced polymerisation of crystalline acrylamide starts in areas containing extended defects and occurs at interfaces between the amorphous polymer and the crystalline monomer. In the eutectic mixture acrylamide-water, the chain polymerisation in the quenched high pressure phase was found to be hindered very strongly when the samples that had been exposed to radiolysis at 77 K were heated.⁶⁵ The most likely reason for the inhibition of this process is the small size of eutectical acrylamide crystals, the contacts between which are disturbed as the metastable ice phase passes into the equilibrium phase, with the accompanying sharp increase in the volume of the system and its strong dispersion. In fact, if the sample under study represents monomer microcrystals that have virtually no contacts between each other (which hinders strongly the transfer of the growing polymer chain from one crystal to another) and the linear size of these crystals does not exceed 100 molecules (the length of polymer chains is ~ 100 units), the polymerisation in such a sample will be hampered strongly in comparison with a monolithic sample (at equal concentrations of active sites). The estimated size of such crystals is $\sim 0.1 \mu m$.

III. Chain reactions in glasses

Amorphous bodies feature only short-range ordering where only the mutual arrangement of a few molecules is correlated. Owing to the absence of long-range order, amorphous bodies are isotropic, *i.e.*, their macroscopic properties do not depend on direction. At temperatures above the melting point, the compound is in a thermodynamically stable liquid state, while on cooling below the melting point it is transformed to another equilibrium state, *i.e.*, a crystal. However, sufficiently fast cooling can give a liquid in a non-equilibrium supercooled state; its subsequent cooling below the glass transition point (T_g) results in yet another non-equilibrium solid amorphous state, which is commonly referred to as glass. In fact, the transition from the supercooled liquid state to the glassy state occurs within a narrow temperature range. The glass-transition point is not a thermodynamic characteristics of a compound and may vary widely depending on conditions of the sample preparation and the measurement procedure used. Species in a glass are only capable of oscillation and small-scale rotational movement. The translational mobility typical of liquids is lost almost completely.

In our subsequent discussion, the following fact is very important: both the transition from the supercooled liquid state to the glassy state and the reverse transition (called devitrification) are accompanied by an abrupt change in the properties of the compound, such as viscosity, elastic modulus, thermal expansion factor, *etc.* Certainly, the most impressive phenomenon is the huge jump of viscosity (by 10–12 orders of magnitude) in the narrow glass-transition range.⁶⁶ From the chemical viewpoint, this means that the molecular mobility, which defines the dynamics of a chemical conversion, changes abruptly in this region. The nature of the chemical process should change considerably when the glass softening region is passed owing to the abrupt change in the mobilities of the reactants (in this case, the mobilities of molecules change stepwise on increasing or decreasing the temperature by only a few degrees).

Radiolysis of glassy matrices gives rise to reactive radical or ionic species which are stabilised in more or less deep traps and which may preserve reactivities for a long time. The absence of molecular mobility in the glass prevents mutual recombination of such stabilised radicals. When the matrix is heated and the glass

passes to the supercooled liquid state (devitrification), the translational mobility increases abruptly and, as a consequence, recombination of the accumulated radicals occurs. In the systems where the radicals released upon devitrification can initiate a chain reaction, efficient chain radical processes are realised (see below).

Polymerisation reactions (radical, ionic, copolymerisation, graft polymerisation) occurring quite intensely upon devitrification of glassy matrices that have undergone radiolysis at 77 K are described in detail in a review by Barkalov and Kiryukhin.⁶⁶

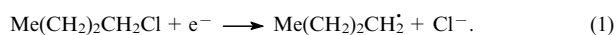
1. Chlorination during matrix devitrification

Specific features of low-temperature radiation-induced chlorination in glassy matrices were studied in a system butyl chloride–molecular chlorine ($T_g = 100$ K). The reaction was studied (i) directly under γ -irradiation and (ii) in the post-radiation effect mode on heating of pre-irradiated samples.^{67,68}

The radiation-induced chlorination of butyl chloride, in both the glassy and supercooled liquid state near the devitrification point (98–107 K), is characterised by a long life time (τ) of active sites (~ 1500 s). As the temperature is increased, the chain growth rate in the supercooled liquid reaches a maximum at 114 K; when the system passes to a thermodynamically stable liquid and the viscosity of the medium decreases, the probability of chain termination increases ($\tau < 100$ s). This decreases the overall rate of the process in the temperature range 115–150 K.

When glassy solutions of chlorine in butyl chloride pre-exposed to γ -irradiation at 77 K are heated in a calorimeter, heat evolution is observed because of chlorination. As the pre-irradiation dose is increased, the heat evolution due to chlorination is detected at progressively lower temperatures. After irradiation with a dose of 100 kGy, the reaction starts at 80 K.

The ESR spectra recorded during the irradiation of the system at 77 K manifest two types of paramagnetic centres, *viz.*, alkyl radicals ($R_A^\bullet$) and Cl_2^- species. The most likely mechanism of the formation of the $R_A^\bullet$ radical involves the dissociative capture of a slow electron:



The formation of Cl_2^- species probably results from direct electron addition:



The chain chlorination in the temperature range 90–110 K occurs by the classical mechanism:



The behaviour of the Cl^- species formed upon radiolysis is quite unusual: in the presence of these species, chlorine atoms are captured from the chain at 80–100 K according to the reaction:



As a consequence, the efficiency of the low-temperature radiation-induced chlorination decreases. It is this that differs radiation-induced chlorination from photochemical chlorination. In fact, photolysis does not produce Cl^- species, and at equal concentrations of alkyl active sites $R_A^\bullet$ the process occurs more intensely in those samples which have undergone photolysis.

Measurements of the rate of the process directly during γ -irradiation and in the post-effect mode (on heating of pre-irradiated samples) gave the following rate constant for the limiting step of chain growth [reaction (4)] in the temperature range 98–114 K:^{67,68}

$$k_4 = 10^{12} \exp\left(-\frac{25000}{RT}\right) \text{ litre mol}^{-1} \text{ s}.$$

Thus, the chain reaction of chlorination of chloroparaffins (both in the glassy and supercooled liquid state near the devitrification region) features long life times of active sites. With an increase in temperature, the chain growth rate reaches a maximum in the supercooled liquid; when the system passes to the thermodynamically stable state and the viscosity of the medium decreases, the probability of chain termination increases. Hence, similarly to polymerisation processes,⁶⁶ the suppression of chain termination reactions and simultaneous provision of efficient chain growth (this is the mode which is automatically realised near the devitrification region) makes it possible to increase considerably the overall reaction rate.

2. Hydrobromination of alkenes

The solid-phase hydrobromination of ethylene occurs in an equimolar crystalline complex. Mozhaev *et al.*⁶⁹ studied low-temperature radiation-induced hydrobromination of alkanes (for allyl chloride as an example) in the glassy state.

On cooling to 77 K, an allyl chloride–HBr system passes to the glassy state ($T_g = 88$ K) for all the reagent ratios used (1:1, 10:1 and 60:1). Spontaneous hydrobromination in this system occurs only in the liquid state (in the temperature range 182–220 K); for the allyl chloride:HBr ratio = 1:1, the conversion is 50% in this temperature range. The degree of conversion was determined calorimetrically. Complete conversion of HBr in thermoactivated hydrobromination occurs only in the presence of an excess of allyl chloride. For example, complete conversion of hydrogen bromide is observed in the allyl chloride–HBr system with 10:1 composition. The thermal effect of the reaction (ΔH) determined in a series of experiments is 71.4 ± 2.0 kJ mol⁻¹. This value is in good agreement with the thermal effect of ethylene hydrobromination and the calculated ΔH value.³⁴

Hydrobromination in the allyl chloride–HBr system can give either 2-bromo-1-chloropropane (addition in accordance with the Markownikoff rule) or 3-bromo-1-chloropropane (anti-Markownikoff addition). The difference between the thermal effects of these two reaction pathways is determined by the different strengths of C–H bonds in the methyl and methylene groups. In fact, the strengths of the C–Br bonds in 1-bromopropane and 2-bromopropane are the same,⁶⁹ whereas the energies of the C–H bonds in propane at the C(1) and C(2) atoms are 412 and 395 kJ mol⁻¹, respectively.

Thus, the thermal effect of the Markownikoff addition of bromine is 17 kJ mol⁻¹ higher than that of the anti-Markownikoff addition. Hence, the experimentally measured thermal effect of spontaneous hydrobromination of allyl chloride (which is the same as that of the hydrobromination of ethylene) corresponds to the Markownikoff addition of HBr to give 2-bromo-1-chloropropane.

During radiolysis of the allyl chloride–HBr system (⁶⁰Co γ -irradiation) at 77 K, active sites are stabilised in the matrix; they initiate efficient chain hydrobromination when the sample is unfrozen. This reaction occurs when the molecular mobility increases abruptly, *viz.*, in the devitrification region of the system (in the temperature range 87–95 K). The degree of conversion depends on the pre-irradiation dose; for example, it increases from 12% to 25% as the dose is increased from 1.5 to 20 kGy. A decrease in the HBr concentration in the original mixture increases the degree of conversion. In allyl chloride–HBr systems with 20:1 and 60:1 compositions that have been pre- γ -irradiated with a dose of 10 kGy, complete HBr conversion is observed. Naturally, no spontaneous addition occurs on heating of such samples to 200 K. The thermal effect of the post-radiation reaction (ΔH) determined in a series of experiments⁶⁹ is 55.4 ± 2.0 kJ mol⁻¹. Hence, the post-radiation addition of HBr to allyl chloride results in 3-bromo-1-chloropropane (anti-Markownikoff addition); the thermal effect of the reaction coincides with the calculated⁶⁹ ΔH value.

3. Hydrobromination of allene

Chain addition at low temperatures has also been studied for the first representative of hydrocarbons containing cumulated C=C bonds, *viz.*, allene ($\text{H}_2\text{C}=\text{C}=\text{CH}_2$).⁷⁰

On stirring the allene–HBr equimolar mixture at ≤ 190 K followed by freezing to 77 K, the system passes to the glassy state ($T_g \approx 80$ K). Unlike the equimolar mixture, samples with allene–HBr molar ratios of 1:5, 1:2 or 5:1 pass to the crystalline state upon stirring and cooling to 77 K. An eutectic mixture is formed in the case of the allene–HBr molar ratio of 1:2, and the calorimetric curve shows only the melting of the eutectics around ~ 120 K. In the other reaction mixtures containing a larger excess of one of the components, melting of the excess component is observed as well. Subsequent heating of samples results in spontaneous hydrobromination; calorimetric curves show exothermic reactions at a temperature of ≥ 170 K. The hydrobromination rate increases with an increase in the HBr content in the mixture. The maximum reaction rates in mixtures with allene–HBr molar ratios of 1:2 and 1:5 are observed at 260 and 230 K, respectively.

Spontaneous hydrobromination of allene in this temperature range obeys the Markownikoff rule. In all the systems studied, 2-bromopropene [$\text{MeC}(\text{Br})=\text{CH}_2$] is the major reaction product, irrespective of the original ratio of the reactants. Analysis of absorption IR spectra of the reaction products allows two conclusions to be made. First, spontaneous hydrobromination of allene results in the cleavage of only one C=C bond, since the IR spectrum of the reaction products displays absorption bands near 1650 cm^{-1} , which correspond to the stretching vibrations of the C=C bond. Second, the absorption IR spectra of 2-bromopropene, unlike those of allyl bromide, contain bands originating from the presence of a methyl group in the regions of 800 cm^{-1} (skeleton C–Me vibrations) and $\sim 1380\text{ cm}^{-1}$ (symmetric deformation vibrations of the C–H bond in the methyl group).

The yield of the allene spontaneous hydrobromination product (the reaction occurs in the dark; the heating rate is $\sim 1\text{ deg min}^{-1}$) depends on the original molar ratio of the reactants: it is $\sim 25\%$ (allene:HBr = 1:1) or $\sim 60\%$ (allene:HBr = 1:2 or 1:5). The thermal effect of the reaction (ΔH) determined in a series of experiments⁷⁰ was $70.0 \pm 0.7\text{ kJ mol}^{-1}$.

It should be noted that the conclusion that only one C=C bond is cleaved in the allene molecule during spontaneous hydrobromination under these reaction conditions is confirmed experimentally. Studies of the reaction of allyl bromide (3-bromopropene) and 2-bromopropene with HBr showed that no spontaneous hydrobromination of these compounds occurs in the temperature range 77–290 K.⁷⁰

Studies of the radiation-induced hydrobromination of allene were carried out for the same systems (with the molar ratios allene:HBr = 1:1, 1:2, 5:1) that have been used in studies of the spontaneous reaction. When the allene–HBr equimolar mixture pre-exposed to γ -irradiation with a dose of 2 kGy at 77 K was heated, intense heat evolution due to hydrobromination was observed in the temperature range of system devitrification (82–90 K).

When the allene–HBr system pre-exposed to γ -irradiation at 77 K with 1:2 molar ratio of the reactants was heated, hydrobromination was detected in the temperature ranges 85–95 K and 105–110 K. Subsequent heating results in melting of the remaining eutectic mixture.

If an excess of allene is originally present in the system (molar ratio allene:HBr = 5:1), post-radiation hydrobromination is observed in the temperature range 90–115 K. Subsequent heating of the sample results in melting of the excess allene. It should be noted that the heat of melting of the excess allene remains the same in both systems, *viz.*, intact and subjected to radiolysis. Hence, hydrobromination involves only the amount of allene which corresponds to its content in the eutectic mixture.

Thus, the post-radiation hydrobromination of allene, unlike spontaneous hydrobromination, occurs at much lower temper-

atures (80–120 K). Analysis of hydrobromination products in allene–HBr systems (with original molar ratios of the reactants 1:1, 1:2 and 5:1) makes it possible to conclude that one allene C=C bond is cleaved in the first step, and subsequent hydrobromination involves the cleavage of the second C=C bond. The post-radiation hydrobromination of allene at low temperatures occurs as the anti-Markownikoff addition to give allyl bromide and also a product of more extensive hydrobromination of allene, *viz.*, 1,3-dibromopropane. The absorption IR spectrum of the reaction products is a superposition of two spectra, *i.e.*, those of allyl bromide and 1,3-dibromopropane.

Since the boiling points of allyl bromide and 1,3-dibromopropane differ considerably (344 and 439 K, respectively), it is easy to separate these products. It was found that if the composition of the original mixture is 1:1, then the overall product yield is $\sim 50\%$, while the yield of 1,3-dibromopropane is $\sim 14\%$; if the allene:HBr ratio is 1:2, the overall yield is 70%, while the yield of 1,3-dibromopropane is $\sim 50\%$. The IR spectra of the reaction products that were isolated match completely the spectra of allyl bromide and 1,3-dibromopropane recorded previously.

Thus, the hydrobromination of allene in the temperature range 80–120 K during unfreezing of the allene–HBr system pre-exposed to radiolysis at 77 K occurs as the anti-Markownikoff addition, irrespective of the original ratio of the reactants. In the first stage, allyl bromide is formed; it then undergoes hydrobromination to give 1,3-dibromopropane. The content of allyl bromide and 1,3-dibromopropane in the reaction products depends on the original composition of the reaction mixture and on the pre-irradiation dose.

4. Cryopolymerisation of epichlorohydrin

Epichlorohydrin (ECH) passes to the glassy state on cooling to 77 K at a rate of $50\text{--}100\text{ deg min}^{-1}$. The calorimetric heating curve for ECH (Fig. 4, curve 1) displays the transition from the glassy state to the supercooled liquid state ($T_g = 130\text{ K}$), crystallisation in the temperature range 150–170 K and melting of the monomer (at 210 K).⁷¹ The heat of melting of ECH determined from these calorimetric measurements is $10.0 \pm 0.5\text{ kJ mol}^{-1}$.

Preliminary γ -irradiation of ECH at 77 K followed by heating results in polymerisation of the monomer.⁷¹ The most intense polymerisation is observed in the devitrification region (see Fig. 4, curves 2, 3). As the pre-irradiation dose is increased, the post-polymerisation of ECH during heating is detected calorimetrically at progressively lower temperatures. At sufficiently high pre-irradiation doses ($> 300\text{ kGy}$), the calorimetric curve shows that the polymerisation rate first increases with an increase in temperature, then decreases slightly and eventually increases abruptly in the glass softening region (see Fig. 4, curve 3). This pattern is probably a consequence of the kinetic non-uniformity of the growing active sites. The ‘freezing’ and ‘revival’ of growing polymer chains during solid-phase polymerisation,²³ the decay

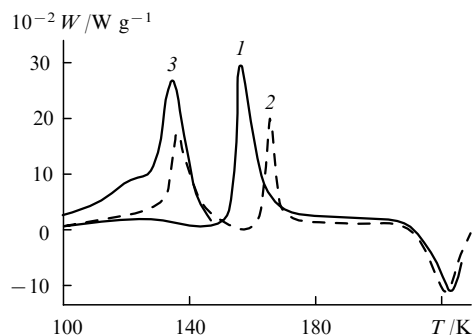


Figure 4. Calorimetric curves of epichlorohydrin heating;²⁵ non-irradiated sample (1); samples exposed to γ -irradiation with doses of 57 kGy (2) and 310 kGy (3). The irradiation was carried out at 77 K.

of stabilised active sites and a number of other processes may be interpreted within the framework of the 'polychronous kinetics' concept.²⁴ In the glass softening temperature range, where the molecular mobility increases abruptly, the post-polymerisation of ECH (like that of the majority of other monomers) occurs efficiently.

In order to elucidate the specific features of the reaction mechanism, Kichigina *et al.*⁷¹ studied the effect of certain additives (pyridine, hydroquinone, ethanol) on the post-polymerisation of ECH. The addition of ~4% pyridine (a typical inhibitor of cationic polymerisation) to the system suppressed completely the ECH post-polymerisation. On the other hand, the addition of hydroquinone (a typical inhibitor of radical polymerisation) did not affect the ECH post-polymerisation. The yield of the polymer from samples containing hydroquinone was almost the same as in the case of pure ECH. Hence, the post-radiation polymerisation of ECH in the temperature range 85–150 K occurs according to the cationic mechanism. It is of note that a polymer is also formed in the region of the system devitrification during the radiation polymerisation of ECH in a glassy matrix of dichloromethane, which is a typical solvent for cationic polymerisation.

Ethanol was found to exert an unusual effect on the post-radiation polymerisation of ECH. The addition of ethanol (to a concentration of 5%) does not virtually affect the post-polymerisation in the temperature range 77–120 K and suppresses strongly the polymerisation in the devitrification region (130–150 K). Ethanol is a weaker inhibitor of cationic polymerisation than pyridine. This is probably the reason why it suppresses the ECH polymerisation in this way. At low temperatures, far from the devitrification region where the matrix is sufficiently rigid, ethanol does not affect polymerisation. In the devitrification region, where softening of the matrix occurs with an abrupt decrease in the viscosity and hence an increase in molecular mobility, ethanol suppresses the cationic polymerisation of ECH. In this case, the yield of the polymer is 5% for the irradiation dose of 150 kGy (for the pure monomer, the yield of the polymer is 12% for the same irradiation dose).

The dynamics of the post-radiation polymerisation of crystalline ECH differs considerably from that of the glassy monomer. Crystalline ECH is obtained by 'annealing' a sample in a calorimeter: glassy ECH is heated to the pre-melting region and then frozen to 77 K.⁷¹ Unlike the glassy monomer, insignificant heat evolution associated with polymerisation is only observed in the pre-melting region for the crystalline sample pre-exposed to radiolysis. At equal pre-irradiation doses at 77 K (170 kGy), the yield of the polymer from crystalline ECH is 3%, while that from glassy ECH is 12%.

It is well known that the epoxide ring is highly resistant against high-energy ionising radiation.^{72,73} Efficient chain polymerisation of ethylene oxide could be carried out only by heating a glassy solution of the monomer in butyl chloride pre-exposed to radiolysis at 77 K.⁷⁴ In the case of ECH, post-polymerisation during devitrification makes it possible to carry out the reaction without the use of glass-forming solvents, since the monomer itself readily passes to the glassy state on cooling to 77 K. This analogy may be extended. As shown previously,⁷⁵ heating of a pre-irradiated glassy ethylene oxide–hydrogen cyanide mixture results in their copolymerisation. It was found that a solution of HCN in ECH (molar ratio 1 : 3) passes to the glassy state on cooling to 77 K (the glass softening temperature is ~130 K). Cooling of this solution pre-irradiated at temperatures in the glass softening region results in copolymerisation of ECH with HCN. The brown reaction product is soluble in ECH. Its IR spectrum displays a band near 1680 cm⁻¹ characteristic of the stretching vibrations of the C=N bond, which indicates that HCN molecules are involved in the copolymer.

5. Polymerisation of ketene in glassy matrices

Solutions of ketene (25 mol.%) in butyl chloride pass to the glassy state on cooling to 77 K (Fig. 5a, curve 1).⁷⁶ Heating of this

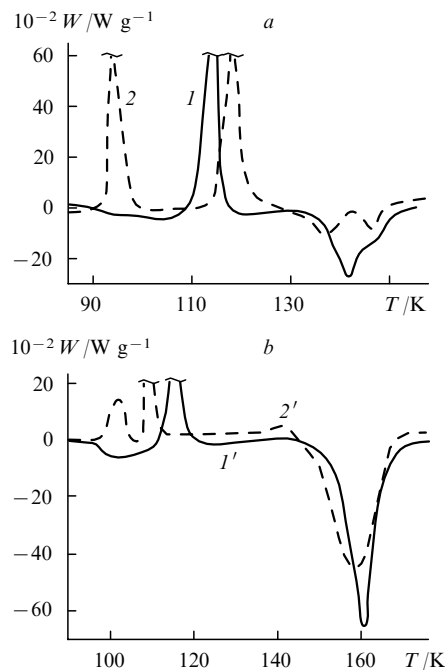


Figure 5. Calorimetric curves of the unfreezing of ketene solutions in butyl chloride (25 mol.%) (a) and in diethyl ether (33 mol.%) (b);⁷⁶ non-irradiated solutions (1, 1'); solutions γ -irradiated with doses of 250 kGy (2) and 330 kGy (2').

glassy system pre- γ -irradiated at 77 K results in ketene polymerisation in the devitrification temperature range ($T_g = 95$ K) (see Fig. 5a, curve 2). Subsequent heating results in crystallisation, which (due to the presence of the polymer) is shifted to a higher temperature range with respect to the crystallisation of a non-irradiated sample; in addition, melting of the mixture occurs (see Fig. 5a).

The dependence of the yield of the polymer on the pre-irradiation dose is shown in Fig. 6. In the case of ketene polymerisation in a glassy butyl chloride matrix, the yield of the polymer reached the limit of ~20% at a dose of 50 kGy (see Fig. 6, curve 2). The resulting polymer is yellow; it is partially soluble in ethyl methyl ketone. Its solubility increases with an increase in the pre-irradiation dose: the soluble polymer fraction is 10% at a dose of 10 kGy and 75% at 250 kGy. The polymer was isolated without exposure at room temperature.⁷⁶

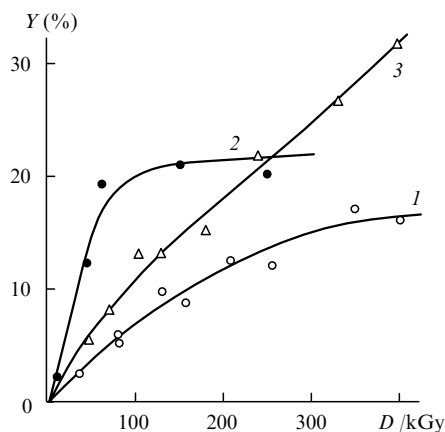


Figure 6. Dependence of the yield (Y) of the ketene polymerisation product on the dose (D) of preliminary γ -irradiation;⁷⁶ (1) ketene, (2) solution of ketene (25 mol.%) in butyl chloride, (3) solution of ketene (33 mol.%) in diethyl ether.

The specific heat of ketene polymerisation in a glassy matrix of butyl chloride differs considerably from the heat of polymerisation of crystalline ketene. The mean specific heat of ketene polymerisation in the devitrification region of the system determined in a series of experiments is $74 \pm 3 \text{ kJ mol}^{-1}$, which is almost fourfold larger than the specific heat of polymerisation obtained for crystalline ketene.

The IR spectrum of polyketene resulting from the reaction in the ketene–butyl chloride system also differs considerably from that of the polymerisation product of crystalline ketene. The former contains an intense absorption band characteristic of the stretching vibrations of the C=O bond and a weak band corresponding to the C=C bond. The absorption IR spectra and the specific heat of ketene polymerisation (which is close to the heat of cleavage of the C=C bond) suggest that the cryopolymerisation of a glassy solution of ketene in butyl chloride predominantly occurs with the cleavage of C=C bonds.

It should be noted that previous studies of low-temperature post-radiation polymerisation of various monomers (cyclopentadiene,⁷⁷ ethylene oxide,⁷⁸ acetaldehyde⁷⁹) in a butyl chloride glass-forming matrix pointed to a cationic reaction mechanism. It is likely that the cryopolymerisation of ketene in butyl chloride also occurs by the cationic mechanism with the cleavage of the C=C bond.

Post-radiation cryopolymerisation of a solution of ketene (33 mol.%) in diethyl ether was studied.⁷⁶ On cooling to 77 K, this solution, like the ketene–butyl chloride system, passes to the glassy state. The calorimetric curve of heating displays devitrification of the system ($T_g = 100 \text{ K}$), crystallisation (110–120 K) and melting of the mixture (150 K) (see Fig. 5*b*, curve 1').

After γ -irradiation at 77 K followed by heating of the irradiated sample, as in the ketene–butyl chloride system, the calorimetric curve displays ketene polymerisation in the devitrification temperature range (see Fig. 5*b*, curve 2'). However, unlike the ketene–butyl chloride system, the formation of a polymer in the devitrification region of the ketene–diethyl ether system shifts crystallisation to a lower temperature range (105–110 K). Post-polymerisation of ketene occurs not only in the devitrification temperature range but also during subsequent heating near the melting point of the system (see Fig. 5*b*, curve 2').

The yield of the polymer increases almost linearly with an increase in the pre-radiation dose to 200 kGy and equals $\sim 35\%$ at a dose of 400 kGy (see Fig. 6, curve 3). The isolated polymer was yellow; it was completely soluble in ethyl methyl ketone.

The IR spectrum of the ketene polymerisation product formed in this system is virtually completely the same as that of the polymer obtained by cryopolymerisation of crystalline ketene. The specific heat of ketene polymerisation in a diethyl ether glassy matrix is $21 \pm 2 \text{ kJ mol}^{-1}$, which is close to the specific heat of polymerisation of pure ketene. These data suggest that, as for pure ketene, its polymerisation in a diethyl ether matrix probably occurs by an anionic mechanism involving the preferential cleavage of C=O bonds and formation of a polyester.

Analysis of experimental data⁷⁶ demonstrates clearly that the low-temperature post-radiation polymerisation of ketene can occur by both the anionic and cationic mechanism depending on the conditions of the process. Using solvents typical of cationic (butyl chloride) or anionic polymerisation (diethyl ether) as the glass-forming matrix, it is possible to govern the predominant reaction pathway.

6. Cryoozonolysis of perfluoroalkenes

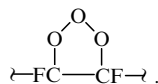
Cryochemical methods have favoured a considerable progress in the studies on perfluoroalkenes. First, it became possible to conduct experiments with pure ozone (which was isolated by low-temperature rectification). Second, the use of low-temperature kinetic calorimetry⁸⁰ made it possible to follow the temperature and rate parameters of chemical processes involved in the cryoozonolysis of perfluoroalkenes.

The low-temperature ozonolysis of neat tetrafluoroethylene (TFE) and hexafluoropropylene (HFP) in the absence of oxygen was studied.^{81,82} It was found that for equimolar perfluoroalkene:O₃ ratios and at low temperatures (140–230 K) ozone adds quantitatively to the double bond to give the corresponding ozonides. The cryoozonolysis products are stable up to temperatures of 250–290 K. They decompose at higher temperatures; however, the ozonide from TFE is more stable than the ozonide from HFP. The resulting decomposition products of TFE and HFP ozonides initiate the polymerisation of TFE and a number of other monomers.⁸³

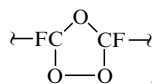
The previously developed technique to prepare samples and perform experiments, which prevents the reaction from occurring in uncontrolled explosive mode, allowed the low-temperature ozonolysis of some other perfluoroalkenes, *e.g.*, perfluoro-4-methylpent-2-ene (HFP dimer, or DHFP) and perfluoro-2,4-dimethyl-3-ethylpent-2-ene (HFP trimer, or THFP) to be studied as well.^{83,84}

On cooling to 77 K, the HFP dimer passes to the glassy state ($T_g = 110 \text{ K}$). On cooling the sample containing equimolar amounts of DHFP and O₃, an exothermic reaction of ozone with DHFP occurs starting from $\sim 210 \text{ K}$. The cryoozonolysis rate increases with an increase in temperature to reach a maximum near ~ 240 – 250 K . The overall activation energy of the reaction in the temperature range 210–240 K is $90 \pm 5 \text{ kJ mol}^{-1}$. On further increase in temperature, the rate of the process decreases because the reactants are depleted. The thermal effect of DHFP ozonolysis determined in a series of calorimetric measurements is $505 \pm 5 \text{ kJ mol}^{-1}$.

As with TFE and HFP, the ozonolysis of DHFP at low temperatures according to the well-known three-step Criegee mechanism⁸⁵ gives the corresponding carbonyl-containing compounds and the DHFP ozonide. Initially, the reaction of ozone with DHFP gives the so-called molozonide



This ozonide is unstable and decomposes quickly to a bipolar ion $-\text{FC}^+ - \text{O} - \text{O}^-$ $\leftrightarrow$ $-\text{FC}^+ = \text{O} - \text{O}^-$ and a carbonyl compound $-\text{FC} = \text{O}$ $\leftrightarrow$ $-\text{FC} = \text{O}$. The resulting intermediates readily reassemble in a different manner to give a more stable ozonide



Like TFE and HFP ozonides, DHFP ozonide initiates polymerisation of a number of monomers, *e.g.*, TFE, methyl methacrylate, acrylonitrile, and also copolymerisation of tetrafluoroethylene with hexafluoropropylene. It should be noted that the use of the ozonides obtained for the initiation of the polymerisation of fluoromonomers has important advantages over the use of other initiators.⁸⁶ DHFP ozonide is non-explosive and storage-stable. The use of perfluoroosonides makes it possible to polymerise TFE under atmospheric pressure and at room temperature with technologically acceptable rates. In principle, such initiators allow continuous polymerisation of fluoromonomers in the gas phase to be performed. The equipment required for the process is simplified considerably because gaseous TFE is used under ordinary pressure; furthermore, the synthesis becomes much more environmentally safe, because no emulsions or water are used.

IV. Autowave processes

In our discussion of the mechanism of an elementary act of a chemical reaction at temperatures near absolute zero (radiation-induced and photochemical polymerisation of formaldehyde, photochlorination of ethylene in a spatially ordered crystalline structure, radiation-induced hydrobromination of ethylene,

etc.^{25–33}), we did not touch upon the mechanism of the chemical transformation chain. However, in addition to the obscure issue of the mechanism of overcoming the activation barrier, yet another important problem remained open, *viz.*, that of the mechanism of the displacement of reagents in an elementary act of attachment of monomeric unit. It should be reminded that in the formation of a macromolecule each van der Waals distance between the monomers in a crystal decreases to the lengths of chemical bonds as a result of the reaction.

The consideration of the mechanochemical aspect of the radiation cryochemistry of solids was stimulated by the discovery of the chain reaction initiation upon local sample destruction.⁸⁷

When destruction of a solid occurs, the mechanical energy of its elastic deformation is concentrated in the vicinity of the newly formed surface. It is well known that upon such energy transformation, the properties of substances on the newly formed surface change considerably in comparison with their bulk properties.^{88,89} Brittle destruction is accompanied by a number of physicochemical phenomena: emission of electrons and ions, luminescence, generation of radicals, sharp acceleration of transfer processes on the split surfaces.^{90–92} It seemed logical that the transition of the reaction from the homogeneous mode to the considerably heterogeneous mode by performing brittle destruction of the sample would 'switch on' the non-equilibrium mechanism of energy transfer to active sites previously stabilised in the solid matrix, and initiate chemical transformations at low temperatures.

Let us consider yet another circumstance that prompted the researchers to reconsider the generally accepted concepts. In the studies performed before, both the kinetic models that describe solid-phase radiation-chemical transformations and the experimental techniques were based on the assumptions about the system uniformity and homogeneity of the chemical reaction. This stage was quite logical, as it is difficult to reveal and study specific features of non-uniform chemical transformation modes by calorimetric and spectroscopic techniques that deal with integral signals. There have always been doubts as to the applicability of zero-dimensional kinetic models in the radiation chemistry of solids, since it is well known that an irradiated sample is never homogeneous on the microscopic scale. The main results obtained at this step of the studies were generalised in a number of reviews.^{13–15}

Polymerisation and copolymerisation are the most interesting processes during which it is possible to observe low-temperature transformation autowaves. Their principal difference from previously studied chain reactions of chlorination and hydrobromination of hydrocarbons is that polymerisation produces long material chains. It is reasonable to expect that this predetermines certain features of the reaction, *e.g.*, an increase in the life time of active polymerisation sites due to the limited molecular mobility in the network formed by a polymeric product. Furthermore, the formation of long polymeric chains under low and ultralow temperature conditions is of undoubted interest for the explanation of the processes of 'cold' chemical evolution of matter in the Universe.

1. Polymerisation autowave of crystalline acetaldehyde

The propagation of the polymerisation front in solid radiolysed acetaldehyde at comparatively high temperatures (117–147 K) close to the monomer melting point (150 K) was observed by thermography and by shooting a film.⁹³ This phenomenon was interpreted within the framework of the classical thermal mechanism of burning. The propagation rate of the reaction front was 1–3 cm s⁻¹ at the temperatures specified above and upon pre-irradiation with doses of 5–100 kGy. Using just one heat transfer equation and a number of assumptions, Pshezhetskii and Tupikov⁹³ calculated the time required to add one monomeric unit to a polymeric chain (10⁻⁸ s). The kinetics of this reaction has been studied in detail by the calorimetric method in a slow temperature scanning mode and directly under γ -irradiation in the absence of

noticeable sample overheating.²⁵ The rate constant of chain growth in the crystalline monomer was determined at 130–140 K:

$$k \approx 3 \times 10^{17} \exp\left(-\frac{46000}{RT}\right) \text{ litre mol}^{-1} \text{ s}^{-1};$$

it was found that the time required for the addition of one monomer unit is as short as 0.1–0.01 s. In view of this, a question appeared whether the theory of burning was rightfully used⁹³ to describe the process of the layer-by-layer propagation of the polymerisation front.

The development of the concept of autowave processes stimulated Kichigina *et al.*⁹⁴ to analyse specific features of the polymerisation of crystalline acetaldehyde on a new qualitative level. This reaction is of particular interest owing to two factors. First, the discovery of the autowave mode during the polymerisation of acetaldehyde would allow one to state that a cryochemical wave is possible in a one-component system. Second, the thermal effect of this reaction is virtually an order of magnitude lower than those of systems studied previously.

The main concepts regarding the mechanochemical feedback in the autowave process^{13–15} were confirmed by a study of this system. The polymerisation wave, which appears as a result of local brittle destruction of crystalline pre-radiolysed acetaldehyde in the temperature range 4.2–77 K, was observed in bulk (cylindrical) and thin-film samples immersed in a nitrogen or helium bath.⁹⁴

The principal features of the structure of the running polymerisation fronts in acetaldehyde are similar to those found for other cryochemical reactions (Fig. 7). These include an indistinctly expressed stage of inert heating and the abrupt reaction 'turn-on' at considerably lower temperatures than in the case of thermoactivated processes. However, unlike the systems studied before, more time is required for the temperature decrease after the polymerisation front has passed. The characteristic time of this decrease is 2–3 times longer than the thermal inertia of the system. Hence, the polymerisation reaction is not 'turned off' after the wave front has passed, and part of the polymer is formed behind the front.

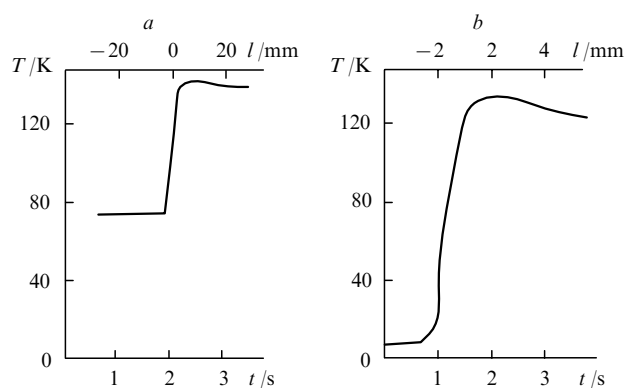


Figure 7. Time and spatial scanning of characteristic temperature profiles of the propagation waves of acetaldehyde polymerisation at 77 K (a) and 4.2 K (b).⁹⁴

The γ -irradiation dose is 700 kGy; the wave propagation rates are 26 (a) and 4 mm s⁻¹ (b).

When the front passes through a sample immersed into a helium bath, the maximum temperature in the polymerisation front does not exceed 130 K, which is much lower than the monomer melting temperature (150 K). Thus, this system may be used to analyse the changes in the structure and phase state of a crystalline sample caused by the passage of a cryopolymerisation mechanochemical wave through the sample. According to the concept developed in a series of studies,^{13–15} the front of a chemical reaction is a mechanical dispersion zone that moves

through a solid reagent. The cinegrams obtained by Kichigina *et al.*⁹⁴ for the polymerisation of acetaldehyde show that a polycrystalline sample becomes transparent after the wave has passed. It may be assumed that, as the polymerisation wave passes, amorphisation of polycrystalline acetaldehyde occurs due to both the formation of an amorphous polymer phase and mechanical dispersion.⁹⁴

This assumption was checked by the calorimetric method, which allows determination of the ratio of amorphous and glassy phases in a solid matrix, based on changes in the thermal effect of melting. In order to perform this analysis, a cylindrical sample of acetaldehyde through which an autowave has passed in liquid helium was transferred to a liquid nitrogen bath and then cut into several parts at different heights. Each of the parts was placed in a separate calorimeter at 77 K and its calorimetric curve of unfreezing was recorded. It was found that the crystalline phase was absent in the entire sample after the wave has passed. The calorimetric experiments only manifested a jump of the thermal capacity which accompanies devitrification, whereas the thermal effect of melting was not observed. However, if the process is carried out not in the autowave mode but by slow heating of the entire sample in a calorimeter (without brittle destruction that initiates an autowave), then the nonconsumed monomer maintains its crystallinity. This confirms that the passage of a mechanochemical wave through a crystalline sample results in its amorphisation.

The autowave propagation rate depends on the pre-irradiation dose. For samples immersed into liquid nitrogen, the propagation rate of the polymerisation autowave increases linearly with an increase in the irradiation dose up to 1200 kGy. It was logical to assume that the increase in the wave propagation rate resulted from the accumulation of active sites. However, active sites (radical ions and radicals) are accumulated linearly during the radiolysis of polycrystalline acetaldehyde at 77 K as the irradiation dose increases to 50 kGy; after that, the process slows down and ceases completely at doses above 650 kGy.

The increase in the wave propagation rate with an increase in the irradiation dose may be explained as follows. The low-temperature radiolysis of acetaldehyde gives rise to methane and carbon monoxide, which exist in a condensed state at 77 K. When the reaction front passes, these radiolysis products turn into gases (the melting points of CH₄ and CO are 111 and 81 K, respectively). The gases evolved can facilitate brittle dispersion of the sample and thus accelerate the movement of the running transformation front.⁹⁴

2. Acetaldehyde polymerisation autowave in a glassy matrix

Pure acetaldehyde could not be transformed to the glassy state even by fast cooling. Solutions of acetaldehyde (up to 30 mass %) in butyl chloride are completely transformed to the glassy state on cooling. As the content of acetaldehyde in the original solution is increased (> 30 mass %), a crystalline phase appears in samples cooled to 77 K (the cooling rate is ~150 K min⁻¹). Such samples are mixtures of a glassy and crystalline phases.

On slow cooling (in a calorimeter) of the acetaldehyde–butyl chloride system radiolysed at 77 K, efficient polymerisation of the monomer occurs in the devitrification region. Convincing proof of the cationic mechanism of the post-polymerisation of acetaldehyde in a glassy butyl chloride matrix has been obtained.²⁵

An autowave polymerisation mode initiated by local brittle destruction was realised in a glassy acetaldehyde–butyl chloride system pre-irradiated at 77 K.⁹⁵ It is interesting to compare the characteristics of the cryopolymerisation waves for crystalline and glassy acetaldehyde samples. The main parameters of the autowave polymerisation process are qualitatively the same in polycrystalline and glassy matrices, but differences are observed as well.

The maximum temperature at the running wave front in a glassy system is 110–130 K; in the case of crystalline acetaldehyde, it may reach 150 K. The critical dose of pre-irradiation, *i.e.*,

the dose starting from which autowave propagation of the process is ensured, is 60 kGy for the glassy system, whereas in the crystalline monomer, it is above 300 kGy.⁷⁹

There is a minimum threshold concentration of acetaldehyde in the original solution that still supports the autowave mode. In fact, the reaction cannot be run in autowave propagation mode in samples containing less than 20 mass % of acetaldehyde at a pre-irradiation dose of 300 kGy.

It is reasonable to relate the observed differences between the cryopolymerisation waves in the crystalline and glassy acetaldehyde with differences in the reaction mechanisms (ionic mechanism in glass and radical mechanism in crystal) and in the strength characteristics of the systems in question. It should be reminded that the devitrification temperature of the acetaldehyde–butyl chloride system ($T_g = 95$ K) is much lower than the melting point of crystalline acetaldehyde (150 K).

Thus, while autowave modes have previously been observed for reactions that were believed to involve radical processes, the acetaldehyde–butyl chloride system features a polymerisation autowave which occurs by a cationic mechanism.

3. Cyclopentadiene cryopolymerisation autowave

It has been shown previously⁷⁷ that the post-radiation polymerisation of cyclopentadiene vitrified in a butyl chloride matrix occurs by a cationic mechanism in the devitrification temperature range of the system ($T_g = 97$ K). These results gave grounds for the search for autowave modes in this system. The local brittle destruction of a cyclopentadiene sample in a glassy butyl chloride matrix pre-radiolysed at 77 K initiates polymerisation that propagates through the sample as an autowave.⁹⁶ As in other autowave processes, this reaction ‘switches on’ at 77 K, and the temperature at the wave front quickly reaches a maximum value. However, considerable time is required for the decrease in temperature after the front has passed, just as in the case of the acetaldehyde cryopolymerisation wave. The polymerisation is not ‘turned off’ after the wave front has passed, and part of the polymer is formed behind the front. The mean degree of conversion calculated from the adiabatic heating at the reaction wave front is ~25%, whereas the yield of the polymer determined gravimetrically is ~55%.

Thus, unlike the autowave processes that give low-molecular-mass products (chlorination and hydrobromination), considerable additional conversion occurs behind the wave front in the case of polymerisation. It may be assumed that the low degree of conversion, *e.g.*, in the butyl chloride–chlorine system, is due to the heating of the wave front to the devitrification temperature, where the molecular mobility increases abruptly; this results in the efficient decay of active sites due to recombination. On the contrary, the limited molecular mobilities of active sites during the polymerisation increase the life time of these sites and hence the degree of conversion.

The velocity of the cyclopentadiene polymerisation autowave increases linearly with an increase in the pre-irradiation dose up to 1200 kGy. Most likely, this behaviour of the wave rate does not result from the dynamics of the accumulation of cationic active sites, since their concentration ceases to increase at much lower doses. It has been shown in special experiments that the radiolysis of the cyclopentadiene–butyl chloride system at 77 K produces a gas mixture with an overall radiation yield of ~1 molecule per 100 eV of absorbed energy.⁹⁶ The fraction of hydrogen in this mixture is ~75%. The passage of the polymerisation wave through a sample (heating to 110–130 K occurs at the wave front) results in intense evolution of dissolved and frozen gases from the glass and their transfer to the gas phase. The pressure of the gas micro-bubbles may favour the brittle destruction of the system. An increase in the pre-irradiation dose increases the quantity of evolved gases almost linearly; hence, brittle destruction should be facilitated. Analysis of the cinegrams of the reaction propagation through the sample confirms this assumption qualitatively.

At high pre-irradiation doses, strong swelling of a sample upon passage of the polymerisation wave is observed; as a result, its volume increases almost twofold after the process has ended. At low pre-irradiation doses and hence smaller amounts of gaseous radiolysis products, no swelling of the sample occurs upon passage of the wave.

Depending on the autowave 'startup' conditions, the character of the autowave process may differ considerably. For the same pre-irradiation doses, the propagation rate of the polymerisation wave initiated in the lower part of the sample is much higher than if the wave is initiated in the upper part. It is of note that if the wave is initiated in the lower part of the sample, the temperature profile of the running wave is steeper. This fact can also be explained by the role of radiolytic gases. When the polymerisation wave propagates from above downwards, the gaseous products can exit to the evacuated space above the sample. However, if the reaction is initiated in the bottom part of the sample, the gases evolved at the wave front have no free way to exit; as a result, the disjoining pressure of the gases increases and accelerates the front movement.

Yet another reason for the linear increase in the wave propagation rate with an increase in the pre-irradiation dose is possible.⁹⁷ Part of the irradiation energy absorbed during the low-temperature radiolysis can be accumulated by means of lattice deformations and formation of metastable phases. Under certain conditions, this accumulated energy will facilitate the brittle destruction of the system. When the wave is launched in the top part of the sample, there are conditions for its 'relief'; however, when it is launched in the bottom part of the sample, 'relief' is hindered considerably owing to the permanent solid 'plug' created by the top part of the sample. In the latter case, the deformation energy accumulated during radiolysis is spent more efficiently, which accelerates the movement of the wave.

The IR spectra of the polymer isolated after the passage of the polymerisation wave coincide completely with the spectra of the product obtained in the post-radiation polymerisation mode during devitrification. However, the conversion of the monomer is much higher if polymerisation is carried out in the autowave mode. The maximum yield of the polymer is 20% for post-polymerisation during devitrification (at a pre-irradiation dose of 50–500 kGy) and from 30% at a dose of 100 kGy to 55% at a dose of 1200 kGy in the autowave mode. The molecular mass of polycyclopentadiene obtained in the autowave mode decreases from 10^6 to 10^4 with an increase in the pre-irradiation dose, but it is by almost an order of magnitude higher than the molecular mass of the polymer formed upon post-radiation polymerisation during devitrification.⁷⁷ This difference may result from the fact that polymerisation in the autowave mode commences at lower temperatures (almost at 77 K) than thermally activated post-polymerisation ($T_g = 97$ K).

It should be noted that the 'explosive' polymerisation of cyclopentadiene was observed in films obtained from molecular beams of the monomer and TiCl_4 as a catalyst, after pricking the film with a metal needle at 77 K.^{98,99} In these experiments, the reaction propagated through the sample at high rate. The highest propagation rates of cryochemical reactions initiated by local brittle destruction of samples pre-radiolysed at 77 K were achieved by Kiryukhin *et al.*¹⁰⁰ These facts suggest that such cryochemical processes may involve a detonation mechanism. It is possible that the 'gas-free detonation' mechanism is realised in this case. According to this mechanism, the shock wave appears and is then supported by the system owing to changes in the density of the compound during the conversion.¹⁰⁰ A model of an autowave process that occurs due to appearance of a density gradient in the reacting layer upon formation of reaction products was suggested.^{101–103} These calculations allowed evaluation of the size of the fragmentation grain of the reactant matrix. The resulting value (~ 10 μm) agrees well with experimental data for autowave modes of cryochemical transformations in thin-film samples.

4. Autowave of acetaldehyde–HCN cryocopolymerisation

The autowave mode has also been realised for cryocopolymerisation.¹⁰⁴ On cooling to 77 K, an HCN–acetaldehyde mixture containing 25 mol.% of hydrogen cyanide passes to the glassy state. Its devitrification temperature (transition to the supercooled liquid state) is 90 K, the crystallisation temperature is 110–115 K, and the melting point is 140 K. The local brittle destruction of such a sample pre-radiolysed at 77 K gives rise to an autowave of copolymerisation of acetaldehyde with HCN. The copolymerisation wave front rapidly propagates over the entire sample from the top downwards (this may be observed visually by the changes in the sample colour). The maximum temperature at the wave front increases from 125 K at an irradiation dose of 15 kGy to 148 K at a dose of 140 kGy; the yield of the copolymer increases similarly.

The dependence of the propagation rate of the cryocopolymerisation autowave front on the pre-irradiation dose was found to be unusual (Fig. 8, curve 2). It should first be noted that, as in the systems studied previously in which the autowave low-temperature transformation mode was observed, the acetaldehyde–HCN system features a critical dose of preliminary γ -irradiation below which autowave cryocopolymerisation is not initiated. In this case, the threshold γ -irradiation dose is ~ 15 kGy. The propagation rate of the acetaldehyde–HCN copolymerisation wave front increases with an increase in the pre-irradiation dose to ~ 8 cm s^{-1} at 100 kGy. If the irradiation dose is increased, the propagation rate of the copolymerisation wave front decreases.¹⁰⁴

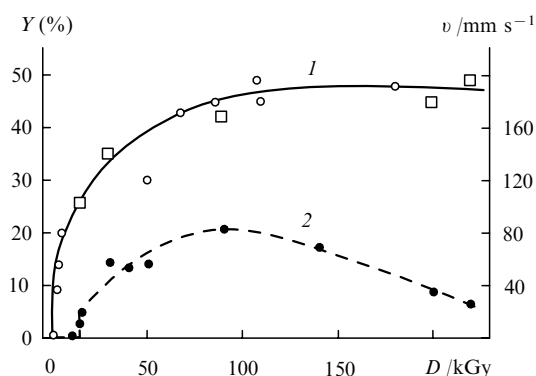


Figure 8. Dependence of the yield (Y) of the copolymer (1) and the rate (v) of the copolymerisation propagation wave front (2) on the pre-irradiation dose (D).¹⁰⁴

The open squares show the values for the reaction in the thermoactivated post-radiation effect mode.¹⁰⁵

The model of the autowave phenomena studied is based on a concept of the existence of a positive feedback between (i) the heat evolved in an exothermic reaction and (ii) destruction of the matrix. As follows from this concept, the chemical reactivity of a radiolysed system is determined not only by the concentration of active sites but also by the potential mechanical energy accumulated in the sample and the strength parameters of the matrix. In fact, autowave transformation modes have been realised at 4.2 K whereas the thermally activated mode requires much higher temperatures for these reactions to occur (near the melting point or the system devitrification temperature). The linear relationship between the propagation rate of the transformation wave and the concentration of the active sites accumulated during radiolysis is violated considerably. It was assumed¹⁰⁴ that the slowing down of the acetaldehyde–HCN copolymerisation propagation wave at doses above 100 kGy results from changes in the accumulating properties of this matrix during the radiolysis.

After the passage of the copolymerisation wave at 77 K, the sample was unfrozen to room temperature and the copolymerisa-

tion yield was determined.^{105, 106} On increasing the pre-irradiation dose, the copolymerisation yield increases to reach a maximum value of 45%–50% (see Fig. 8, curve 1). Figure 8 also shows the dependences of the yield of the copolymer on the irradiation dose during thermally activated post-polymerisation.^{105, 106} During slow unfreezing of a pre-irradiated acetaldehyde–HCN system in a calorimeter, post-polymerisation occurs in the devitrification temperature range. The dependences of the yield of the copolymer on the irradiation dose are similar for both reaction modes.

The copolymer obtained in the autowave mode is colourless; it is completely soluble in ethyl methyl ketone, and its molecular mass decreases with an increase in the pre-irradiation dose.¹⁰⁵ On the contrary, the content of nitrogen in the copolymer increases with an increase in the pre-irradiation dose (Table 1). Based on these experimental results and the data on the yield of the copolymer at different irradiation doses, it is possible to calculate the mean number of HCN and acetaldehyde molecules in one polymeric macromolecule and the concentration of polymeric chains in the system during the reaction. The calculated values are listed in Table 1.¹⁰⁴ It is of note that the number of macromolecules formed increases monotonically with an increase in the pre-irradiation dose; this number is larger than that of the initiating active sites accumulated during pre-radiolysis, especially at high doses.^{107–109} These data are evidence of the existence of chain transfer.

Table 1. Characteristics of acetaldehyde–hydrogen cyanide copolymers.¹⁰⁴

Pre-irradiation dose /kGy	Molecular mass	Nitrogen content (mol.%)	Mean number of units in a macromolecule		Number of macromolecules, $10^{-19} A / g^{-1}$
			HCN units	MeCHO units	
15	13 500	0.8	2.4	306	1.2
40	9 000	1.28	2.6	204	2.6
50	7 800	1.59	2.8	176	3.2
90	5 000	3.95	4.5	111	5.6
140	4 000	—	—	—	7.8
200	2 200	—	—	—	13.3
220	2 200	18.6	9.1	34	14.8

The principal difference between the autowave polymerisation mode described above and classical liquid-phase processes is that in the former case the reaction initiation rate at the wave front quickly attains a maximum value (in approximately 0.1 s) and then decreases (the active sites accumulated during irradiation are consumed during the process). The observed characteristics of copolymerisation are evidently due to this feature of the process kinetics.

It should be noted that autowave copolymerisation does not give cross-linked insoluble fractions formed as a result of a thermally activated reaction (slow heating of pre-irradiated samples) at different acetaldehyde : HCN starting ratios.

A scheme of thermally activated copolymerisation of acetaldehyde and HCN was suggested, which involved a combination of two mechanisms (cationic and radical).¹⁰⁶ At low pre-irradiation doses, the copolymer is mostly formed by the cationic mechanism. As the pre-irradiation dose is increased, the radical mechanism starts to predominate, and the fraction of HCN in the copolymer increases. Taking into account that the characteristics of the copolymers obtained in different reaction modes (autowave and thermoactivated) are similar, it may be assumed that a similar mechanism is realised in the autowave cryocopolymerisation of acetaldehyde with HCN.

V. Cosmochemical aspects of low-temperature reactions

It is very likely that a very long period of chemical evolution of compounds preceded the origination of living matter and its subsequent biological evolution. This pre-biological development provided ‘building materials’ for the creation and development of living substance: the formation and accumulation of progressively more complex molecular structures, *viz.*, amino acids, nucleotides, polysaccharides, *etc.*, that could subsequently be utilised as a basis for building the main elements of the living cell in the process of biological evolution.

It is hard to imagine, based on the generally accepted concepts about the dynamics of chemical transformations, that a sufficient amount of the ‘building material’ could have been formed in a specific place over any period when favourable physical conditions existed on the Earth (temperatures within 250–450 K, pressure within 1–1000 bar, virtual absence of radiation fields). Probably, the main obstacle was that there had never existed a sufficiently long time interval during which the required conditions were maintained. Previously, the idea was put forward that the cosmic time and space scales may be used to describe the pre-biological evolution process (see, *e.g.*, the monograph by Zigel’¹¹⁰). However, the common concepts about the dynamics of chemical transformations hampered the development of this idea. The impossibility of chemical reactions at temperatures near absolute zero had to be doubted after it had been established experimentally that chain polymerisation of solid formaldehyde can occur at temperatures within 4–100 K. Later, low-temperature chain processes were also observed for a number of other chemical transformations.

The autowave cryopolymerisation processes considered above demonstrate that macromolecules can be formed under conditions similar to those in outer space, *i.e.*, at low temperatures and in weak radiation fields. It is quite rightful to apply the ideas considered in the present review to the explanation of the processes of ‘cold’ chemical evolution in the Universe, *i.e.*, formation of progressively more complex molecules from elements under conditions of interstellar dust and cold planets.

Since the time of their origination in the ‘big bang’,^{110, 111} the matter in the Universe may have passed through a number of cycles involving strong heating. The end of any such cycle may have served as a starting point for the subsequent chemical evolution of matter. Certainly, matter only existed as chemical elements during any heating cycle. Subsequent cosmic processes resulted in a more or less fast temperature decrease almost to absolute zero. The formation of molecules from elements and their subsequent complication could only occur during such cooling. For example, molecular gases were formed: hydrogen, oxygen, nitrogen, carbon monoxide. If these gases froze on interstellar dust particles, then, according to the classical concept, their subsequent chemical transformations were quite doubtful, even on the cosmic time scale. On the other hand, ‘oceans’ of ammonia and methane have been discovered on many outer planets and their satellites. In addition, the interstellar space also contains large amounts of these gases and water.

We can attempt to describe the formation of such compounds as ammonia and methane from a frozen mixture of elements that originally existed on the surface of cold planets and their satellites in the following way. The thermal stress in the solid planet cover was a means for its continuous destruction. The multiple brittle destruction events of the frozen element mixture pre-activated by radiation may have resulted in the chemical binding of the components. This scenario may have been realised in interstellar clouds, *i.e.*, huge suspensions of dust grains in a gas. It is believed^{8, 48} that space dust particles contain silica or graphite nuclei coated with a ‘coat’ of ‘dirty ice’, *viz.*, a mixture of frozen gases.

The next stage of chemical evolution, during which solid ammonia and hydrocarbons were transformed to the simplest

amines due to the positive feedback between brittle destruction and chemical reactions on the freshly formed surface, is also quite believable. The fact that long polymeric chains are formed upon brittle destruction under conditions of cosmic cold may be regarded as proven experimentally for the polymerisation of formaldehyde and acetaldehyde.

The information presented above is also of interest in relation to other cosmochemical problems. Hydrogen cyanide is a widespread molecular compound in outer space, specifically, in huge clouds of interstellar dust, in comets and in other galactic structures. The HCN molecule is generally considered to be the basis for further chemical evolution, because its transformations provide a direct route to proteins and other large molecules. The chemical behaviour of this simple molecule under conditions that are close to those in outer space (low temperatures and radiation) and the role it plays in the 'cold' chemical evolution of the Universe are of considerable interest for researchers.

VI. Conclusion

Studies on the cryochemical reactions in crystals have made it possible to observe experimentally chain processes at temperatures near absolute zero. These results, which are beyond the scope of the classical concepts of chemical kinetics, have stimulated studies on the mechanisms of 'non-Arrhenius' elementary events of chemical transformations.^{8, 12, 35–41} However, there are not so many reactions that occur by the chain mechanism at $T < 77$ K: radiation-induced polymerisation and photopolymerisation of formaldehyde^{5, 25, 27, 30} and acetaldehyde;^{25, 31} photochlorination of ethylene in a spatially ordered structure,³⁶ radiation-induced hydrobromination of ethylene,^{34, 35} and others.^{20–22, 26}

The next step important in principle which favoured the expansion of studies at low temperatures involved the discovery and investigation of the autowave modes of chemical transformations initiated by local brittle destruction of solid samples at 4.2–77 K.^{13–15, 87} Results of recent studies suggest that autowave processes are rather widespread in the cryochemical transformations of solids. Autowave modes of cryochemical transformations have been observed for polymerisation and copolymerisation, chlorination and hydrobromination of saturated and unsaturated hydrocarbons.²⁵ The realisation of high chemical transformation rates at such low temperatures is also very attractive.¹⁰⁰ The results obtained open up new approaches to the explanation of the mechanism of chain cryochemical reactions; these approaches take the potential energy accumulated by a solid and the high reactivity of surfaces formed upon brittle destruction in an autowave transformation mode into account.

If a chemical reaction is carried out during matrix devitrification, transformations of the reactants can be studied at temperatures much lower than the melting points of these compounds.²⁵ Obviously, a chain reaction in a crystal lattice is hindered owing to the low translational mobility of the reactants and the necessity of destruction of the lattice. On the other hand, the selection of an appropriate vitrifying matrix makes it possible to perform a reaction at very low temperatures.^{22, 66} The interest in such low-temperature chemical processes is due to the fact that, as the temperature is decreased, selection from among the possible reaction pathways occurs: those reactions that have the lowest activation energy 'survive'.

Thus, a decrease in the reaction temperature should increase the selectivity of the process. Furthermore, the entropy factors that are so important in the thermodynamics of chemical reactions become less important at lower temperatures; therefore, the equilibria of transformations are shifted in favour of exothermic reactions, even if the latter give rise to highly ordered systems.

The data presented in this review are of interest because they can help explain the 'cold' chemical evolution of matter in the Universe.

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Modern applications of matrix isolation technique to investigation of radical species generated in atom – molecular chemical reactions

E Ya Misochko, A V Akimov, I U Goldshleger

Contents

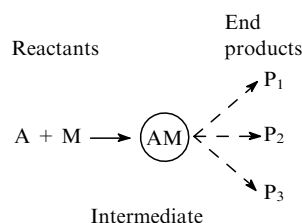
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Abstract. The potential of using the translational mobility of hydrogen, oxygen and fluorine atoms in the crystals and solid matrices of inert gases for initiating solid-phase cryochemical reactions and for investigating the stabilised intermediate particles generated in these reactions is discussed. The main spectroscopic methods used to study the stabilised particles are considered. Particular emphasis is placed on elucidation of the spectroscopic characteristics required for reliable identification and determination of the structure of new reactive intermediates. Methodological approaches to the solution of this problem are discussed. Examples of successful implementation of these approaches by various research groups are given. The bibliography includes 205 references.

I. Introduction

Atom–molecular chemical reactions play an important role in various chemical and biological processes. Therefore, considerable attention has been given to applied studies of and basic research into such reactions. Experimental determination of the rate constants for most of the practically important atom–molecular reactions in the gas phase dates back to the latter half of the 20th century. However, the mechanisms of cleavage and formation of new chemical bonds in this type of reactions cannot always be described at the molecular level due to the lack of information on the dynamics of the reacting systems in the vicinity of the transition state.

A particular avenue of research in the field of modern chemical physics is the investigation of the dynamics of atom–molecular chemical reactions in which the formation of end products is preceded by binding the reactants into a long-lived (compared to the period of intramolecular vibrations) intermediate complex.



Of particular interest are the investigations of intermediate species (radical intermediates) involved in these reactions. This is due to a noticeable and sometimes even determining effect of these species on the ratio of the reaction products and on the energy distribution over their internal degrees of freedom. Experimental kinetic data as well as quantum-chemical calculations on this type of reactions in the gas phase indicate the possibility for a variety of reactive intermediates to exist. Nevertheless, spectroscopic information on the intermediate species of most of the reactions in question is unavailable as yet. Detection of such intermediates in the gas phase is a rather complicated problem since the intermediate products usually have short lifetimes because of high collision energies of reactants in the reactions occurring under normal conditions.

Traditionally, information on the reaction dynamics of elementary processes in the gas phase has been obtained using the molecular beam technique which allows measurements of the energy and angular distributions of products formed in the atom + molecule collision reactions. However, these experiments provide indirect information on the reactive intermediates, since the behaviour of the reacting system in the vicinity of the transition state is reconstructed from the data on the state of the end reaction products. Improved experimental techniques combining supersonic cooling of gas jets and spectroscopic methods with high temporal resolution^{1,2} are based on the concept of studying the chemical dynamics of a system with a temporal resolution that is better (shorter) than the characteristic times of intramolecular motions. This permits obtaining information on the potential energy surface (PES) of reactions in the vicinity of the transition state. However, these methods are applicable to a narrow range of objects due to the requirement of high sensitivity and temporal resolution imposed on the measurements carried out under conditions when the system is 'frozen' in configuration on the femtosecond time scale.

Another approach to the investigation of short-lived intermediates in the gas phase involves freezing of reactive intermedi-

E Ya Misochko, A V Akimov, I U Goldshleger Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 524 96 76. Tel. (7-096) 720 49 59 (ext. 2-1404). E-mail: misochko@icp.ac.ru (E Ya Misochko), shura@icp.ac.ru (A V Akimov), ilya@icp.ac.ru (I U Goldshleger)

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ates at cryogenic temperatures. In the simplest version of this technique products of a gas-phase reaction are trapped and frozen in a matrix consisting of a large excess of inert gas. The use of inert gases as solid matrices for spectroscopic investigations of radical species was proposed in the studies of research groups headed by Pimentel and Porter in 1954.^{3,4} These studies marked the beginning of intensive development of the matrix isolation technique. The vast majority of species trapped in the matrices of inert gases exhibit no translational mobility at temperatures up to the melting (sublimation) temperature of the crystal of inert gas. This allows accumulation of sufficiently high concentrations of radicals and their detection by continuous-wave spectroscopic techniques. It is these methods that were employed to obtain spectroscopic data for most of the known free radicals; this information is generalised and systematised on a regular basis.⁵ An essential drawback of the technique is the interaction between the species under study and the crystalline environment, which inevitably causes changes in their spectroscopic characteristics. Therefore, molecular beam spectroscopy provides more accurate information on subtle features of the molecular structure and properties of reactive intermediates. Nevertheless, versatility and the possibility of using continuous-wave spectroscopic equipment for detecting new molecules and obtaining primary characteristics of their structures make the matrix isolation technique a basic experimental method of research in such fields of science as chemical physics and molecular spectroscopy.

During the last 50 years the concept of matrix isolation of radical species developed in two main directions, namely, search for new conditions for generation of reactive intermediates and the use of various spectroscopic methods for their studies. These research avenues have been reviewed.^{6–8} In the mid-1960s, Milligan and Jacox proposed⁹ that, would the atoms of light elements (*e.g.*, hydrogen) have sufficiently high translational mobility in low-temperature matrices, the reactive intermediates could be stabilised by generating them *in situ* in the reactions of the mobile atoms with molecules of the other reactant trapped in the inert matrices.

Indeed, at ultralow temperatures (≤ 50 K) the solid matrix acts as an inert chemical microreactor which permits fast relaxation of the excess energy of the reaction and prevents the reaction products from flying apart. The matrix also provides ideal conditions for stabilisation of the reactive intermediates characterised by short lifetimes in the gas phase. To illustrate their hypothesis, Milligan and Jacox carried out spectroscopic studies of the products of photolysis of HI molecules in dilute Ar/HI/O₂ solid mixtures and first determined the vibrational frequencies of the HO₂ radical. They assumed that this radical is produced in the reaction of the migrating photogenerated hydrogen atom with oxygen molecule trapped in the inert matrix,



Obtaining new experimental data on the mobility of various atoms in cryogenic crystals and solid matrices in the last decade gave an impetus to further development of this concept. Since the early 1990s a large number of studies on the conditions for generation of atoms in solid matrices by photolysis of trapped molecules have been reported. It was established that in some cases the ‘cage effect’, which precludes photodissociation of molecules in solids, is insignificant and generation of atoms in inert matrices can occur with quantum yields close to unity. A large number of studies provide only qualitative data which permits ambiguous interpretation from the standpoint of physical mechanisms. Nevertheless, they point to the possibility for particular atoms to migrate over rather long distances in the crystals and matrices of inert gases. The results obtained were generalised in a review¹⁰ which also concerns possible mechanisms of translational mobility of atoms at ultralow temperatures, namely,

migration and thermalisation of a translationally excited ‘hot’ atom generated upon photodissociation of precursor molecule as well as thermal and photostimulated diffusion of atoms.

In this review we discuss the potentialities of using mobile atoms in cryogenic solid matrices for generation and investigation of reactive intermediates. The data on the mobility of various atoms are presented, methodological approaches aimed at solving the problem posed are outlined and some examples of their practical implementation are given.

We will consider reactions with participation of reactive atoms of only three elements, that is, hydrogen, fluorine and oxygen, involved in various practically important processes. The relatively simple electronic structure of these atoms facilitates analysis of the various elementary processes they are involved in. Two different [from the standpoint of their chemical reactions in solid matrices (crystals) of inert gases] types of mobile atoms considered in this review are translationally excited ‘hot’ atoms and diffusing thermalised atoms.

To generate reactive intermediates in a solid-phase chemical reaction in crystals at ultralow temperatures, the following conditions should be met:

- the molecules of reactant and photolytic precursor of atoms must be initially isolated in the sample;
- the atom must be mobile to migrate in the solid matrix;
- the energy of the atom must be high enough to overcome the barrier to reaction.

This shows the interrelation between matrix isolation techniques and preparative-scale cryochemistry. They have much in common from the standpoint of methodology but are mutually excluding in their basic formulations, namely, matrix isolation implies the absence of chemical transformations while the subject of cryochemistry is specific features of chemical reactions at ultralow temperatures.^{11,12}

In this review cryochemical reactions of mobile atoms are treated as a means of generation of reactive intermediates while spectroscopic methods of investigation are considered as experimental techniques for studying matrix-isolated particles. This concept predetermines the issues that have attracted primary attention in this review. First of all, investigations of chemical transformations require relevant kinetic measurements to establish the principal reaction channels in the reacting system and to identify the primary and subsequent reactions. Carrying out spectroscopic measurements, one should choose spectroscopic characteristics necessary for reliable identification of particles. This is of particular importance in studies of novel open-shell species that were not observed earlier by other experimental methods.

Isotope substitution has been traditionally employed in analysis of vibrational and EPR spectra. Until recently, in most cases analysis of the spectra of isotopomers with the same stoichiometry served as the only objective argument when identifying new stabilised particles and establishing their structure. Improvement of computer hardware and development of new methods of quantum-chemical calculations in the last 10–15 years brought about radical changes in the procedure for identification and characterisation of trapped intermediates. Experimental data on the structure of most reactive intermediates are scarce, which precludes evaluation of the reliability and accuracy of calculations. It should be noted that quantum-chemical calculations should be treated as a kind of prediction until confirmation by corresponding experimental data. However, the use of modern methods of quantum-chemical calculations permits reliable identification of new chemical compounds based on comparison of the calculated and experimental spectroscopic data. In this review particular emphasis has been placed on joint use of experimental (both spectroscopic and kinetic) data and the results of quantum-chemical calculations of reactive intermediates.

II. Low-temperature spectroscopy of matrix-isolated species as a tool for investigations of reactive intermediates

1. Vibrational spectroscopy

The absorption IR spectroscopy is the most widely used method of investigation of matrix-isolated particles. Using this technique implies that the interaction of impurity particles with the lattice of inert gas is weak and has only little effect on the structure and vibrational dynamics of the species under study. The relative matrix shifts of vibrational frequencies (ratio of the frequency difference between the molecular vibration in the solid matrix and in the gas phase to the vibrational frequency in the gas phase) of various molecules and radicals have been analysed.¹³ For most molecules the matrix shifts were found to lie between -2% and 2% (Fig. 1). The matrix shift histogram presented is centred at $\sim 0.5\%$ while the dispersion is at most 1% . The magnitude and sign of the matrix shift are related to the character of intermolecular interactions between the particle and environment. In some cases one should take into account the dynamic effects in addition to static guest–host interactions. Modern computational approaches to determination of matrix shifts have been documented.^{14, 15}

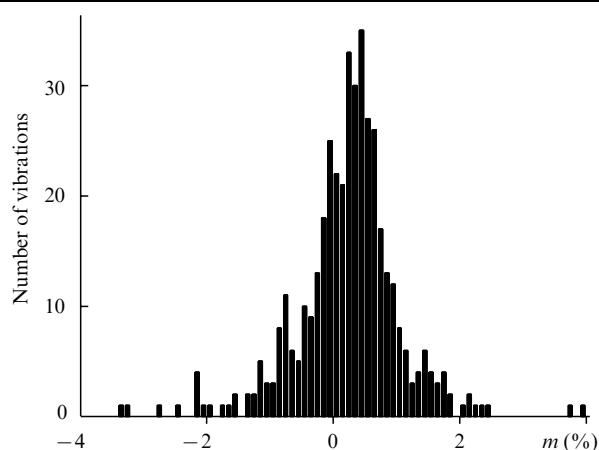


Figure 1. Relative matrix shifts (m) of vibrational frequencies of intermediates isolated in argon matrices.¹³

Head-Gordon *et al.*¹⁶ reported comparative analysis of the accuracy of calculations of vibrational frequencies for various molecular compounds using the most widely used *ab initio* computational methods (in the harmonic approximation). The accuracy of B3LYP density functional calculations of fundamental frequencies was shown to be comparable with that of the frequency calculations by the CCSD(T) method. For instance, the frequencies obtained from B3LYP/cc-pVDZ calculations deviate from the corresponding frequencies measured in the gas phase by $\sim 5\%$ on the average, while the relative error of CCSD(T)/cc-pVDZ calculations can be as high as 1.5% . At the same time, all computational methods employed give a rather wide scatter of deviation values (dispersion of the deviations from the experimental values amounts to $10\%–12\%$). The most complicated problems are associated with calculations of the vibrational frequencies of light atoms (in particular, hydrogen atom) in polyatomic molecules.

The potentialities of IR spectroscopy are extended with improvement of corresponding equipment. Currently, the technique permits reliable detection of molecular compounds under study at concentrations that are low enough to provide conditions for spatial isolation of these species in a solid matrix. A conventional procedure for preparation of solid samples of an inert gas, containing trapped impurity molecules, involves condensation of

the gas molecular beams *in vacuo* on a substrate cooled to helium temperatures. Thin films of inert gas thus obtained have a polycrystal morphology and are characterised by the presence of nonequilibrium defects and a large specific surface. Usually, such films are called ‘solid matrices’; however, one should keep in mind a basic difference between these films and crystals grown under equilibrium conditions. It is nonequilibrium conditions for condensation and low concentrations of impurity particles that allow trapping of virtually any particle in the matrix without their association. Long-range order in the vicinity of the small impurity molecules trapped in a solid matrix corresponds, as a rule, to substitutional impurity or to interstitial impurity occupying the O_h site in the face-centred cubic (f.c.c.) lattice of inert gas.¹⁴ An impurity trapped in a solid matrix is considered isolated if its nearest environment contains no analogous particle. If the trapped molecules are randomly distributed over the substitutional sites of a f.c.c. crystal lattice, the probability, p , for a particular molecule to be spatially isolated is given by the following expression,

$$p \approx 1 - zx_m,$$

where $z = 12$ is the number of atoms in the first coordination sphere of the impurity molecule and x_m is the relative concentration of impurity particles ($x_m = [m]/[Ar]$). To consider a total of 99% of impurity particles isolated, their concentration x_m should be less than 10^{-3} . In real experiments the number of trapped dimers and higher clusters of impurity molecules much exceeds the statistical average. This is usually explained by limited mobility of the molecules on the surface of the growing film during condensation and by their interaction in the gas mixture. If only van der Waals intermolecular interactions occur, the fraction of clusters amounts, as a rule, to $1\%–5\%$ of the total number of trapped molecules at $x_m \approx 5 \times 10^{-4}$. If the molecules are capable of forming hydrogen-bonded clusters (*e.g.*, NH_3 and HCN , see Refs 17–19), this proportion increases to $10\%–20\%$.

The sensitivity of IR spectroscopic measurements in the conventional spectral range ($400–4000\text{ cm}^{-1}$) under conditions of matrix isolation of the particles under study can be estimated based on the characteristic values of the integrated intensity ($B \approx 10^7\text{ cm mol}^{-1}$) and spectral halfwidth ($\Delta \approx 3\text{ cm}^{-1}$) of absorption bands. At optical densities $D > 2 \times 10^{-3}$, these values correspond to a measurable number of particles, $N > 5 \times 10^{14}\text{ cm}^{-2}$. In this case, assuming that the thickness of the matrix film is $\sim 100\text{ }\mu\text{m}$, the average relative concentration of the particles to be recorded is greater than 10^{-6} . These values allow measurements of the IR spectra using low concentrations (sufficient for spatial isolation) of reactant molecules. Usually, the relative concentrations of impurity molecules are of the order of $10^{-3}–10^{-4}$. This permits both reliable detection of weak bands in the IR spectrum (with the integrated absorption coefficient of about $10^5–10^6\text{ cm mol}^{-1}$) and measurements of changes in the concentrations of initial reactants in the course of chemical transformations with an error of at most 0.5% .

IR spectroscopy allows detection of different types of particles (molecules, radicals, ions, molecular complexes). Therefore, this method is a universal tool for kinetic measurements. The potential of the technique, as applied to differentiation between particular bands in the IR spectrum of products of the reactions of mobile atoms based on the results of kinetic measurements, was demonstrated taking reactions of fluorine atoms with CO molecules in solid argon at 20 K as examples.^{20, 21} In this case, where only one reactant (fluorine atom) is mobile in the matrix, the principal channels of consumption of the reactants are as follows: recombination of diffusing fluorine atoms



primary reaction of fluorine atoms



secondary reaction of fluorine atoms



The experimentally observed changes in the band intensities in the IR spectrum of the reactant molecule (CO) and reaction products correspond to this simple kinetic scheme. Namely, in the initial stage, the intensities of the bands of the molecular product (F_2CO) increase quadratically with respect to the increase in the intensities of the bands of FCO^* radicals and those of the consumption of the molecular reactant. This allows one to distinguish between the IR bands of the primary and secondary products of the reactions of the mobile atoms. One can also measure the absolute intensities of the bands by comparing the increase in the band intensity and the corresponding decrease in the intensities of the bands of the reactant molecules. Taking into account the mass balance equation for the CO group,

$$\Delta[\text{CO}] = \Delta[\text{FCO}^*] + \Delta[\text{F}_2\text{CO}] \quad (3)$$

one gets a linear relation between the product band intensities, A_{FCO^*} and $A_{\text{F}_2\text{CO}}$, normalised to the corresponding decrease in the intensity of the band of the molecular reactant, ΔA_{CO}

$$\frac{A_{\text{FCO}^*}}{\Delta A_{\text{CO}}} = -\beta_1 \frac{A_{\text{F}_2\text{CO}}}{\Delta A_{\text{CO}}} + \beta_2, \quad (4)$$

where β_1 and β_2 are the ratios of the integrated intensities of the bands

$$\beta_1 = \frac{B_{\text{FCO}^*}}{B_{\text{F}_2\text{CO}}}, \quad \beta_2 = \frac{B_{\text{FCO}^*}}{B_{\text{CO}}}. \quad (5)$$

Since the ratio of the concentrations of the primary and secondary reaction products varies in the course of transformations, the relative absorption coefficients for the products and reactant, $B_{\text{FCO}^*}/B_{\text{CO}}$ and $B_{\text{F}_2\text{CO}}/B_{\text{CO}}$, can be determined from the linear dependence of the relative intensities of the product bands in Eqn (4). Experiments showed²⁰ that the band intensities of the

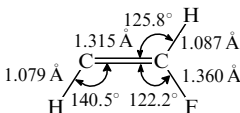
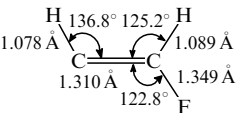
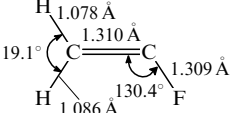
molecular product (F_2CO) thus obtained are in agreement with those determined earlier by other methods and that the band intensities of the radical product (FCO^*) are in reasonable agreement with the results of corresponding quantum-chemical calculations.

Despite high sensitivity and versatility of IR spectroscopy, identification of radical intermediates and determination of their structure faces some problems. For instance, if we deal with condensation of reaction products from the gas phase, the IR bands of different products cannot always be reliably distinguished and identified. As mentioned above, carrying out solid-phase reactions eliminates this problem. Another type of severe problem is associated with the fact that the vibrational frequencies measured by IR spectroscopy are dynamic characteristics of molecular compounds. Therefore, in some cases determination of the molecular structure based on the vibrational spectra only is complicated and additional information is required. This is of particular importance in studies of loosely bound molecular complexes or various isomers and conformers of trapped intermediates. Registration of characteristic low-frequency vibrations ($\nu \leq 300 \text{ cm}^{-1}$) of loosely bound complexes using conventional instruments is also difficult. Moreover, both static deformations of the structure and dynamic lattice effects predetermine large shifts of the vibrational frequencies of complexes.

When studying various isomers of the same stoichiometry, one should take into account minor changes in the vibrational dynamics of different isomers, especially if changes in position of the hydrogen atom are concerned. In this case changes in the characteristic vibrational frequencies are comparable with the accuracy of calculations. Therefore, identification of a particular isomer of a stabilised radical by comparing the experimental and calculated vibrational spectra is complicated.

As an example, Table 1 lists the geometric parameters, vibrational frequencies and isotropic hyperfine coupling constants (IHFC) of structural isomers of the $2\text{-C}_2\text{H}_2\text{F}^*$ radical generated in the reaction of a mobile fluorine atom with a C_2H_2 molecule in

Table 1. Calculated and experimental vibrational frequencies and isotropic hyperfine coupling constants of structural isomers of $2\text{-C}_2\text{H}_2\text{F}^*$ radical. Calculations were carried out by the B3LYP/6-311++G(3df,2p) method.

Parameter (vibration)	Calculated value ^a			Experi- mental value ^a	Experi- mental value ^b
	<i>trans</i> - $2\text{-C}_2\text{H}_2\text{F}^*$	<i>cis</i> - $2\text{-C}_2\text{H}_2\text{F}^*$	$1\text{-C}_2\text{H}_2\text{F}^*$		
					
Vibrational frequencies / cm^{-1}					
1a' (CH_α stretching)	3307	3308	3236	3193	3178
2a' (CH_β stretching)	3184	3122	3111	3026	—
3a' (CC stretching)	1664	1678	1701	1631	1623
4a' (H_βCC bending)	1305	1291		1263	1211
(CH_2 bending)			1395		
5a' (CF stretching)	1024	1093	1149	1070	1066
6a' (H_αCC bending)	779	734		698	678
(CH_2 rock)			943		
7a' (FCC bending)	433	479	454	—	462
1a'' (wagging)	883	827	831	785	785
2a'' (twist vibrations)	661	645	615	643	631
IHFC constant /mT (see ^c)					
a_{F}	10.12	6.69	13.37	6.50	7.30
a_{H_β}	1.69	3.81	4.16	3.86	3.81
a_{H_α}	0.14	0.17	1.20	0.25	—

^a The data were taken from Ref. 22; the vibrational frequencies were calculated in the harmonic approximation. ^b The vibrational frequencies were taken from Ref. 23 and the IHFC constants were taken from Ref. 24. ^c Only absolute values of IHFC constants were measured experimentally.

solid argon²² as well as the results of an earlier study²³ in which the 2-C₂H₂F[•] radicals were stabilised by condensation of reaction products in gas discharge. Analysis of the vibrational dynamics in the model structure of the *trans*-2-C₂H₂F[•] isomer suggested²³ that the radical stabilised corresponds to this isomer. However, as can be seen in Table 1, the vibrational frequencies of the *trans*-2-C₂H₂F[•] and *cis*-2-C₂H₂F[•] isomers calculated by modern quantum-chemical methods are close and the experimental IR spectra cannot be assigned to a particular isomer even taking into account the results of analogous measurements for the deuterated analogue (2-C₂D₂F[•]). Comparison of the spectra of the radicals^{22,23} reveals close values of all vibrational frequencies (to an accuracy of $\pm 15\text{ cm}^{-1}$), except for the relatively weak bending vibration $\text{H}\beta\text{CC}$, for which the frequency difference is 52 cm^{-1} . However, the reason for such a large difference is still to be clarified (this can be different matrix shifts due to a different manner of arrangement of the radical in the lattice, or these are different isomers, or incorrect assignment of the weak IR band!). Moreover, identification of another structural isomer, 1-C₂H₂F[•], faces analogous problems since the patterns of the vibrational spectra of all three particles are similar and exhibit no characteristic distinctive features (see Table 1). Unambiguous establishment of the structure of radical intermediates in the two above-mentioned cases can be made only by joint use of vibrational and EPR spectroscopy.^{22,25}

2. EPR spectroscopy

Electron paramagnetic resonance is widely used in various applications of the matrix isolation technique as well as in cryochemical and radiation chemistry studies. Some key aspects of the use of this method in studies of matrix-isolated reactive intermediates are considered below.

High spectral resolution and sensitivity of the EPR technique under conditions of generation of radical intermediates in solid-phase reactions of mobile atoms with isolated reactant molecules are due to the following factors: perfect isolation of the radicals stabilised and the absence of radical pairs in the nearest environment (this eliminates the dipole–dipole interaction between radicals), the absence of super-HFC on the matrix nuclei due to zero nuclear spins of argon and neon atoms (and the ⁴He and parahydrogen molecules), and fast (incoherent) rotation of radicals in the lattice, which averages anisotropic magnetic interactions.

These factors are due to both the procedure for generation of radicals and the properties of the inert matrices. Under conditions of ideal matrix isolation of the radicals the widths of individual components of the hyperfine structure (HFS) are at most 0.1 mT in solid argon and at most 0.01 mT in solid p-H₂. Therefore, the spectral resolution under these conditions is no worse than in liquids²⁶ and much better than in organic crystals and glasses.²⁷ The spectroscopic parameters of ethyl radicals measured in different media are listed in Table 2. As can be seen, the intrinsic widths

of the lines in the spectra of radicals stabilised in solid parahydrogen or argon is comparable with the linewidths in the EPR spectra recorded in the liquid phase.^{28–33}

A feature of small polyatomic molecules is rotation in solid matrices and crystals at ultralow temperatures. Depending on the species size and on site occupied by the particles in the crystal lattice, both free rotation (with population of nonzero rotational quantum states) and rotational diffusion (incoherent rotation) characterised by the rotational correlation time, τ_c , can occur. Fast incoherent rotation of radicals in the lattice causes averaging of anisotropic interactions, thus providing high resolution of the hyperfine structure and the possibility of determining the absolute values of the IHFC constants if they exceed 0.1 mT.

As an example illustrating the influence of various factors on the resolution of the EPR spectra of trapped radicals, Fig. 2 presents the spectra of the 2-C₂H₂F[•] radicals generated in the solid-phase reaction $\text{F} + \text{C}_2\text{H}_2$. Spectrum 1 was obtained in an argon matrix with high concentration of C₂H₂, while spectrum 2 was recorded in a krypton matrix containing magnetic nuclei (the nuclear spin of ⁸³Kr atom is 9/2). In the former case most of the reactant molecules (C₂H₂) exist as dimers and more complex associates. This leads to stabilisation of the radicals bound in complexes with the neighbouring C₂H₂ molecules. The radical–molecule interaction in these complexes stabilises the structure formed and hinders rotation of the radical. Probably, that is why no resolved hyperfine structure of these radicals in photolysed mixtures $\text{Ar}:\text{F}_2:\text{C}_2\text{H}_2(\text{C}_2\text{D}_2) = 200:1:1$ was recorded earlier.³⁴ A hyperfine splitting of 0.25 mT on the α -proton of the 2-C₂H₂F[•] radical was first observed under conditions of perfect isolation of the radicals generated in the reactions of

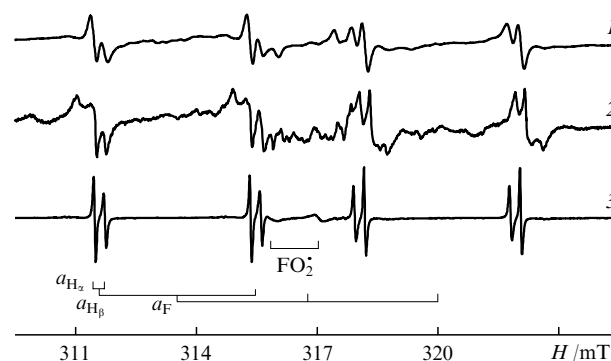


Figure 2. EPR spectra of 2-C₂H₂F[•] radicals produced by photolysis at 15 K and subsequent annealing of the samples at 25 K.²²

The spectra were recorded at 30 K; shown are the HFS of 2-C₂H₂F[•] and FO₂[•] radicals. Sample composition: $\text{Ar}:\text{F}_2:\text{C}_2\text{H}_2 = 300:1:1$ (1), $\text{Kr}:\text{F}_2:\text{C}_2\text{H}_2 = 3000:1:1$ (2) and $\text{Ar}:\text{F}_2:\text{C}_2\text{H}_2 = 3000:1:1$ (3).

Table 2. Characteristic EPR linewidths, parameters of the hyperfine coupling (mT) and *g*-factor tensors of C₂H₅[•] radical in different media.

Matrix	Generation technique	Linewidth	<i>g</i> -Factor	$ a_x $ ^a	$ A_{\perp}^{\alpha} - A_{\parallel}^{\alpha} $	$ a_{\beta} $	$ A_{\perp}^{\beta} - A_{\parallel}^{\beta} $	Ref.
p-H ₂ (>99.5%)	UV photolysis of C ₂ H ₅ I	0.02	2.0031 ($\Delta g \leq 0.0001$)	2.27	0.98	2.68	0.31	28
Ar	addition reaction $\text{H} + \text{C}_2\text{H}_4$	0.1	2.0023 ($\Delta g \leq 0.0003$)	2.28	1.02	2.68	0.28	29
C ₂ H ₆ (liq.)	electron beam irradiation	0.01	2.0026	2.238	—	2.687	—	30
p-H ₂ (>95%)	UV photolysis of C ₂ H ₅ I	0.14	—	2.24	—	2.69	—	31
Ar	the same	0.2	—	1.99	—	2.65	—	32
Xe	addition reaction $\text{H} + \text{C}_2\text{H}_4$	0.3	2.0026 ($\Delta g \leq 0.0015$)	2.25	0.93	2.72	0.36	33
Xe	abstraction reaction $\text{H} + \text{C}_2\text{H}_6$	0.3	2.0028 ($\Delta g \leq 0.0024$)	2.20	0.96	2.70	0.31	33

^a Calculated using the formula $a = \frac{2A_{\perp} + A_{\parallel}}{3}$.

mobile atoms in solid argon (see spectrum 3 in Fig. 2). Experiments with heavier isotopomers of acetylene (C_2D_2 and C_2HD) allowed assignment of a complete set of IHFC constants of this type of radicals.²² Analogously, frozen van der Waals complexes $\text{FCO}^{\bullet}\cdots(\text{CO})_n$ were produced in the samples with relative concentrations of the reactant molecules, $[\text{CO}] > 10^{-3}$ (see Refs 35 and 36). The EPR spectra of $\text{FCO}^{\bullet}$ radicals at 4.2 K provide a classical example of the EPR spectra of frozen radicals with strong anisotropy of the constants of HFC with the fluorine atom. Recently,³⁷ it was found that anisotropic spectra of the $\text{FCO}^{\bullet}$ radicals (they are similar to the spectra reported earlier^{34,35}) in photolysed $\text{Ar}/\text{F}_2/\text{CO}$ samples with a high concentration of the molecular reactant ($[\text{CO}] > 5 \times 10^{-3}$) remain unchanged up to 30 K. However, the shape of the EPR spectra of $\text{FCO}^{\bullet}$ radicals in the samples with much lower concentration of the reactant molecules ($[\text{CO}] < 10^{-3}$) changes dramatically upon temperature variation.

The EPR spectrum of $\text{FCO}^{\bullet}$ radicals is presented in Figure 3. This is a superposition of an anisotropic spectrum, which varies only slightly with temperature, and a spectrum whose pattern closely resembles that of an isotropic spectrum. The linewidths in the latter spectrum drastically decrease as the temperature increases at $T > 13$ K. The samples with the relative concentration of the reactant molecules of less than 10^{-4} are characterised by a virtual absence of radicals exhibiting anisotropic spectra at high temperatures. The time τ_c of the isolated radicals, estimated from changes in the linewidths under conditions of fast incoherent rotation, is $\sim 10^{-9}$ s at 30 K. Averaging of the anisotropy due to fast rotation of radicals in inert matrices at ultralow temperatures was also pointed out in other studies (*e.g.*, Refs 38 and 39). These examples demonstrate that under perfect isolation conditions, the anisotropy of magnetic interactions of not only small radicals (*e.g.*, $\text{FCO}^{\bullet}$) but also larger structures, (*e.g.*, $\text{C}_2\text{H}_2\text{F}^{\bullet}$) is averaged due to fast rotation of the species in the lattice.

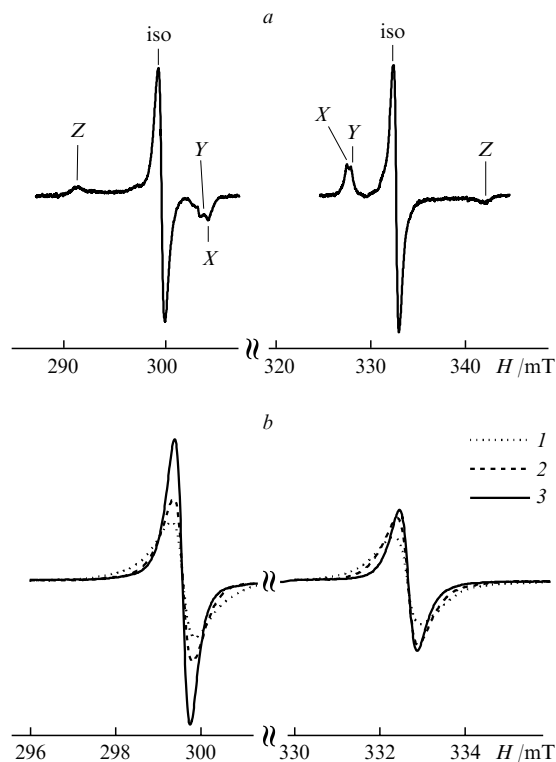


Figure 3. EPR spectra of $\text{FCO}^{\bullet}$ radicals in $\text{Ar}:\text{F}_2:\text{CO} = 300:1:1$ (a) and $\text{Ar}:\text{F}_2:\text{CO} = 3000:1:1$ (b) recorded at 15 (1), 22.5 (2) and 35 K (3).³⁷ The components of the HFC tensor are labelled X, Y and Z and the isotropic line is labelled 'iso'.

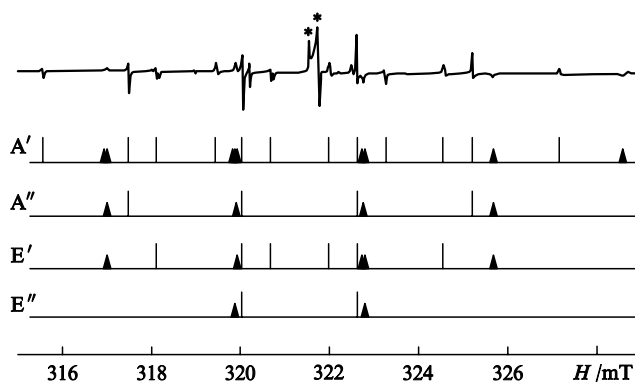


Figure 4. EPR spectrum of $p\text{-H}_2:\text{C}_2\text{H}_5\text{I} = 5000:1$ sample after UV photolysis at 4.7 K.²⁸

The intense signal at the centre of the spectrum (asterisked) is due to the presence of paramagnetic particles in the quartz ampoule. Shown are the calculated positions of the components of the anisotropic spectrum of ethyl radicals with A' , A'' , E' and E'' symmetry. Vertical lines and triangles denote positions of the components in the spectrum of ethyl radicals in which the C—C bond is respectively perpendicular and parallel to the direction of the external magnetic field.

Kumada *et al.*²⁸ reported the EPR spectra of $\text{C}_2\text{H}_5^{\bullet}$ radicals isolated in solid parahydrogen (Fig. 4). High spectral resolution achieved in this study (< 0.01 mT) allowed both determination of the anisotropic components of the HFC tensor in the absence of rotation of the whole radical and distinguishing between the spectral lines corresponding to different rotational states of the methyl group. The rotational energy level splitting in solid parahydrogen (5.3 ± 0.7 K) determined from temperature-induced variations of the line intensities was found to be close to that measured earlier by IR spectroscopy in the gas phase. Resolved EPR spectra of 2-fluoroethyl radicals can be recorded in solid argon under conditions of perfect isolation (Fig. 5).⁴⁰ Fast (incoherent) internal rotation and the dependence of the IHFC constants on the angle of rotation of the CH_2 group around the CH_2F fragment is responsible for a sharp temperature dependence of the EPR linewidths in the temperature range from 20 to 35 K. Anisotropy of the HFC tensor of the fluorine atom is retained upon warming up the system; therefore, changes in the spectral pattern are due to internal rotation of the CH_2 group only. Variation of the angle of rotation causes modulation of the HFC, thus leading to temperature-induced line broadening. The energy barrier, E_a , to internal rotation was estimated from the Arrhenius dependence of the linewidth at $\approx 920\text{--}1050$ J mol⁻¹,

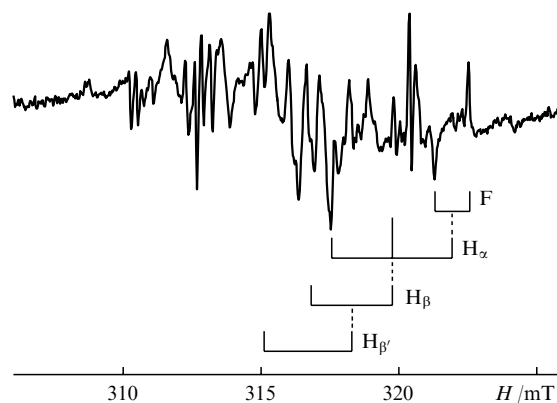


Figure 5. EPR spectrum of $2\text{-C}_2\text{H}_4\text{F}^{\bullet}$ radicals generated in reactions of diffusing fluorine atoms with C_2H_4 molecules and isolated in solid argon.⁴⁰

which is close to the barrier height calculated⁴¹ for a free radical in the gas phase. However, this value is much smaller than that measured in viscous liquids ($\sim 4000 \text{ J mol}^{-1}$).⁴²

The aforesaid indicates that perfect isolation of radical species in inert matrices containing no magnetic nuclei permits both determination of the principal HFC parameters and characterisation of internal rotation of molecular fragments and atomic groups in the absence of rotation of the whole radical.

The experimentally measured IHFC constants provide a reliable structure-sensitive parameter suitable for identification of new radical intermediates. Their structures can be determined by comparing the experimental values of spectroscopic characteristics with the corresponding values calculated using modern quantum-chemical methods. This approach was substantiated^{43–45} when analysing the experimental data and results of quantum-chemical calculations of different types of radicals. These investigations have demonstrated the practical applicability of density functional calculations to the studies of the interrelation between structure and spectroscopic characteristics. The IHFC constants are determined by the distribution of the unpaired electron density over the corresponding magnetic nuclei in the molecular structure. Therefore, these characteristics are rather sensitive to the changes in the electron wave function on the magnetic nuclei. The error in calculations of the IHFC constants using modern methods is usually at most 10%.⁴⁴ The vibrational frequencies can be calculated with better accuracy; however, they are much less sensitive to changes in the electronic structure. This is of crucial importance for the identification of reactive intermediates and for the determination of their structure in at least two critical situations. The first case concerns identification of a particular isomer of the stabilised intermediate. A typical example is provided by the *cis*- and *trans*-isomers of the $2\text{-C}_2\text{H}_2\text{F}^\bullet$ radical. The vibrational spectra of these isomers were discussed above. As can be seen from Table 1, the values of the IHFC constants of the radicals stabilised in solid argon correspond to *cis*- $2\text{-C}_2\text{H}_2\text{F}^\bullet$ rather than *trans*- $2\text{-C}_2\text{H}_2\text{F}^\bullet$, as was reported earlier.^{24,34} In this case both the chemical intuition (assignment of the experimental EPR spectrum was based on the assumption of analogy between the electron density distributions in the $2\text{-C}_2\text{H}_2\text{F}^\bullet$ and $\text{C}_2\text{H}_3^\bullet$ radicals and on the predicted thermodynamic properties of the *cis*- and *trans*-isomers) and vibrational analysis²³ led to erroneous conclusions. This was first pointed out by Barone *et al.*⁴³ Reliable identification of the other structural conformer, $1\text{-C}_2\text{H}_2\text{F}^\bullet$ radical, is possible only based on measurements of the IHFC constants. Insertion of a fluorine atom at the α -position causes a twofold increase in the IHFC constant a_F (and simultaneous increase in the IHFC constants on protons) compared to the corresponding constants of the isomers of the $2\text{-C}_2\text{H}_2\text{F}^\bullet$ radical.

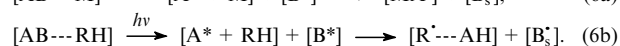
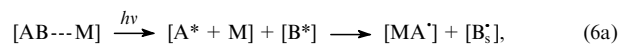
Another practically important problem is to determine the structure of weakly bound radical – molecular complexes. It has been shown^{46,47} (for detailed analysis, see below) that reaction products of hydrogen abstraction from RH molecules can be stabilised in matrices in the form of radical – molecular complexes $\text{R}^\bullet \cdots \text{HF}$. Taking into account the spectral resolution that can be achieved in the experiments with inert matrices, the EPR technique seems to be promising for the investigation of the structure of such intermediates. If the radical and the molecule in a complex are separated by at most 0.3 nm and the individual components of the HFS are no wider than 0.1 mT, the EPR spectra exhibit a resolved hyperfine structure corresponding to interactions of the unpaired electron of the radical with the magnetic nuclei of the other molecule (nuclear spin of the H and F atoms of the HF molecule is $1/2$). The constants of magnetic interactions are rather sensitive to the distances and orientation of fragments in complexes; this permits their structure and sometimes the type and characteristic times of hindered internal motions of the fragments in the complex to be determined reliably.

3. Optical spectroscopy and photoinduced transformations of stabilised reactive intermediates

The main fields of application of the optical studies of cryogenic matrices involve spectroscopy of electronically excited states, photoinitiation of chemical transformations in the complexes comprised of molecular reactants, generation of radical species in the photodissociation of isolated molecules and photoinduced intramolecular conversion of isolated species as well as photo-stimulated translational mobility of atoms.

The electronic and vibronic transitions in the condensed phase are strongly affected by the environment, even if the molecular species under study are isolated in inert matrices. For this reason, spectroscopic investigations of matrix-isolated particles are to a greater extent focussed on the studies of the mechanisms of relaxation of excitation energy in the solid phase (see review⁴⁸) rather than spectroscopic characterisation of excited states. Besides, instrumental problems due to strong scattering of the visible and UV light by crystalline matrix films, as well as the effects of nonradiative relaxation in the matrices reduce the sensitivity of absorption spectroscopy and limit the use of the laser-induced fluorescence (LIF) technique in these studies. Most spectroscopic data on the excited states of radical species were obtained in the gas-phase LIF and laser-induced magnetic resonance studies (these methods are characterised by high sensitivity and the possibility of carrying out experiments with spectral and temporal resolution). Detailed investigations of the $\text{OH}^\bullet$ (see Ref. 49), $\text{CN}^\bullet$ (see Refs 50 and 51) and $\text{ClO}_2^\bullet$ (see Refs 52–54) radicals were performed, and considerable attention has been given to the studies of perturbations of the lower electronic states by the crystalline environment and of the dynamics of relaxation processes in solid matrices.

Photoinduced transformations in molecular complexes is an interesting branch of cryochemistry. The key feature of these investigations is to preliminarily prepare molecular complexes of reactants in the matrix. Further chemical reactions in the complexes are initiated by photo-excitation of one of the reactants. In most cases these studies are limited to identification of reaction products and determination of the relative yields of the principal reaction channels.⁵⁵ Description of chemical transformations on the molecular level taking into account the dynamics of molecular rearrangements and the energy relaxation in the lattice is a rather complicated task. Some approaches to the molecular dynamics simulation of these transformations using semiempirical methods of calculations of the PES of corresponding reactions have been reviewed by Raff.⁵⁶ If the initial reactants are closed-shell species chemical transformations within the matrix cage will also result in the molecular products. To trap the radical intermediates, the radical fragment of the reacting system should escape the reaction cage and then be trapped outside it. For instance, photodissociation of a complex of a diatomic molecule (AB) with a reactant (M) can yield radical adducts or radical – molecular complexes, if one of the atoms is stabilised outside the reaction cage:



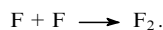
However, different research groups (see, *e.g.*, Refs 57–59) reported that photolysis of halogen molecules bound into a complex with the molecules of the other reactant results mainly in the molecular products and that the yield of radical pairs in the reactions (6a) and (6b) is negligible. These results were expected for the complexes containing molecules of heavy halogens (Cl, Br and I). At the same time, the reaction channels (6a) and (6b) can be significant for the complexes with HI (HBr) or F_2 molecules due to weakening of the cage effect for the hydrogen and fluorine atoms compared to the heavy halogen atoms.⁶⁰

Photolysis of isolated molecules in cryogenic matrices is a conventional method of generation of stabilised radicals. Spectro-

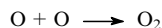
scopic data for the radical species thus produced served as the basis for further studies of these objects (see, *e.g.*, Ref. 6). At the same time the cage effect precluding spatial separation of the photodissociation products, the formation of tight radical pairs as well as photolysis of primary products of photodecomposition reduce the efficiency of generation of stabilised radicals and make the interpretation of the spectroscopic and kinetic data more difficult.

Another method for generation of new matrix-isolated particles involves photo-excitation of an isolated particle followed by intramolecular rearrangements. In contrast to the gas phase, photo-excitation to the dissociative absorption band under conditions of the crystalline environment, which impedes spatial separation of the photodissociation fragments, can cause stabilisation of various structural conformers of the same stoichiometry. In most of such studies the molecules were matrix isolated using conventional techniques (see, *e.g.*, Refs 61 and 62). Despite the fact that this procedure for generation of new molecular species has found a rather wide application, there are only a few examples of generation of radical species in this manner. Methodological difficulties in such studies are associated with the necessity of obtaining sufficiently high concentrations of radicals in the absence of other products.

Electronically excited halogen – Rg complexes (Rg is the atom of inert gas) have been traditionally used as a working substance for gas lasers. Basic research into the optical properties of halogen atoms in the solid matrices and crystals of inert gases^{63,64} was mainly stimulated by the idea of creation of solid-state excimer lasers. It was found that in most cases the effects of multibody interactions in crystals preclude radiative deactivation of diatomic exciplexes. For instance, the energy of electronic excitation of an ArF complex in solid argon is close to that determined in the gas phase (Fig. 6). However, the excited state undergoes fast relaxation (during $\sim 10^{-13}$ s) into a more stable triatomic exciplex (Ar_2^+F^-) (see Ref. 65). Radiative deactivation of diatomic exciplexes in solid krypton is also preceded by the formation of triatomic excited states, *e.g.*, $(\text{Kr}_2)^+\text{F}^-$ (see Ref. 66). Since exciplexes are characterised by electron transfer from the halogen atom to the atoms of the inert gas, the equilibrium distances in such structures are much shorter than the van der Waals interatomic distances in the ground electronic state. As a result, radiative deactivation of an electronic excitation causes transformation of a large portion of the exciplex energy (1 to 2 eV) into the kinetic energy of the atoms of the dissociating particle (see Fig. 6). This brings about a unique phenomenon, namely, photo-induced migration of ‘hot’ fluorine atoms in the crystals of inert gases.^{65,66} For instance, experiments on photogeneration of fluorine atoms in argon crystals showed that excitation to the ArF exciplex absorption band with light at $\lambda = 193$ nm upon continuous irradiation of the samples leads to bimolecular recombination of fluorine atoms



The average migration length of a ‘hot’ F* atom with an initial kinetic energy of ~ 0.7 eV was estimated at ~ 7 nm.⁶⁶ An analogous effect of photoinduced migration was also observed for the oxygen atoms isolated in solid krypton or xenon.^{67–69} Studies of continuous photolysis of xenon or krypton crystals containing stabilised $\text{O}(^3\text{P})$ atoms with light at $\lambda = 248$ nm showed that radiative deactivation of charge-transfer Rg^+O^- exciplexes induces migration of the atomic oxygen in the crystal and, finally, loss of the oxygen atoms by a bimolecular mechanism



Photoinduced migration of reactive atoms in the crystals of inert gases opens up unique prospects for practical implementation of chemical reactions involving these atoms at ultralow temperatures. This is possible if two conditions are met. First, the atom must possess the ability to migrate in the crystal. Second, it must have an excess kinetic energy required to overcome a reaction barrier. Methodologically, there is a feature which complicates a correct interpretation of the results of such experiments. To make atoms mobile, the sample should be irradiated with UV light at a wavelength of about 200 nm. This can cause photoinduced conversions of both the reactant molecules and the primary products of the reactions of the mobile atoms. Nevertheless, this effect can be insignificant since diatomic exciplexes are, as a rule, characterised by extremely large absorption cross sections ($\sim 10^{-16} - 10^{-17}$ cm², see Ref. 66).

III. Translational mobility of hydrogen, fluorine and oxygen atoms in the crystals and solid matrices of inert gases

1. Translationally excited ‘hot’ atoms produced by photodissociation of isolated molecules

Photodissociation dynamics of small molecules in the crystals of inert gases have been well studied experimentally. Efficient photodecomposition of an isolated precursor can be achieved if the kinetic energy of one reactant (in this case, the atom) is high enough to overcome the lattice barrier which precludes spatial separation of the dissociation products. Possible mechanisms of photodissociation of a number of small molecules, accompanied by generation of H, F and O atoms in the crystals of inert gases, have been considered in detail by Apkaryan and Schwentner.¹⁰ Fundamental difficulties which arise when simulating such processes include the necessity of taking into account the effects of multibody interactions at short distances, which make the pair atom – atom potentials non-additive. Nevertheless, the results of the molecular dynamics simulation are in reasonable agreement with the available experimental data.

The dynamics of ‘hot’ atoms in the crystal is controlled by the following factors. The $\text{F}(^2\text{P})$ and $\text{O}(^1\text{D})$ atoms are characterised by relatively short effective interaction ranges in the crystals of inert gases. If such atoms occupy octahedral interstitial sites (O_h) of the f.c.c. crystal lattice, they interact with adjacent lattice atoms (Ar, Kr or Xe) in the attraction region of the pair interaction potentials $U(r)$. At the same time the repulsive part of the interaction potentials at short distances determines the optimum trajectory of the motion of the atom to an adjacent O_h site through the edge of a face of the octahedron.^{70,71} Since the masses of the F and O atoms are comparable with those of the atoms of the argon lattice, the energy of a translationally excited ‘hot’ atom efficiently dissipates by collisions with the lattice atoms. Therefore, efficient escape of the atoms from the cage and spatial separation of the photodissociation products require that the bond cleaved in the photolytic precursor be oriented towards a face of the cell. In this case the atom can migrate in the crystal in a ballistic regime, thus avoiding direct collisions with the lattice atoms.⁷²

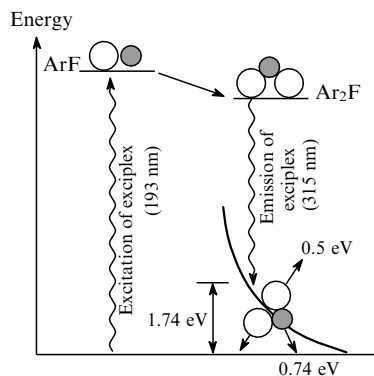


Figure 6. Scheme of excitation and deactivation of ArF exciplex in solid argon.⁶⁵

Quite different are the dynamics of photolytically generated hydrogen atoms. The effective radius of the interaction between the $\text{H}(^2\text{S})$ atom and Ar, Kr and Xe atoms is comparable with the interatomic distances in the lattice. Therefore, the $\text{H}(^2\text{S})$ atom interacts with adjacent lattice atoms only in the repulsive region of the pair interaction potentials and the optimum trajectory of the motion of the atom between interstices passes through the centres of the triangular faces of the f.c.c. crystal lattice.⁷³ It is believed¹⁰ that this predetermines another (compared to the F and O atoms) trajectory of the escape of the 'hot' atom from the reactant cage. In addition, due to the small mass the hydrogen atom loses a small portion of the kinetic energy by collisions with the lattice atoms. Therefore, the requirements on the orientation of the photolytic precursor in the lattice are not so severe as in the case of the $\text{F}(^2\text{P})$ or $\text{O}(^1\text{D})$ atoms. In this case the trajectory of motion of the 'hot' hydrogen atom during thermalisation should be close to the diffusion trajectory.

2. Thermally activated diffusion of atoms

Thermally activated mobility of H, O and F atoms in the crystals and matrices of inert gases has been reported by different research groups. The available literature data suggest that fluorine atoms possess extremely high translational mobility in the crystals of argon and krypton. The diffusion coefficients of hydrogen and oxygen atoms have been determined under conditions providing efficient recombination of the atoms, corresponding to typical kinetics of bimolecular reactions. Detailed consideration of these studies is given below.

IV. Chemical reactions involving hydrogen atoms

Hydrogen atoms isolated in cryogenic matrices have been the subject of intensive physicochemical studies using the matrix isolation technique. These investigations were mainly focussed on the problems of creation of high-energy systems, studies of quantum motions of light atoms and on specific features of multibody interactions in the condensed phase. After establishment of the fact that accumulation of high concentrations of stabilised hydrogen atoms in the solid phase is limited due to involvement of these atoms in chemical reactions, the emphasis was placed on the investigation of mechanisms of photoinduced generation of the atoms and subsequent chemical processes with their participation in low-temperature crystals and matrices.

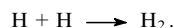
1. Photogeneration of hydrogen atoms

EPR is a very sensitive method for detection of hydrogen atoms in inert matrices. It was found that the lines of the hydrogen doublet in the EPR spectra in solid matrices exhibit a multiplet structure, which is due to the presence of several possible atomic sites in the crystal lattice. Analysis of distortions of the HFC and g -factor tensors by the crystal field showed that photogenerated hydrogen atoms are mainly stabilised in the interstitial sites (O_h and T_d) and to a lesser extent in the substitutional sites.^{74–78}

The HBr and HI molecules are convenient photolytic precursors for generation of hydrogen atoms in the solid phase. In the early studies (see, *e.g.*, Ref. 6) photolysis of these molecules was used to produce hydrogen atoms that entered into reactions with various reactants. Spectroscopic data for the radical species $\text{HO}_2^\bullet$, $\text{PHCO}^\bullet$, $\text{H}_2\text{NO}^\bullet$, *etc.* were first obtained using this experimental technique. It was shown⁷⁹ that 'hot' hydrogen atoms produced by photodissociation of HBr in solid xenon are stabilised at rather long distances (up to 10 nm!) from the dissociation site. This conclusion was drawn based on the study of the kinetics of HBr consumption and accumulation of bromine atoms during continuous photolysis of HBr with light at a wavelength of 248 or 193 nm. It was found that the kinetic dependences obey a second-order law due to reactions of the 'hot' atoms (characterised by long migration length) with the distant HBr molecules



This conclusion was confirmed in a study carried out using the EPR and LIF techniques and molecular dynamics simulation.⁷⁸ It was established that only a fraction of photogenerated H atoms is stabilised in the Xe and Kr matrices. Other H atoms either enter into reactions (8) or recombine during thermalisation



A quite different situation was shown to occur in solid argon where hydrogen atoms are trapped near the dissociation site. Therefore, nearly 100% of the precursor molecules are converted into trapped hydrogen atoms. The molecular dynamics simulation of thermalisation of a 'hot' atom showed that the hydrogen atom with an initial excess energy of 2.5 eV can move from the parent cage over long distances (up to 4 nm in solid krypton). In view of these results, one should expect that reactions of photogenerated 'hot' hydrogen atoms with various molecules should be efficient in solid krypton and xenon.

2. Thermally activated diffusion of hydrogen atoms

Consumption of hydrogen atoms during temperature annealing of solid Rg matrices was reported by different authors.^{80–84} It was found that consumption of hydrogen atoms in Kr and Xe matrices at $T > 30$ K obeys a second-order kinetic law, which corresponds to bimolecular recombination. Loss of H atoms in solid argon at temperatures above 12 K was observed. However, analysis of the kinetic dependencies of the loss of H atoms suggested⁸⁴ predominance of geminate recombination



of the atoms produced during low-temperature photolysis of HBr molecules.

The available literature data allow one to assume that solid matrices of inert gases (Ar, Kr and Xe) can serve as convenient media for studying the interactions of hydrogen atoms with small concentrations of various dopants. Chemical reactions of hydrogen atoms involving cleavage of molecular bonds are, as a rule, characterised by rather high activation barriers ($\geq 6–8$ kJ mol^{−1}). At ultralow temperatures, such thermally activated reactions must occur very slowly and therefore the use of photogenerated 'hot' atoms to produce reaction products seems to be more promising than the reactions of diffusing 'cold' atoms. At the same time stabilisation of a long-lived pre-reaction complex $\text{H} \cdots \text{M}$ formed by collision of the mobile atom with the isolated molecule in the absence of efficient thermal activation of chemical reactions provides the possibility of studying the interactions in the stage where the reactants approach each other.

Studies of tunnelling reactions of hydrogen exchange with hydrogen isotopes in solid hydrogen^{85–87} were also carried out in solid argon where the bound state of reactants was first detected by EPR.^{88,89} Stable complexes of reactants were formed as a result of diffusion of the H and D atoms at temperatures above 17 K. In particular, the atoms diffusing in solid Ar/HD mixtures form pre-reaction complexes upon collisions with the HD molecules. Among subsequent exchange reactions,



a tunnelling transition resulting in complexes of the products is possible only in reaction (9a). This allows one to expect stabilisation of two complexes, $\text{H} \cdots \text{HD}$ and $\text{H} \cdots \text{D}_2$, in this system. Their EPR spectra (Fig. 7) exhibit a resolved HFS on the doublet lines of the H atoms due to the interaction of the unpaired electron of the atom with the magnetic nuclei of the molecules in the complexes $\text{H} \cdots \text{HD}$ and $\text{H} \cdots \text{o-D}_2$. Besides, the hyperfine splitting on the hydrogen atom in the complex ($a_\text{H} = 51.18$ mT) differs from the characteristic a_H values of the atoms trapped in solid

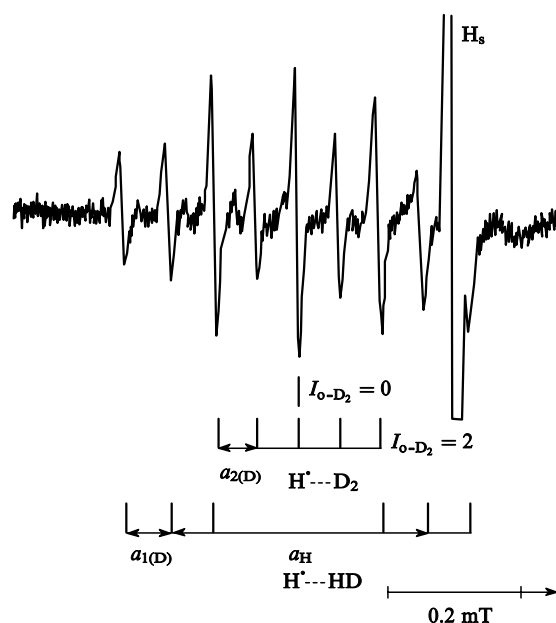


Figure 7. EPR spectra of van der Waals complexes $\text{H}'\cdots\text{HD}$ and $\text{H}'\cdots\text{D}_2$ formed in an argon matrix at 20 K.⁸⁹

The intense line denoted by H_s is due to hydrogen atoms stabilised in the substitutional site O_h . Shown are the characteristic splittings for individual complexes.

argon ($a_{\text{H}} = 50.73, 51.42$ and 51.54 mT for the substitutional site and the O_h and T_d interstitial sites, respectively).

The spectra of complexes $\text{H}'\cdots\text{H}_2$ generated analogously in Ar/ H_2 mixtures exhibit no super-HFS since the more stable parahydrogen molecule has a zero nuclear magnetic moment in the ground rotational state. Nevertheless, the formation of this complex was detected by the appearance of the hydrogen doublet with $a_{\text{H}} = 51.18$ mT. Specific features of the EPR spectra, such as narrow isotropic HFS lines and equal values of the constants of super-HFC with both atoms of the H_2 , HD and o- D_2 molecules (with allowance for correction for different gyromagnetic ratios, $\mu_{\text{H}}/\mu_{\text{D}} = 6.5$) were attributed to fast internal rotation in the complex. Quantum-chemical QCISD/aug-cc-pvqz calculations of hyperfine interactions in the complex showed that the experimental superhyperfine splitting $a_{\text{H}}' = 0.386$ mT corresponds to a distance of 0.245 nm between the atom and the geometric centre of the molecule.⁸⁹ This is much shorter than the value calculated earlier for free van der Waals complex $\text{H}'\cdots\text{H}_2$ on the PES of the H_3 system (0.34 nm). These data are in agreement with the results of investigations of tunnelling reactions of H atoms in solid hydrogen (H_2 , D_2 and HD), according to which the distances between the reactants in the crystalline environment are shortened.⁹⁰

3. Formation of chemical bonds with atoms of inert gases

A unique feature of heavy atoms of inert gases (xenon and krypton) is their ability to form chemical bonds with other atoms or molecular fragments that are efficient electron acceptors. This is due to a relatively low ionisation energy of the closed-shell atoms. This type of stable compounds can be exemplified by XeF_2 and XeF_4 which were first synthesised more than three decades ago.^{91,92} Data on binding xenon atoms into chemical compounds with fluorine and oxygen atoms have been generalised in some reviews (see, e.g., Refs 93–95).

Quantum-chemical calculations predict that the formation of weak chemical bonds with the light atoms of inert gases is possible.⁹⁶ Such chemical compounds can be stabilised only at ultralow temperatures. Therefore, the crystals of inert gases, which interact with free atoms under these conditions, are, strictly

speaking, not chemically inert. For instance, the XeCl_2 and KrF_2 molecules were first synthesised and characterised under matrix isolation conditions.^{97–99}

Convincing proofs of the possibility for chemical bonds with the atoms of inert gases were provided by researchers from Finland who detected a number of new chemical compounds, namely, $\text{H}-\text{Xe}-\text{H}$, $\text{H}-\text{Xe}-\text{Y}$ and $\text{H}-\text{Kr}-\text{Y}$ (Y is the halogen atom or a CN^* or OH^* radical). These compounds are formed in the reactions of diffusing hydrogen atoms in the solid matrices of xenon and krypton.^{100–102} Studies of these reactions have been reviewed.^{103,104} It is believed that neutral molecules $\text{H}-\text{Rg}-\text{Y}$ are formed as a result of the interaction of two close-lying diabatic PES corresponding to the interaction between neutral and charged fragments (Fig. 8). The low-lying bound state $^1\Sigma^+$ is treated as an ion pair $(\text{HRg})^+ \text{Y}^-$ in which the covalently bound fragment $(\text{HRg})^+$ is involved in electrostatic interaction with the negatively charged fragment Y^- . Based on this model, a molecular structure with ionic bond, $(\text{HXe})^+ \text{Cl}^-$, was predicted by semiempirical quantum-chemical calculations even in 1988.¹⁰⁵ The structure $\text{H}-\text{Xe}-\text{H}$ is treated analogously, that is, as a resonance hybrid between $(\text{HXe})^+ \text{H}^-$ and $\text{H}-(\text{XeH})^+$. Quantum-chemical calculations predict a linear geometry of $\text{H}-\text{Rg}-\text{Y}$ and the molecular energies lying between 38 and 135 kJ mol^{-1} relative to the energy of dissociation into neutral atoms. Global potential minima of such systems correspond to neutral HY molecules and Rg atoms. Because of the ionic type of chemical bonding the molecules $\text{H}-\text{Rg}-\text{Y}$ are characterised by high IR band intensities and by an extremely large dipole moment of the electronic transition $\text{A}^1\Sigma \leftarrow \text{X}^1\Sigma$ between two close-lying electronic states.^{106,107} Therefore, such particles are mostly studied by IR and optical spectroscopy. Table 3 lists the experimental and calculated frequencies of the $\text{H}-\text{Rg}$ stretching vibrations as well as the calculated bond lengths for a number of compounds.

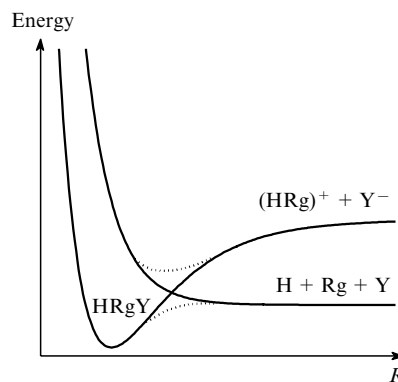
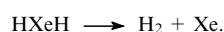


Figure 8. Scheme illustrating the nature of the chemical bond in HRgY molecules. Diabatic PES for the ionic $[(\text{HRg})^+ + \text{Y}^-]$ and neutral ($\text{H} + \text{Rg} + \text{Y}$) states of the system are shown by solid lines.¹⁰³ The abscissa is the sum of the $\text{H}-\text{Rg}$ and $\text{Rg}-\text{Y}$ distances in the linear configuration HRgY .

It was also found that HXeOH and HXeH stabilised in solid xenon dissociate over $\sim 10^3$ s at temperatures of 54 and 66 K, respectively.¹⁰⁷ Thermal decomposition was explained by decay of metastable states upon activation of bending vibrations



and



However, no formation of H_2O and H_2 molecules that would provide confirmation of the existence of such a dissociation channel was observed. The energy of IR quantum necessary to decompose a compound by multilevel IR excitation or the long-

Table 3. Experimental and calculated parameters of compounds H – Xe – Y and H – Kr – Y.^{103, 104}

Compound	ν_1/cm^{-1}	ν_2/cm^{-1}	l_1/nm	l_2/nm
H – Xe – Cl	1648	1799	0.1685	0.2663
H – Xe – Br	1504	1730	0.1694	0.2837
H – Xe – I	1193	1560	0.1747	0.3095
H – Xe – CN	1624	1817	0.1707	0.2392
H – Xe – OH	1578	1823	0.1718	0.2208
H – Xe – H	1166/1181 (asym.)	1334 (asym.)	0.1861	–
H – Kr – Cl	1476	1758	0.1435	0.2666
H – Kr – CN	1497	1738	0.1466	0.2349

Notations: ν_1 and ν_2 are the experimental and calculated frequencies of H – Rg vibrations; l_1 and l_2 are the calculated H – Rg and Rg – Y bond lengths, respectively; the bond lengths and vibrational frequencies were calculated at the MP2 level of theory in the harmonic approximation.

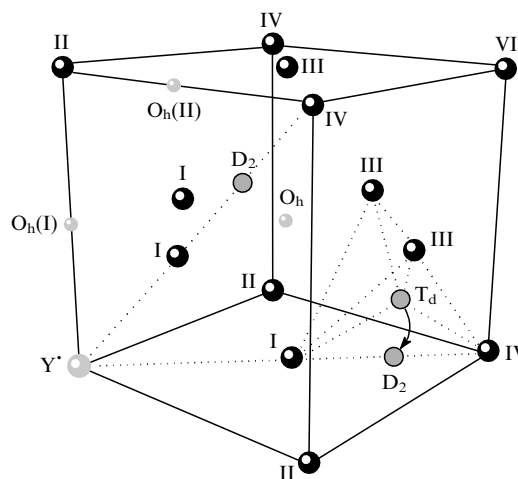
wavelength edge in the electronic absorption spectra are used as the upper limit of the binding energies. The H – Rg – Y particles have rather large intrinsic dipole moments; hence, polarisation interactions between them and the surrounding atoms can strongly affect the spectroscopic and energy characteristics of the intermediate. Therefore, the problem of stability of both free and matrix isolated particles is still to be clarified. Currently, the H – Rg – Y particles have been the subject of intensive research^{107–109} and one can expect to obtain new data on these interesting objects by the time of publication of this review.

The procedure for generation of the H – Rg – Y particles employed in the above-mentioned studies included (i) preparation of thin films of inert gas, containing a controlled amount of HY molecules (e.g., HI, HCl or HCN), (ii) low-temperature photolysis of the impurity molecules, resulting in the formation of spatially separated radical pairs $\text{H}^\bullet \cdots \text{Y}^\bullet$ and (iii) annealing of the matrix up to the temperatures at which thermally activated diffusion of hydrogen atoms is possible. The results of a joint study by IR, optical and EPR spectroscopy showed that the kinetics of loss of the hydrogen atoms correlates with the kinetics of formation of the H – Xe – H and H – Xe – Y molecules.^{83, 107} In the course of the reactions the loss of the stabilised radicals $\text{Y}^\bullet$ amounts to 40%, and virtually no recombination of the molecules of the photolytic precursor HY occurred. With allowance for these facts it was concluded that the three-body interactions $\text{H} + \text{Rg} + \text{H}$ and $\text{H} + \text{Rg} + \text{Y}$, which are responsible for stabilisation of the xenon- and krypton-containing compounds, are the principal channels of loss of the diffusing atoms. Detailed quantitative balance for the reactions of the diffusing atoms has not been determined as yet; however, the results of kinetic measurements suggest that high-energy processes of direct recombination of the radicals,



are inefficient under such conditions due to stabilisation of triatomic intermediates H – Rg – Y.

Quantum-chemical calculations of the PES of a free HRgY particle (in the ground electronic state $^1\Sigma^+$) showed that the reaction can follow two routes as the hydrogen atom approaches the RgY fragment. If the angle of attack, H – Rg – Y, is larger than 90° and the H – Rg distance is shorter than 0.4 nm, the system tends to reach an intermediate bound state with a linear configuration H – Rg – Y. In contrast, if the angle of attack is smaller than 90° , the system tends to arrive at a global minimum corresponding to recombination $\text{H}^\bullet + \text{Y}^\bullet$ (see Refs 103 and 104).

**Figure 9.** The O_h , T_d and D_2 interstitial sites occupied by hydrogen atom in the f.c.c. crystal lattice of an inert gas.

Impurity particle $\text{Y}^\bullet$ occupies the substitutional site. Roman numerals I – IV and VI denote the atoms in the first to fourth and in the sixth coordination spheres of the crystal surrounding the impurity $\text{Y}^\bullet$.

Realisation of a particular reaction channel in the crystal is determined by the trajectory of the motion of the hydrogen atom in the vicinity of the trapped impurity (heavy fragment $\text{Y}^\bullet$). Diffusion of hydrogen atoms in the f.c.c. crystal lattice of inert gas has been traditionally treated as random jumps between octahedral interstitial sites O_h , which occur in such a way that in the intermediate states the H atom is located at the tetrahedral site T_d (Fig. 9). If a heavy fragment of primary photodissociation ($\text{Y}^\bullet$) occupies a lattice site, recombination $\text{H}^\bullet + \text{Y}^\bullet$ should occur when the H atom arrives at a tetrahedral T_d (I) or octahedral site O_h (I) adjacent to the fragment $\text{Y}^\bullet$. The formation of a bound species H – Rg – Y must occur with participation of an Rg(I) atom (one of the twelve lattice atoms in the first coordination sphere of the $\text{Y}^\bullet$ species). Linear structure H – Rg(I) – Y can be formed if the hydrogen atom occupies the interstitial site D_2 . There are several T_d and O_h (II) sites outside the first coordination sphere of the $\text{Y}^\bullet$ fragment (see Fig. 9). Jumping between them, the hydrogen atom arrives at the attraction region on the PES of the triatomic system H – Rg(I) – Y and becomes bound into the intermediate H – Rg(I) – Y. As a consequence, its recombination with the fragment $\text{Y}^\bullet$ is now impossible. If the H atom arrives at other tetrahedral sites T_d surrounding the first coordination sphere of the fragment $\text{Y}^\bullet$, the H – Rg₂(I) – Y configurations comprised of adjacent atoms are formed.

It is known that cations of the type $(\text{HRg}_2)^+$ can be stabilised in low-temperature matrices. Therefore, analogous ionic bonds $(\text{H} - \text{Rg}_2)^+ - \text{Y}^-$ can also be formed in such T_d configurations and these T_d sites can be considered as saddle points for binding the H atom into a more stable linear configuration H – Rg(I) – Y. In this case all trajectories of the H atom, which lead to recombination of fragments, are blocked by the interactions responsible for stabilisation of the intermediate. This treatment demonstrates the necessity of taking into account multibody interactions to gain a deeper insight into the mechanisms of the reactions of diffusing hydrogen atoms with isolated impurity $\text{Y}^\bullet$.

The synthesis of a compound called hydrido argon fluoride, H – Ar – F, in solid argon has been reported.¹¹⁰ Changes in the vibrational frequencies of the stabilised intermediate upon isotope substitutions $\text{H} \rightarrow \text{D}$ and $^{40}\text{Ar} \rightarrow ^{36}\text{Ar}$ are thought to be the most important argument in favour of the formation of the H – Ar and F – Ar bonds. According to quantum-chemical calculations carried out at the CCSD(T)/aug-cc-pVQZ level of theory (see Ref. 111), the energy of HArF is 14.7 kJ mol^{-1} relative to the energy of dissociation into neutral atoms while the barrier to

dissociation is 17.2 kJ mol^{-1} . In addition, calculations predicted a high stability of the intermediate towards internal conversion into neutral systems corresponding to the global potential minimum



Such a conversion can occur involving the bending vibration. The calculated barrier to reaction along the coordinate of the $\text{H}-\text{Ar}-\text{F}$ bending vibration was $\sim 96.4 \text{ kJ mol}^{-1}$.

Taking into account successful stabilisation of chemical compounds $\text{H}-\text{Rg}-\text{Y}$ (see above), one can suggest that the use of experimental methods employed for the synthesis of such compounds will allow detection of new compounds with the atoms of inert gases including light Rg atoms. Calculations predict that the reaction barriers responsible for the intrinsic stability of such intermediates are at most $10\text{--}15 \text{ kJ mol}^{-1}$; therefore, stabilisation of these particles requires operation at temperatures below 20 K . Bondybey *et al.*¹⁰⁸ succeeded in using solid neon for stabilisation of intermediate particles ($\text{H}-\text{Kr}-\text{Br}$) under conditions where thermal diffusion of hydrogen atoms unfreezes at temperatures below 10 K . Low-density solid media (*e.g.*, impurity–helium solid phase, which is stable at temperatures below 10 K) can also be considered as solid matrices suitable for stabilisation of loosely bound compounds of various atoms with the atoms of inert gases.^{112, 113} The morphology of such structures is not known with certainty; however, Boltnev *et al.*¹¹⁴ have demonstrated the possibility of doping solid phases of composition $\text{Rg}(\text{He})_n$ ($\text{Rg} = \text{Ne}, \text{Ar}, \text{Kr}, \text{Xe}; n > 10$) with reactive species.

V. Chemical reactions involving fluorine atoms

Chemical reactions with participation of fluorine atoms have been the subject of intensive basic and applied research.^{115, 116} These reactions are characterised by high exothermicity and low energy barriers (usually, the gas-phase barriers are at most 8 kJ mol^{-1}), which predetermines high reaction rates and the formation of excited products. The matrix isolation technique has been traditionally used for detection and studies of the products of such reactions. Comprehensive reviews of investigations in this field carried out to the late 1980s have been reported by Jacox.^{6, 117} Because of this we will concern ourselves with more recent studies.

1. Translational mobility of fluorine atoms

The unique properties of fluorine atoms produced by photodissociation of F_2 molecules isolated in solid argon or krypton matrices have been reported in the early 1990s. Experiments⁶⁶ showed that the quantum yield of photodissociation of F_2 is close to unity, if the excess energy per atom,

$$\Delta E = \frac{h\nu - D_e(\text{F}_2)}{2},$$

where D_e is the dissociation energy of the F_2 molecule, exceeds 1 eV . As can be seen from Fig. 10, at $\Delta E > 1 \text{ eV}$ the cage effect is insignificant and the efficiency of photodissociation of F_2 in solid argon is close to the efficiency of the corresponding gas-phase process. Photodissociation of F_2 in solid matrices is basically different from the photodissociation of the molecules containing heavy halogens (Cl_2 , ICl , Br_2), since in the latter case the quantum yield is at most 10^{-5} at moderate excess energies ($< 3 \text{ eV}$).^{118–120} The thermalisation length of a ‘hot’ atom F was estimated at $3\text{--}8 \text{ nm}$.⁶⁶

The possibility for a long-range migration of ‘hot’ fluorine atoms to occur was also confirmed by other researchers,¹²¹ though estimates of the thermalisation length were smaller. Using the molecular dynamics simulation, it was shown⁷² that migration of a ‘hot’ atom in the crystal occurs as ballistic motion (*i.e.*, the trajectory of the fluorine atom passes through the lattice interstices) until the first strong collision with the lattice atom. This is due to efficient dissipation of the energy of the ‘hot’ fluorine atom

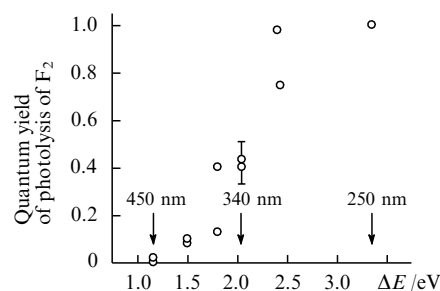


Figure 10. Quantum yield of photodissociation of F_2 molecules isolated in solid argon as a function of excess photon energy.⁶⁶ The arrows denote the characteristic wavelengths of photolysing radiation.

in the interaction with the argon atoms. Yet another feature of the fluorine atoms is that their diffusion mobility unfreezes at temperatures much below the melting (sublimation) temperature of the crystal. Consumption of the fluorine atoms produced by photolysis of F_2 in the crystals of argon and krypton is illustrated in Fig. 11. At concentrations of the order of 10^{17} cm^{-3} , the lifetime of the F atoms stabilised in argon is nearly 10^3 s at 20 K . Kinetic measurements revealed the absence of geminate recombination of the atoms produced by photodissociation of one F_2 molecule.⁶⁶ In the course of diffusion the atoms migrate in the crystal over long distances and the kinetics of loss of the atoms corresponds to bulk recombination

$$\frac{d[\text{F}]}{dt} = -k_d[\text{F}]^2, \quad (12)$$

where $[\text{F}]$ is the volume average of the concentration of the atoms.

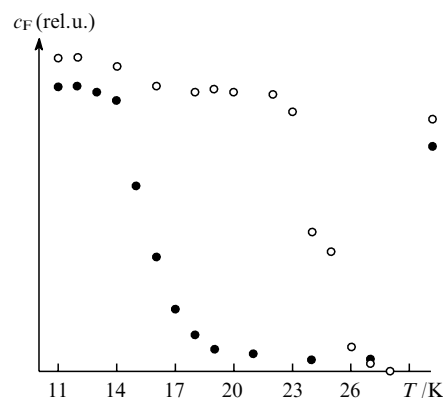
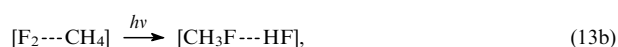


Figure 11. Temperature dependence of the concentration of fluorine atoms (c_F) in argon (1) and krypton (2) crystals.⁶⁶ Heating of samples from 10 K at a rate of $\sim 0.5 \text{ K min}^{-1}$.

2. Reactions of photogenerated ‘hot’ fluorine atoms

As photogenerated ‘hot’ atoms escape the parent cage, they can react with distant molecules of the other reactant. The formation of stabilised radicals generated by low-temperature photolysis of solid $\text{Rg}/\text{F}_2/\text{M}$ mixtures was established in the early studies (see, *e.g.*, Refs 33, 35, 122, 123). However, no reaction channels responsible for the formation of such products were found. The point is that the radical species can be produced both in the interaction of the migrating atom with the isolated impurity molecule, $\text{F} + \text{M}$, and by photolysis of F_2 contained in heterodimers $[\text{F}_2 \cdots \text{M}]$, if the photogenerated atom escapes the cage [see reactions (6a) and (6b)]. However, in a series of studies^{58, 124, 125} it

was shown that photolysis of heterodimers $[F_2 \cdots M]$ results in predominant formation of molecular (closed-shell) products. Therefore, the emphasis was placed on studies of hydrogen-bonded molecular complexes generated in photoinduced reactions



In our joint investigations carried out in collaboration with Prof. C Wight (University of Utah, USA) we succeeded in distinguishing between the reaction channels associated with the formation of molecular and radical products in such systems.^{20, 21} Figure 12 presents the kinetic curves of consumption of the reactants and of accumulation of the products during photolysis of Ar/F₂/CO mixtures prepared using a conventional matrix isolation technique. Exponential fit of the kinetic curves of consumption of the CO molecules and binary complexes $[F_2 \cdots CO]$ in the course of continuous photolysis shows a nearly twofold difference in the rates of the processes. The rate of accumulation of the F₂CO molecules equals the rate of consumption of the $[F_2 \cdots CO]$ complexes, whereas an increase in the concentration of the FCO[•] radicals correlates with consumption of isolated CO molecules. Spectral and kinetic studies of the reactants and reaction products revealed two principal reaction channels with participation of photogenerated fluorine atoms:

(1) reaction in the complex of reactants



(2) reaction of a 'hot' F* atom with an isolated CO molecule



Analysis of changes in the band intensities in the IR spectra of the reactants and reaction products showed that the mass balance for consumption of complexes $[F_2 \cdots CO]$ and accumulation of F₂CO is kept constant within the limits of experimental error ($\pm 10\%$). This means that photolysis of complexes of the reactants causes no exit of the fluorine atoms from the reaction cage; rather, they react with the neighbouring CO molecule. Only $\sim 3\%$ of the CO molecules in the samples of composition Ar:F₂:CO =

1000:1:1 undergo conversion into the FCO[•] radicals following reaction (16). The proportion of binary complexes $[F_2 \cdots CO]$, which produce the F₂CO molecules in reaction (14), is $\sim 7\% - 10\%$ of the total amount of CO molecules. Thus, the amount of molecular products of the cage reaction exceeds the amount of radicals generated in the reactions of the migrating 'hot' fluorine atoms by a factor of 2 to 3. This product ratio remains unchanged for the samples of various compositions (at x_{F_2} and $x_{CO} < 10^{-3}$), since the amounts of the radical products and $[F_2 \cdots CO]$ complexes vary in proportion to the concentrations of F₂ and CO in the sample. Analogous measurements were also carried out in argon crystals doped with F₂ and CO molecules.²¹ The principal channels of the reactions of photogenerated atoms in the crystal and in the argon matrix were found to be similar. However, a basic difference between them is that the yield of radicals in reaction (16) in the crystal was 10 to 15 times higher than in the matrix at equal initial concentrations of the reactants in the samples.

The ratio of the amount of radicals produced to the initial amount of F₂ molecules in the sample was used^{20, 21} as a measure of the efficiency of reaction (16) between the migrating F* atoms and the isolated molecules. If the relative concentration of the molecules of the second reactant, x_m , is less than 10^{-2} , this ratio increases in proportion to x_m for all the systems studied

$$\frac{[R]}{[F_2]_0} = Kx_m, \quad (17)$$

where K is the coefficient characterising the yield of stabilised radicals in the reactions of photogenerated fluorine atoms with impurity molecules in the solid argon matrix.

The coefficient K determined from the concentration dependencies for reactions of F* atoms with CO molecules in an argon matrix was found to be 27 ± 8 . Analogous measurements in argon crystals gave a much larger value, 340 ± 120 . Even with allowance for the error of measurements the efficiency of the reaction of 'hot' fluorine atoms in argon crystal is more than an order of magnitude higher than in the matrix.

The coefficient K characterises the number of lattice atoms which are 'surveyed' by two migrating, photogenerated fluorine atoms (in order to react with impurity molecule). This value must depend on both the mean thermalisation length, $\langle l \rangle$, and the reaction cross-section, σ_m . The reaction of the thermalised atom with the nearest environment should also be taken into account. If migration occurs in the ballistic regime up to the first strong collision followed by thermalisation⁷² (provided a uniform distribution of reactants over the sample), the yield of radicals can be evaluated from the simple expression

$$\frac{[R]}{[F_2]_0} = (2\sigma_m \langle l \rangle N_0 + 2Z)x_m, \quad (18)$$

where N_0 is the density of atoms in the argon crystal and $Z = 6$ is the coordination number for the O_h interstitial site in the crystal.

According to Eqn (18), the maximum value, $K(\text{matrix}) \simeq 50$, corresponds to a mean thermalisation length of the atom of $\langle l \rangle \simeq 1.5$ nm, or nearly three lattice constants of the argon crystal. A higher yield of radicals in the crystal can be due to a much larger $\langle l \rangle$ value compared to the matrix. The mean thermalisation length in the crystal estimated from the experimental $K(\text{crystal})$ value is as long as 17 nm. Expression (18), as applied to the atomic dynamics in the solid phase, is not rigorous since the atom moves in the crystal field and continuously loses its energy. Therefore, these $\langle l \rangle$ values should be treated as estimates. Nevertheless, they are in agreement with the results of earlier studies in which different scales for migration of 'hot' atoms in argon crystals and in solid matrices were obtained.^{66, 121} The relatively low reactivity of such atoms in the matrix can be rationalised by shortening of the thermalisation length due to the small size of crystallites and to high concentration of defects. Taking into

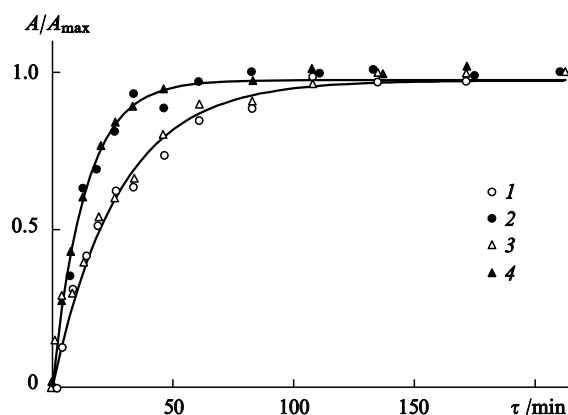


Figure 12. Kinetic curves of consumption of CO molecules (1) and $[F_2 \cdots CO]$ binary complexes (2) and those of accumulation of reaction products for FCO[•] radicals (3) and F₂CO molecules (4) during continuous photolysis of a ternary sample (Ar:F₂:CO = 2000:1:1) with light ($\lambda = 355$ nm) at 16 K.²⁰

The experimental band intensities were normalised to their values after 215 min of photolysis. The curves denote exponential fits to the experimental data.

account the mass ratio of the F and Ar atoms, one can suggest that the fluorine atom with an initial energy of ~ 1 eV must undergo thermalisation after 1–3 successive collisions with the lattice atoms. Without considerable loss of energy the ‘hot’ atom can migrate in the crystal only by moving along specific trajectories passing through the interstices of the crystal lattice, thus avoiding strong collisions with the lattice atoms. Only in this case can the migration length of a ‘hot’ atom be as long as ~ 10 nm,⁷² the lattice defects being a ‘heat sink’ for the excess energy of the atom, thus accelerating its thermalisation in the matrix.

Table 4 lists the K values measured in an argon matrix for the reactions of ‘hot’ fluorine atoms with various molecules. The most efficient is the interaction of such atoms with small diatomic molecules; the interaction with large molecules (*e.g.*, C_2H_2 or C_2H_4) is 2 to 3 times less efficient. Hydrogen abstraction reactions are characterised by the smallest K values. In contrast to nearly barrierless reactions of addition to diatomic molecules O_2 , CO , NO (energy barriers to these reactions in the gas phase are at most 2 kJ mol⁻¹), the barriers to hydrogen abstraction from NH_3 , CH_3 and H_2 molecules in the gas phase vary from 4 to 7.5 kJ mol⁻¹. An important factor, which also reduces the probability for the ‘hot’ atom to react, is high stereospecificity of the hydrogen abstraction reactions in which the atom must attack the molecule along the C–H bond (collinear collision).

Table 4. Values of K coefficient in formula (17).

Reaction	Products	K	Measuring technique
F + O ₂	FO ₂ [•]	45 ± 13 29 ± 8	IR spectroscopy EPR
F + CO	FCO [•]	27 ± 8 19 ± 5	IR spectroscopy EPR
F + NO	FNO	24 ± 7	IR spectroscopy
F + O ₃	FO ₃ [•]	22 ± 7	"
F + C ₂ H ₂	2-C ₂ H ₂ F [•]	15 ± 4	"
F + C ₂ H ₄	2-C ₂ H ₄ F [•]	11 ± 3	EPR
F + NH ₃	H ₂ N [•] ---HF	3.8 ± 1.0	IR spectroscopy
F + CH ₄	H ₃ C [•] ---HF	1.8 ± 0.5	EPR
F + H ₂	H [•] ---HF	0.9 ± 0.3	"

3. Reactions of diffusing fluorine atoms

Thermally activated chemical reactions in thin argon films doped with fluorine atoms and molecules of the second reactant have long been observed (see Refs 6 and 117). Transformations observed were explained by unfreezing of the local mobility of the atoms at high temperatures. More recent studies revealed a key feature of the diffusing atoms, namely, the absence of geminate recombination of photogenerated atoms and the ability of such atoms to diffuse over long distances in crystals and argon matrices.^{65,66} In this case chemical reactions of mobile atoms are limited to their bulk recombination [see Eqn (2a)]. Assuming a uniform distribution of molecules throughout the sample, the kinetics of processes can be described using the volume averaged concentrations of reactants and the rate constants for bimolecular reactions (2a) and (2b). In the framework of this approach the efficiency of reactions of diffusing atoms can be characterised by the ratio of the concentration of radicals produced to the initial concentration of atoms¹²⁶

$$\frac{[R]_{\max}}{[F]_0} \cong \frac{k_r}{k_d} \frac{[x_m]_0}{[F]_0} \ln \left(1 + \frac{k_d}{k_r} \frac{[F]_0}{[x_m]_0} \right), \quad (19)$$

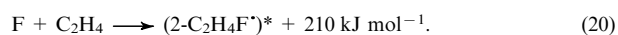
which is in turn determined by the ratio of the initial concentrations of the reactants, $[F]_0/[x_m]_0$, and by the ratio of the rate constant for reaction (2b) to the rate constant for recombination of atoms (2a), k_r/k_d . The k_r/k_d ratios for various reactions are

Table 5. The k_r/k_d ratios for reactions of thermal fluorine atoms in an argon matrix at 26 K. (The recombination constant of F atoms is $\sim 2 \times 10^{-21}$ cm³ s⁻¹ at 26 K.)

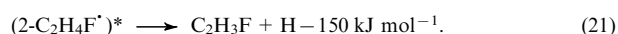
Reaction	k_r/k_d	Measuring technique
F + CO	0.4–0.6 0.35–0.45 0.45–0.6	IR spectroscopy EPR IR spectroscopy in crystal
F + O ₂	0.6–0.8 0.5–0.65	IR spectroscopy EPR
F + C ₂ H ₄	0.2–0.3 0.15–0.25	IR spectroscopy EPR
F + NH ₃	0.02–0.03	"
F + CH ₄	0.001–0.002	"
F + H ₂	0.0003–0.001	"

listed in Table 5. As can be seen, the values of this parameter vary by three orders of magnitude. The O₂ and CO molecules are the most efficient scavengers of diffusing atoms. The rate constants for the reactions with these molecules are close to the rate constant for recombination of the atoms. The smallest k_r/k_d values were obtained for the reactions of hydrogen abstraction from the CH₄ and H₂ molecules.

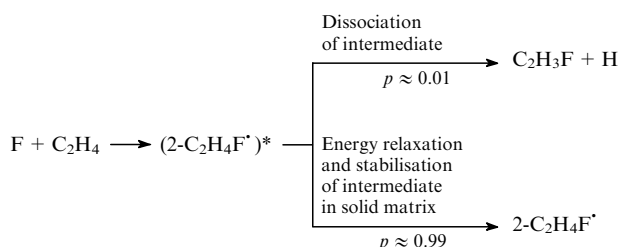
An example illustrating the efficiency of stabilisation of the reactive intermediate in the matrix is provided by the interaction F + C₂H₄, resulting in addition of fluorine at the double bond of ethylene and the formation of a vibrationally excited radical



In the gas phase the radical dissociates in $\sim 10^{-9}$ s (see Ref. 127)



Stabilisation of 2-C₂H₄F[•] in the matrix requires transfer of an energy of ~ 60 kJ mol⁻¹ into the matrix, the transfer time being shorter than the dissociation time. In contrast to the gas-phase reaction, the reaction of diffusing fluorine atoms in solid argon results in stabilised intermediate as the major product.^{39,128,129}



p is the reaction channel probability.

High resolution of the HFS in the EPR spectra of isolated radicals 2-C₂H₄F[•] allowed detailed analysis of the spectra and determination of the character of internal motions in the stabilised radical. Eight vibrational frequencies of this radical were first determined by IR spectroscopy.¹²⁹

New reactive intermediates generated in solid-phase reactions of mobile fluorine atoms are considered below.

4. Radical – molecular complexes R[•]---HF

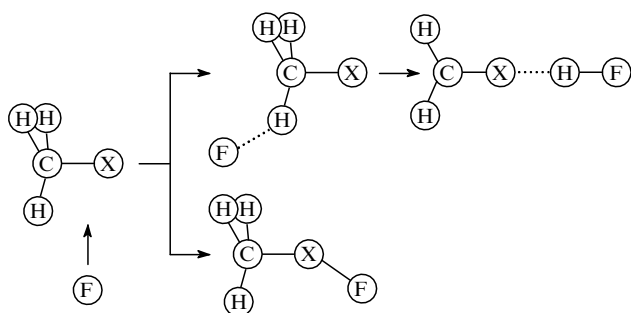
According to published data obtained from studies in the gas phase and from quantum-chemical calculations, most hydrogen abstraction reactions



occur in a collinear complex where the fluorine atom attacks the reactant molecule along the R–H bond.^{130,131} No bound intermediate states of such reactions were observed earlier, though the possibility for them to exist in the vicinity of the transition state both in the product and the reactant valleys was discussed in the literature. Different ways of trapping the products of chemical

reactions (22) in low-temperature matrices have been considered.¹¹⁷ It was pointed out that stabilisation of the bound state of products, $R^{\bullet} \cdots HF$, can be achieved only if the solid-phase reaction is carried out. Information on such complexes provided by IR spectroscopy is insufficient. High-frequency vibrations of radicals change only slightly upon binding into complexes, while the frequencies of characteristic intermolecular vibrations in the complexes appear in the region below 300 cm^{-1} and are unavailable for conventional measuring techniques. The frequency shift of the HF stretching vibration (difference between the frequency in complex and the vibrational frequency of isolated HF molecule) can be indicative of binding the molecule into complex. However, it provides only qualitative information on the binding energy of the complex.

The possibility of stabilisation of pre-reaction complexes $F \cdots RH$ was shown taking low-temperature co-condensation of fluorine atoms and CH_3X ($X = Cl, Br, I$) molecules in excess of argon as an example. The processes with participation of these reactants, occurring in the solid matrix, can be schematically depicted as follows:¹³²



Complexes $H_3CX \cdots F$ are the major products. Weak additional satellite IR bands characterised by small frequency shifts relative to the intense bands of isolated CH_3X molecules were assigned to the pre-reaction complexes $F \cdots HCH_2X$. No reactions with participation of CH_3X in the ground electronic state were observed; however, photolysis of the samples by visible light ($\lambda > 420\text{ nm}$) led to disappearance of complexes $F \cdots HCH_2X$ and production of complexes $H_2XC' \cdots HF$. The experimental HF vibrational frequencies in a number of related radical – molecular complexes isolated in a solid argon matrix are listed in Table 6. This seems to be the only spectroscopic characteristic of intermediates obtained under such experimental conditions by IR spectroscopy.

Table 6. HF stretching vibration frequencies (cm^{-1}) of complexes $R^{\bullet} \cdots HF$ and $M \cdots HF$ trapped in a solid argon matrix. (The stretching vibration frequency of HF molecule trapped in a solid argon matrix is 3916 cm^{-1}).

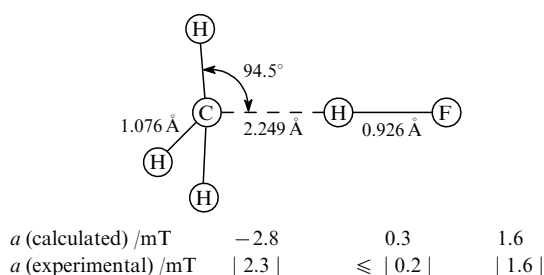
Complexes	Frequency	Ref.
$NC^{\bullet} \cdots HF$	3753	133
$HC_2^{\bullet} \cdots HF$	3756	133
$H_2FC^{\bullet} \cdots HF$	3854	134
$H_3C^{\bullet} \cdots HF$	3764	24, 135
$H_2N^{\bullet} \cdots HF$	3267	47
$HF \cdots HF$	3825	136
$HCN \cdots HF$	3626	137
$H_3N \cdots HF$	3041	138

A radical – molecular complex $H_3C^{\bullet} \cdots HF$ was stabilised in solid argon and identified by IR spectroscopy as an intermediate of the reaction $F + CH_4$.¹³⁵ Experiments with isotope substitution of the reactants ($CH_4 \rightarrow CD_4$) permitted the determination of the HF vibrational frequency (3764 cm^{-1}) and the frequency of the CH_3 out-of-plane vibration (664 cm^{-1}) in the complex. Both vibrations in the complex are characterised by rather large

frequency shifts relative to the frequencies of the corresponding vibrations of isolated HF molecule and $CH_3^{\bullet}$ radical (3916 and 619 cm^{-1} , respectively).

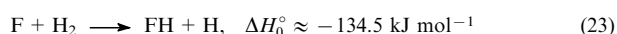
The assignment of these frequencies to complexes $H_3C^{\bullet} \cdots HF$ generated in the reactions of diffusing fluorine atoms with CH_4 molecules in solid argon was confirmed in more recent IR and EPR studies.^{24, 126}

Using the EPR technique it was found that reactions of ‘hot’ fluorine atoms with isolated CH_4 molecules result in isolated radicals $CH_3^{\bullet}$ as the major product (quartet of HFS lines with the splitting $a_H = 2.3\text{ mT}$). The reactions of diffusing fluorine atoms give a product characterised by a sixteen-component EPR spectrum. Each component of the HFS of radical $CH_3^{\bullet}$ is additionally split into four components due to interaction between the unpaired electron and the magnetic nuclei of the HF molecule ($a_F = 1.6\text{ mT}$, $a_H \leq 0.2\text{ mT}$). The structure of free complex $H_3C^{\bullet} \cdots HF$ corresponding to the bound state on the PES in the product valley has been calculated.²⁵



According to calculations, the complex has a collinear configuration of C_{3v} symmetry and a binding energy of $\sim 8.4\text{ kJ mol}^{-1}$. The frequency of intermolecular vibration in the complex is 125 cm^{-1} while the frequency of the H–F vibration in the complex is $\sim 130\text{ cm}^{-1}$ lower than in the free molecule. The calculated IHFC constants of the complex are in good agreement with the experimental values. The IHFC constants of the F and H atoms dramatically decrease upon small variations of orientation of the HF molecule relative to the equilibrium configuration. Therefore, it was concluded that most of the reaction products are stabilised in the form of collinear complex $H_3C^{\bullet} \cdots HF$. This lattice-stabilised complex of reaction products retains the symmetry of the transition state of the reaction.

Gas-phase chemical reaction



has been the subject of numerous studies aimed at investigating the reaction dynamics in elementary chemical processes (see, *e.g.*, Refs 139–141). Quantum-chemical calculations¹⁴² predicted a collinear configuration of complex $H^{\bullet} \cdots HF$ in the output channel of the reaction. The authors¹⁴² pointed out that the presence of such a bound state in the product valley affects the angular and energy distribution of the end reaction products. Complex H_2F produced in the reactions of diffusing fluorine atoms with H_2 molecules was first studied experimentally in solid argon by EPR spectroscopy.¹⁴³ Two bound configurations of the complex were shown to exist. Their relative concentrations vary in the temperature range from 10 to 30 K due to hindered internal rotation of the HF molecule. Temperature dependence of the shape of the EPR spectra was described using a model with allowance for exchange between the energetically inequivalent configurations of the complexes $A \rightarrow B$ and $B \rightarrow A$. The IHFC on ^{19}F and ^1H nuclei of the HF molecule were found to be $a_F = 3.2$ and $a_H < 0.1\text{ mT}$ for complex A and $a_F = 0.5$ and $a_H \approx 0.4\text{ mT}$ for complex B. Complex B appears to be more stable, since its contribution to the EPR spectrum increases as the temperature decreases.

Figure 13 presents the isolines of the constants of IHFC with the nuclei of fluorine atoms of the HF molecule calculated for different configurations of the complex. The experimental IHFC a_F and a_H of complex B are consistent with collinear configura-

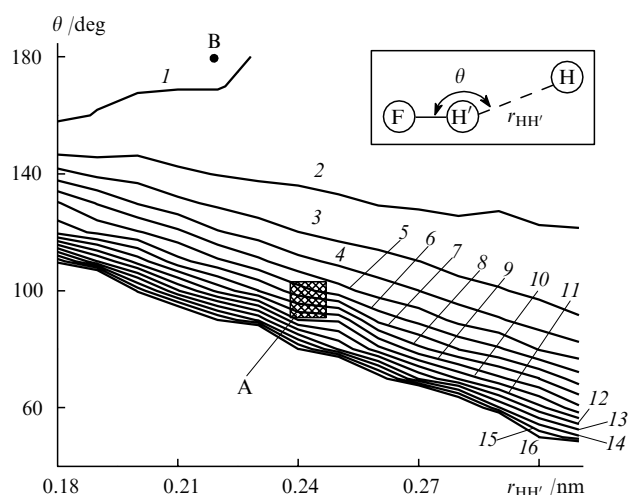


Figure 13. Isolines of IHFC constants on the ^{19}F nucleus in radical–molecular complex $\text{H}'\cdots\text{HF}$ obtained from B3LYP/aug-cc-pVTZ calculations.

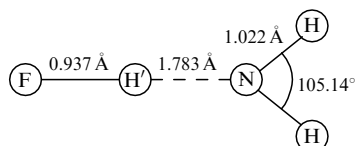
The regions corresponding to the measured IHFC constants are labelled A and B; -0.46 (1), -0.05 (2), 0.27 (3), 0.75 (4), 1.82 (5), 2.33 (6), 2.70 (7), 2.83 (8), 2.92 (9), 3.16 (10), 3.44 (11), 4.07 (12), 4.39 (13), 4.49 (14), 4.70 (15) and 4.71 (16).

tion $\text{H}'\cdots\text{HF}$ with a $r_{\text{HH}'}$ distance of 0.22 nm, which corresponds to a local minimum in the product valley on the PES of the reaction.¹⁴² The nature of the second configuration of the complex (A) is still unknown. The experimental IHFC constants of this complex are in agreement with the calculated IHFC constants for a bent configuration $\text{H}'\cdots\text{H}-\text{F}$ characterised by the angle $\theta \approx 100^\circ$ and the distance $r_{\text{HH}'} = 0.24$ nm. We were unable to find in the literature reliable computational data that would help to decide between the presence or absence of the bound state on the PES in this region of geometric parameters of the system.

Interest in gas-phase reaction



was due to attempts at implementing the process in gas lasers to create an inverse population of rovibrational states of HF molecules. However, no inverse population could be created despite the high exothermicity of the reaction.^{144, 145} The existence of a strongly bound complex in the output channel of the reaction was predicted theoretically and discussed in the literature based on indirect gas-phase kinetic data.¹⁴⁶ Complex $\text{H}_2\text{N}'\cdots\text{HF}$ was first stabilised in solid argon as a product of reactions of mobile fluorine atoms with NH_3 molecules.^{46, 47, 147} Table 7 lists the spectroscopic characteristics of the complex, obtained by EPR and IR spectroscopy as well as the results of quantum-chemical calculations, which predict that the free complex has a planar structure of C_{2v} symmetry



The $\text{N}\cdots\text{H}'$ binding energy in the complex is 51.5 kJ mol^{-1} . Comparison of the experimental and calculated vibrational frequencies and IHFC constants reveals good agreement between them. The calculated binding energy of the complex is comparable with those of strongly bound hydrogen-bonded molecular complexes (*e.g.*, $\text{H}_3\text{N}\cdots\text{HF}$). This conclusion is confirmed by the IR spectrum of the complex: a large shift of the HF vibrational frequency and intense librations with frequencies lying between ~ 800 and 900 cm^{-1} (see Table 7) are characteristic of the

Table 7. Calculated and experimental vibrational frequencies and IHFC constants of radical–molecular complex $\text{H}_2\text{N}'\cdots\text{HF}$.⁴⁷

Parameter (vibration)	Calculated ^a	Experimental
Vibrational frequency / cm^{-1}		
$1a_1$ (HF stretching)	3486	3267
$2a_1$ (NH_2 stretching symmetrical)	3401	—
$3a_1$ (NH_2 scissoring)	1527	1512
$4a_1$ (NH' intermolecular)	257	—
$1b_2$ (NH_2 stretching asymmetrical)	3497	3211
$2b_2$ (HF in-plane libration)	860	797
$3b_2$	221	—
$1b_1$ (HF out-of-plane libration)	817	791
$2b_1$	280	—
IHFC constant / mT		
a_{N}	1.15	$ 1.20 $
a_{F}	-0.70	$ 0.70 $
a_{H}	-2.30	$ 2.40 $
$a_{\text{H}'}$	0.02	$< 0.05 $

^a Obtained from B3LYP/EPR-III calculations in the harmonic approximation.

complexes with the binding energies of $\sim 50\text{--}70 \text{ kJ mol}^{-1}$. According to quantum-chemical calculations, even small distortions of the geometry of the complex must cause significant changes in the IHFC constants. Taking into account the results of geometry optimisation and the arrangement of the complex at the substitutional site of the argon lattice, it was concluded that the geometry of the complex stabilised in solid argon is similar to that calculated for free complex (Fig. 14).

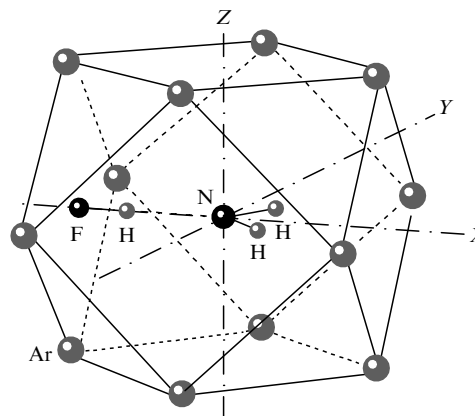


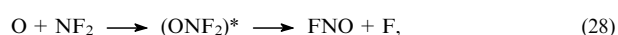
Figure 14. Arrangement and equilibrium geometry of radical–molecular complex $\text{H}_2\text{N}'\cdots\text{HF}$ in the argon crystal lattice.⁴⁷ Shown are twelve nearest Ar atoms.

5. Radical $\text{F}_2\text{NO}^\bullet$

Fox *et al.*^{148, 149} postulated the formation of a radical species $\text{F}_2\text{NO}^\bullet$ in the synthesis of F_3NO molecules



Vibrationally excited radical $\text{F}_2\text{NO}^\bullet$ was considered¹⁵⁰ as an intermediate species in other chemical reactions, *e.g.*,



$$\Delta H_0^\circ \approx -277 \text{ kJ mol}^{-1}.$$

Attempts at detecting this species experimentally in the elementary reactions (25)–(27) failed. The EPR spectra of radical $\text{F}_2\text{NO}^\bullet$ were obtained in the experiments on radiolysis of solid F_3NO .¹⁵¹ This species was stabilised in solid argon (radical was generated in successive reactions of diffusing fluorine atoms with isolated NO molecule).^{152, 153} IR and EPR spectroscopic studies revealed that in the temperature range 17–35 K the radical $\text{F}_2\text{NO}^\bullet$ exists in dynamic equilibrium with the pre-reaction complex $\text{F} \cdots \text{FNO}$



At high temperatures, the equilibrium is shifted to the right, while at low temperatures it is shifted to the left. The enthalpy and entropy of direct reaction (28) determined using a linear approximation of the temperature dependence of the experimental equilibrium constant are respectively

$$\begin{aligned} \Delta H &= 1240 \pm 180 \text{ J mol}^{-1}, \\ \Delta S &= 62 \pm 10 \text{ J mol}^{-1} \text{ K}^{-1} \end{aligned} \quad (30)$$

per mole of reactants isolated in solid argon. This indicates that the formation of the second N–F bond in radical $\text{F}_2\text{NO}^\bullet$ in the solid-phase reaction is an endothermic process. At the same time the formation of this radical is accompanied by a substantial increase in entropy. It is the large positive entropy of reaction (29) that plays a key role in stabilisation of a high equilibrium concentration of radicals upon warm-up of the system when $T\Delta S > \Delta H$. Radicals $\text{F}_2\text{NO}^\bullet$ can also be detected at $T < 20 \text{ K}$, since the characteristic time of their dissociation at these temperatures exceeds 10 h.

A feature of the electronic structure of radical $\text{F}_2\text{NO}^\bullet$ is that it is characterised by low energy of the N–F bond and a rather high N–F stretching vibration frequency ($> 700 \text{ cm}^{-1}$). Because of this, reasonable agreement between the calculated and experimental vibrational frequencies can be obtained only using computational methods with correct inclusion of configuration interactions [QCISD(T)].¹⁵³ According to calculations, the N–F bond dissociation energy is merely $\sim 10 \text{ kJ mol}^{-1}$. However, the formation of $\text{F}_2\text{NO}^\bullet$ in solid-phase reaction (29) is endothermic (by 1.2 kJ mol^{-1}). Direct comparison of these two values is impossible, since the initial reactant in the solid-phase reaction was the bound complex $\text{F} \cdots \text{FNO}$, whereas the bond dissociation energy was calculated relative to the noninteracting reactants F and FNO. In addition, one should take into account the interaction of the reactants with the atoms of the argon lattice, which must be different for complex $\text{F} \cdots \text{FNO}$ and radical $\text{F}_2\text{NO}^\bullet$.

6. Complex $\text{FO} \cdots \text{O}_2$

Asymmetric chlorine trioxide $\text{ClO}_3^\bullet$ was postulated^{154, 155} as a reactive intermediate and unstable product of photodecomposition of ozone by chlorine. However, it is impossible to draw unambiguous conclusions about the stability of such intermediates based on the results of quantum-chemical calculations.¹⁵⁶ The assumption of the existence of a bound particle FO_3 was never made in the experimental and theoretical studies of fluorine oxides $\text{FO}^\bullet$, $\text{FOO}^\bullet$, FOF , OFO and FOOF . It was found that a product of the reaction $\text{F} + \text{O}_3$ in photolysed solid $\text{Ar}/\text{F}_2/\text{O}_3$ mixtures is characterised by two intense IR bands at 968 and 1522 cm^{-1} in the region of the vibrational frequencies of FO and O_2 , respectively.¹⁵⁷ In the experiments with ^{18}O -enriched ozone these bands were assigned to the F–O and O–O vibrations of reactive intermediate $\text{F} \cdots \text{O} \cdots \text{O} \cdots \text{O}$. Based on the results of kinetic measurements and spectroscopic data, it was concluded that reactions of translationally excited and diffusing fluorine atoms with O_3 molecules result in a highly reactive complex $\text{FO} \cdots \text{O}_2$. However, at present the results of quantum-chemical calculations

prevent us from drawing unambiguous conclusions about the nature of chemical bonding and the geometry of the complex.

7. Structural isomers of $[\text{HFCN}]^\bullet$

The possibility of the existence of two structural isomers in radical systems containing the CN group (*e.g.*, $\text{H}_2\text{C}=\text{N}^\bullet$ and $\text{HC}^\bullet=\text{NH}$, $\text{F}_2\text{C}=\text{N}^\bullet$ and $\text{FC}^\bullet=\text{NF}$, $\text{HFC}=\text{N}^\bullet$ and $\text{FC}^\bullet=\text{NH}$) was predicted by numerous quantum-chemical calculations.^{158–160} However, detailed experimental studies were carried out only for π -radicals $\text{H}_2\text{C}=\text{N}^\bullet$ and $\text{F}_2\text{C}=\text{N}^\bullet$ (see, *e.g.*, Refs 161–165). Therefore, quantum-chemical calculations of the structure and properties of such types of radicals are well substantiated experimentally. Until recently, almost no data on free σ -radicals $\text{HC}^\bullet=\text{NH}$, $\text{FC}^\bullet=\text{NF}$, $\text{FC}^\bullet=\text{NH}$ were available. It was assumed^{162, 163, 166} that radicals $\text{HC}^\bullet=\text{NH}$ and $\text{FC}^\bullet=\text{NF}$ can be the secondary products of photolysis of solid mixtures $\text{Ar}/\text{HI}/\text{HCN}$ and $\text{Ar}/\text{trans-N}_2\text{F}_2/\text{FCN}$. The band at 886 cm^{-1} in the IR spectrum was assigned to radical $\text{HC}^\bullet=\text{NH}$ while the band at 1053 cm^{-1} was assigned to radical $\text{FC}^\bullet=\text{NF}$. This assignment is tentative, since it is to a great extent based on the experience and professional intuition of researchers.

Recent EPR and IR spectroscopic studies^{167, 168} allowed the conditions for stabilisation of radical conformers $\text{HFC}=\text{N}^\bullet$ and $\text{FC}^\bullet=\text{NH}$ in solid argon to be determined for the first time. It was shown that a π -radical is generated in the reaction of diffusing fluorine atoms



while radical $\text{FC}^\bullet=\text{NH}$ is produced in the solid matrix as a result of photoinduced conversion of stabilised radical $\text{HFC}=\text{N}^\bullet$



Selective excitation to the absorption band of the $\tilde{\text{X}}^2\text{A}' \rightarrow \tilde{\text{A}}^2\text{A}''$ electronic transition of radical $\text{HFC}=\text{N}^\bullet$ causes a complete conversion of this species into the other structural isomer. The resolved EPR spectra of both structural isomers are shown in Fig. 15. Based on the results of kinetic measurements and analysis of the absorption and fluorescence spectra of

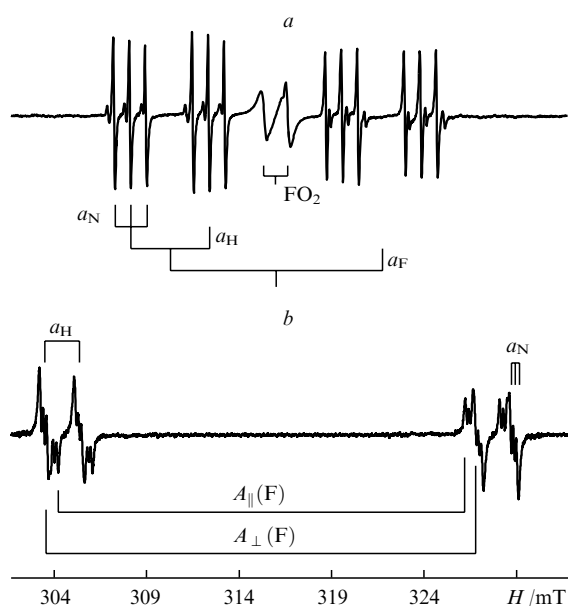


Figure 15. EPR spectra of $\text{HFC}=\text{N}^\bullet$ (a) and $\text{FC}^\bullet=\text{NH}$ (b) radicals stabilised in solid argon at 35 K.¹⁶⁹

The radical was produced in the reactions of diffusing fluorine atoms with HCN molecules (a); the radical was generated by photolysis of trapped $\text{HFC}=\text{N}^\bullet$ radicals with light at $\lambda = 450\text{--}490 \text{ nm}$ (b). Shown are the HFS of the spectra of the radicals.

HFC=N* and DFC=N*, it was concluded that irreversible reaction (32) is due to intramolecular tunnelling of hydrogen atoms on the PES of the electronically excited state.^{169,170} The structure of these species was determined by comparing the calculated and experimental spectroscopic characteristics (a complete set of vibrational frequencies and IHFC constants).

VI. Chemical reactions involving oxygen atoms

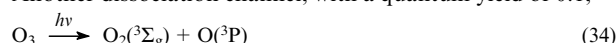
Chemical reactions with participation of oxygen atoms in cryogenic matrices were mostly investigated in order to study the elementary processes initiated by photolysis of ozone molecules. In particular, it was found that the O₃ molecule is an efficient photolytic precursor for generation of oxygen atoms. In the text below we will consider the following aspects of these studies: the behaviour of photogenerated oxygen atoms in inert matrices, photochemical reactions in isolated molecular complexes [O₃–M] and chemical transformations initiated by photolysis of ozone in solid O₃ and O₂.

1. Oxygen atoms in solid matrices and crystals of inert gases

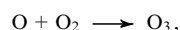
Photolytic generation of oxygen atoms in solid matrices has been studied in the course of photodissociation of isolated molecules O₃, O₂ and N₂O. In the gas phase excitation of O₃ molecules by light to the Hartley absorption band, X¹A₁ → 1¹B₂, causes generation of a singlet oxygen atom with a quantum yield of 0.9



Another dissociation channel, with a quantum yield of 0.1,

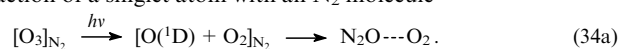


arises due to interception of the excited term 1¹B₂ with the dissociative term that correlates with the ground state of the ozone molecule. UV-Photolysis of ozone in solid argon occurs with a low quantum yield (~10^{−1}–10^{−3}) due to a strong cage effect.^{171–173} The quantum yield of photolysis of ozone monomers in solid argon as a function of temperature is presented Figure 16. A dramatic weakening of the cage effect with an increase in temperature was rationalised by an increase in the amplitude of the O₃ librations at the lattice site.¹⁷¹ The quantum yield of photolysis of ozone in solid xenon is close to unity. However, nearly 80% of the stabilised atoms recombine with the neighbouring oxygen molecules after warm-up to 30–40 K.¹⁷⁴ Other atoms react with distant dioxygen molecules or undergo bulk recombination. By analysing the kinetics of geminate recombination

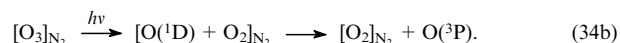


it was concluded¹⁷⁴ that the thermalisation length of ‘hot’ oxygen atoms (~0.2 nm) is comparable with the binding distance between the diffusing atom and the dioxygen molecule. The weak influence of the cage effect on photodissociation of ozone was rationalised by the fact that the effective radius of the interaction R_g–O(¹D) is much smaller than that of the interaction R_g–O(³P).^{71,175} Therefore, ozone molecules are considered as

convenient photolytic precursors for generation of reactive oxygen atoms, O(¹D), in low-temperature matrices.^{173,176,177} For instance, the formation of N₂O in the photolysis of ozone molecules in solid nitrogen¹⁷⁷ is energetically possible only in the reaction of a singlet atom with an N₂ molecule

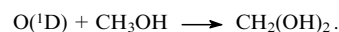


Another channel of O₃ photolysis causes stabilisation of the O(³P) atom outside the reaction cage



The mass-balance equation for the reaction products showed¹⁷⁷ that the formation of one N₂O molecule in reaction (34a) ‘costs’ a total of fifteen dissociated O₃ molecules. The fact that the N₂O molecules are formed only in complexes with O₂ unequivocally indicates that reaction (34a) occurs with participation of the N₂ molecules surrounding the ozone molecule and that the oxygen atoms outside the parent cage do not react with distant nitrogen molecules. At the same time a value of 0.7 was reported¹⁷⁶ for the quantum yield of O₃ photodissociation in a solid nitrogen matrix at 10 K. Taking into account the results obtained by Schriver-Mazzuoli *et al.*,¹⁷⁷ this means that the main process is exit of the ‘hot’ atom from the cage followed by stabilisation of the O(³P) atom [reaction (34b)]. If the atom does not escape the parent cage, either the O + O₂ recombination or ‘concerted’ reaction (34a) with participation of the oxygen atom and O₂ and N₂ molecules occur. Therefore, the efficiency of reaction (34a) should be compared with that of the competing reaction of inverse recombination to the cage. Comparison of the data reported in Refs 176 and 177 suggests that the ratio of yields of these reactions is ~1 : 6.

In the example just considered the reaction involved the O(¹D) atom located within the parent cage. Chemical reactions of photogenerated atoms O(¹D) outside the cage were discovered in studies of photolysis of ternary mixtures Ar/O₃/hydrocarbon.^{178,179} In particular, it was shown that the main channel of the reaction of the O(¹D) atom with methane and methanol molecules is insertion of this atom into the C–H bond, which causes stabilisation of the reactive intermediates:



These results supported the effect of insertion of the oxygen atom into the C–H bond, which was reported earlier.^{180,181} The results of recent studies of the O + CH₄ interaction in molecular beams and analysis of its dynamics in the framework of the Rice–Ramsperger–Kassel–Markus (RRKM) statistical theory showed that the end products (mostly CH₃ + OH and CH₂O + H) are formed after dissociation of vibrationally excited intermediate (CH₃OH)* characterised by a lifetime of ~10^{−11} s. Direct reaction of hydrogen abstraction contributes insignificantly to the balance of end products (see, *e.g.*, Ref. 182).

The problem of distinguishing the reaction channels associated with the oxygen atoms generated by photolysis of O₃ molecules consists in that the van der Waals complexes of ozone with other molecules are, as a rule, characterised by small frequency shifts in the IR spectra. Therefore, discrimination between the reaction products formed by photolysis of binary complexes [O₃–M] and the products of reactions of migrating ‘hot’ atoms with distant molecules is not necessarily successful. The best results were obtained in studies of ozone photolysis in charge-transfer complexes. A correlation was found between consumption of the photolysed [O₃---M] complexes and the formation of the products of photolysis. As a rule, such reactions are completed with transfer of oxygen atom from the photoexcited O₃ molecule to the partner in the complex

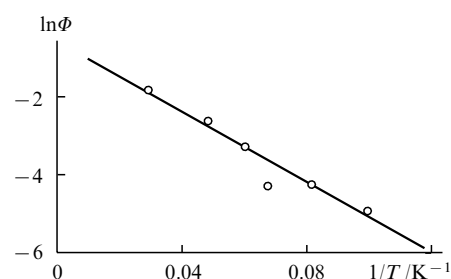
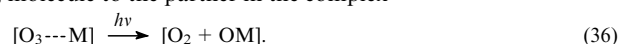
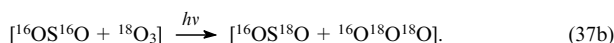
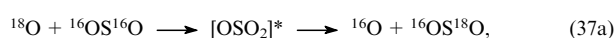


Figure 16. Quantum yield (Φ) of photolysis of ozone monomers in solid argon as a function of temperature.¹⁷¹

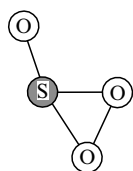
Table 8. Primary products of photoinitiated reactions in [O₃---M] complexes isolated in solid argon.

Complex	Photoinitiation wavelength range /nm	Product	Ref.
[O ₃ ---H ₂ O]	266	H ₂ O ₂	183
[O ₃ ---Cl ₂]	800–360	ClClO	184
[O ₃ ---Br ₂]	800–360	BrBrO	184
[O ₃ ---BrCl]	800–360	ClBrO	184
[O ₃ ---ICl]	750–470	ClIO	185
[O ₃ ---CH ₃ I]	470–360	CH ₃ IO	186
[O ₃ ---C ₂ H ₅ I]	< 800	C ₂ H ₅ IO	187
[O ₃ ---CF ₃ I]	1000–470	CF ₃ IO	188
[O ₃ ---PH ₃]	633–515	H ₃ PO	189
[O ₃ ---PCl ₃]	1000–360	Cl ₃ PO	190
[O ₃ ---PBr ₃]	1000–360	Br ₃ PO	190
[O ₃ ---P ₄]	1000–590	P ₄ O	191
[O ₃ ---AsH ₃]	1000–630	H ₃ AsO	192
[O ₃ ---SO ₂]	266	SO ₃	193
[O ₃ ---H ₂ O ₂]	266	H ₂ O ₃	194

Table 8 lists the data on the products of photoinduced reactions (36). Reliable distinction between the reaction channels was reported recently¹⁹³ in a study of photolytic reactions of O₃ with SO₂ molecules. Using spectral and kinetic methods, they distinguished between the reactions of photogenerated O(¹D) atoms with distant SO₂ molecules and transformations in the photolysed complexes [O₃---SO₂]. The only product detected was a symmetric oxide SO₃. Besides, experiments with the ¹⁶O → ¹⁸O isotope substitution revealed an efficient exchange of oxygen atoms between the reactants



Taking into account the results obtained, the authors suggested the existence of vibrationally excited asymmetric isomer (OSO₂)^{*} as reactive intermediate.



Among five structural isomers of SO₃ predicted by quantum-chemical calculations,⁶¹ the above-mentioned isomer is less stable than symmetric SO₃ (the energy difference is 230 kJ mol⁻¹). The conclusion¹⁹³ that the excited intermediate does not correspond to the symmetric structure of the most stable isomer (*D*_{3h} symmetry) was based on the assumption that the isotope composition of the products of reactions (37a) and (37b) does not correspond to the structure of the (SO₃)^{*} intermediate containing three equivalent oxygen atoms.

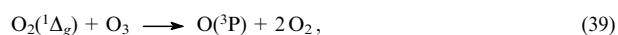
At present, the available experimental data on the mobility of thermalised oxygen atoms in the solid cryogenic matrices and crystals are inadequate to correctly describe diffusion of such atoms even phenomenologically. The kinetics of thermally induced loss of oxygen atoms in a solid xenon matrix in the temperature range 30–40 K^{69,195,196} was described by two rate constants corresponding to the diffusion coefficients of 1.4 × 10⁻¹⁵ and 5.4 × 10⁻¹⁸ cm² s⁻¹ at 32 K. Thermal diffusion of oxygen atoms in the crystals of krypton and xenon was also studied.⁶⁸ The loss of the O atoms was described by three activation barriers assuming the existence of three types of atomic sites in the crystal lattice. Calculations of the mobility of oxygen atoms in a xenon crystal, carried out in the framework of the

transition state theory using various types of pair potentials for the interaction of the O(³P) atom with the atoms of the crystal, gave somewhat contradictory results. For instance, the diffusion coefficients reported by Guo and Thompson¹⁹⁷ are three to five orders of magnitude higher than those calculated by Ford *et al.*,¹⁹⁸ whereas the corresponding experimental values^{68,69} lie between them. These discrepancies can be understood if we take into account the fact that the barriers to diffusion are determined by the short-range terms of the pair interaction potentials and that thermally activated processes occurring at ultralow temperature are very sensitive to the height of the activation barrier. In addition, differences in morphology between the matrices and crystalline samples predetermine a wide scatter of the activation barriers.

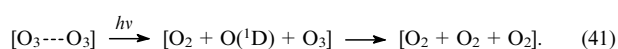
Another phenomenological model of thermally activated mobility of atomic oxygen was proposed by Danilychev and Apkaryan^{68,71} who postulated that the oxygen atom in the ground state, O(³P), in the crystal is immobile. It was also assumed that thermally induced intersystem crossing O(³P) → O(¹D), which occurs with participation of the lattice phonons, is followed by migration of the atom across the singlet PES O(¹D)–(Xe)_n until recrossing and stabilisation in the crystal. According to calculations,⁷¹ O–(Xe)_n intersystem crossing is possible in crystalline xenon. Bringing forward arguments in support of this diffusion mechanism, it was emphasised that the length of thermally activated migration appears to be comparable with the migration length of the O(¹D) atoms generated by photoexcitation of stabilised atoms. Nevertheless, the possibility for this diffusion mechanism to occur is still a moot question (see review¹⁰). The multiplicity of diffusing atoms can be experimentally determined by following their reactions with impurity molecules, which proceed involving the singlet atoms only. Earlier, such reactions were observed for ‘hot’ O(¹D) atoms generated in the photodissociation of ozone molecules in solid argon (see, *e.g.*, Refs 173 and 178).

2. Chemical transformations initiated by photolysis of ozone in solid oxygen and ozone matrices

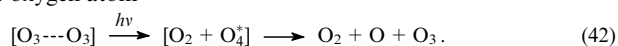
Photodecomposition of ozone upon UV photolysis to the Hartley absorption band in the gas phase occurs with a quantum yield of ~4.¹⁹⁹ Both products of primary photodissociation [see Eqn (33)] participate in further reactions to give a total of six oxygen molecules



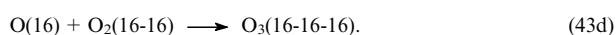
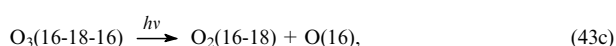
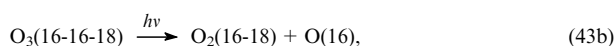
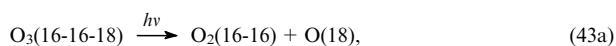
Photolysis of thin films of pure ozone at 10 K occurs with a quantum yield of 2.0 ± 0.3 (see Ref. 171). This means that photodecomposition of ozone in the solid phase involves two successive stages, namely, photodissociation (33) characterised by a quantum yield close to unity and the reaction of one photodecomposition product with the O₃ molecule. Among the three feasible secondary reactions (38)–(40), reaction (38) with participation of the O(¹D) atom seems to be the most probable,¹⁷¹ since the activation barriers to the other two reactions in the gas phase are rather high (> 15 kJ mol⁻¹). Analogous transformations were found in the case of UV photolysis of ozone dimers isolated in solid argon¹⁷¹



The results obtained by Schriver-Mazzuoli *et al.*²⁰⁰ supported high efficiency of photolysis of the [O₃---O₃] dimers in solid argon. However, based on the kinetic data, they proposed another mechanism of loss of the dimers which leads to stabilisation of the oxygen atom



The main difficulty distinguishing between the reaction channels (41) and (42) is that only consumption of the ozone molecules was studied by IR spectroscopy.^{171,200} In this case kinetic measurements cannot provide a means for reliable determination of the product ratios for reactions (41) and (42). The results of IR spectroscopic investigations can be essentially supplemented by carrying out experiments with isotope substitution in the molecules of initial reactants. For instance, photolysis of ozone molecules in solid oxygen was studied using the isotope substitution of oxygen atoms.²⁰¹ The main idea of this experimental strategy was to trap the ¹⁸O-enriched ozone molecules in the solid oxygen matrix containing the ¹⁶O atoms only. Figure 17 illustrates the evolution of the IR spectrum of ozone in the region of the ν_3 vibration during continuous photolysis with light at a wavelength of 693 nm to the Chappuis absorption band. Changes in the spectrum show that the number of the O₃ molecules remains constant during long-term irradiation. However, the isotope composition of ozone molecules changes radically, namely, the ¹⁸O₃(18-18-18) molecules are replaced by the ¹⁶O₃(16-16-16) molecules during photolysis. Kinetic analysis showed that the atom produced upon photodissociation of O₃ is added to the neighbouring O₂ molecule to give an O₃ molecule with altered isotope composition. Subsequent photolysis of products of these reactions causes further transfer of the ¹⁸O atoms in the O₂ molecules and, correspondingly, enrichment of the ozone molecules with the ¹⁶O isotope



In fact this reaction mechanism describes a photoinduced chemical migration of ozone molecules in solid oxygen. The use of isotope substitution allowed reliable establishment of reaction channels in the case where the reactants and products are comprised of oxygen atoms only.²⁰¹

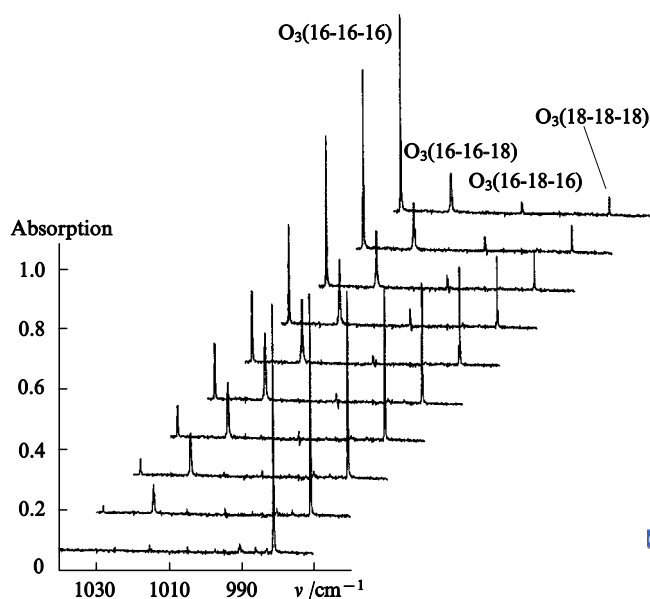


Figure 17. Evolution of the IR spectrum of ozone in the region of the ν_3 vibration during continuous photolysis of a ¹⁸O₃: ¹⁶O₂ = 1:4000 sample with light ($\lambda = 693$ nm).²⁰¹

VII. Conclusion

The results of experimental and theoretical investigations considered in this review show that chemical reactions of mobile atoms, which occur in an inert crystalline environment at ultralow temperature, cause stabilisation of free radicals and radical–molecular complexes (short-lived intermediate particles in the gas phase). The use of mobile atoms for generation of reactive intermediates permitted obtaining spectroscopic data on new metastable molecular structures which were not observed by other methods. This type of reaction is characterised by a rather high extent of conversion of the initial reactants, which makes it possible to detect matrix-isolated products of primary reactions. Stabilisation of a particular type of isolated particles is due to high selectivity of cryochemical reactions. This permits detection of matrix-isolated products of primary reactions using conventional methods of low-temperature spectroscopy. Joint use of the IR, optical and EPR spectroscopy allows reliable identification of products and establishment of their structure by comparing the measured spectroscopic characteristics with the results of quantum-chemical calculations.

The use of mobile atoms for cryochemical synthesis of new compounds is not limited to the atoms of three elements and their reactions considered in this review. In particular, of considerable interest is the use of photostimulated mobility of the rare-earth metal atoms and transition metal atoms. The results of such studies carried out before 1999 were generalised in a monograph.²⁰² Experimental approaches to low-temperature synthesis of particles containing various metal atoms and clusters have been reviewed.²⁰³

The fact that international conferences on the chemistry and physics of matrix-isolated species and on low-temperature chemistry are held on a regular basis (in particular, the last two conferences were held in Poland²⁰⁴ and Finland²⁰⁵) points out that this review is topical. When preparing the manuscript, the authors of this review used not only original communications but also information obtained in discussions, which is useful for refinement of researchers' views of particular (including moot) questions.

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Structure of methane complexes according to the data of experimental and theoretical investigations

V D Makhaev

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Abstract. The results of experimental and theoretical studies of the structures of methane complexes with neutral metal atoms, metal ions M^+ and molecular fragments ML_n are considered and generalised. The influence of the charge and electronic configuration of the central atom and the nature of stabilising ligands L on the mode of coordination of methane in the complexes is analysed. The data from theoretical calculations of the structures of methane complexes are compared with the results of structural studies of some classes of model compounds, namely, borane complexes $M(CO)_5 \cdot BH_3L$ ($M = Cr, Mo, W$) and tetrahydroborate complexes $ML_n(BH_4)_m$ containing BH_4^- anions as ligands. Some rules determining the mode of methane coordination in the complexes are elucidated and assumptions concerning the dependence of the mode of methane coordination on the electronic configuration of the central atom are made. The bibliography includes 173 references.

I. Introduction

The development of methods for mild selective catalytic functionalisation of saturated hydrocarbons (alkanes) is a highly important problem having great potential in organometallic chemistry. As D R H Barton said figuratively,¹ the solution of this problem is the dearest chemists' wish of the last few decades, as desired and unattainable as the Holy Grail for medieval knights. The key stage in alkane functionalisation is the activation of the chemically inert C–H or C–C bonds by metal complexes. Experimental data on the reactions of metal complexes with hydrocarbons have been considered in detail in a number of reviews and monographs (see, for example, Refs 2–12).

Numerous spectroscopic and kinetic data indicate that the addition of metal complexes to C–H bonds in saturated hydrocarbons as well as the reverse elimination of alkanes give intermediate alkane complexes of the corresponding metals containing one or several alkane molecules.^{13–15} The existence of such complexes is now beyond doubt. Some of them have been detected by spectroscopy [for example, $M(CO)_5(\text{alkane})$ complexes, where $M = Cr, Mo, W$].³ Recently, the intermediate formation of alkane

complexes has been observed directly by femtosecond IR spectroscopy during activation of the C–H bonds in alkanes both in low-temperature matrices¹⁶ and in solutions at usual temperatures.¹⁷ The first example of direct NMR monitoring of the formation of an alkane complex of a transition metal, $CpRe(CO)_2(C_5H_{10}\text{-cyclo})$, in solution at -80°C was reported.¹⁸ Similar methane complexes have not been detected experimentally in solutions.⁵

Those involved in experimental investigations of the structures of metal complexes with alkanes are faced with considerable difficulties because these complexes have not been isolated in a pure state. The existing data on these structures were mainly deduced from the results of quantum-chemical calculations.

Methane complexes attract particular attention of researchers because methane is the most naturally abundant hydrocarbon widely applied as an energy carrier and is promising as a cheap, readily available potential raw material for the chemical industry. Catalytic reforming of methane to methanol has been mentioned recently among the ten most important goals of catalysis.¹⁹ Meanwhile, methane is the least reactive hydrocarbon; therefore, its functionalisation is a particularly difficult task.

Of great theoretical interest are items concerning the modes of methane coordination in metal complexes and factors dictating the predominance of one or another coordination mode. A large number of publications have been devoted to the structures of methane complexes with neutral metal atoms, metal ions M^+ and molecular fragments ML_n . According to quantum-chemical calculations, there exist a diversity of possible modes of methane coordination and the difference between the energies of various structures is slight, which is indicative of structurally non-rigid compounds. Therefore, determination of the most stable structure is ambiguous and depends on the particular system (complex) as well as on the calculation method and the basis set of functions used. This ambiguity is inherent in the calculations for any of the three modes of methane complexes, *i.e.*, those with neutral metal atoms, cations and molecular fragments. The lack of uniqueness of calculation results hampers elucidation of the regular structural features of methane complexes. In this connection, there appears to be a need to compare the theoretical data for methane complexes with experimental data obtained for complexes of some species structurally similar and isoelectronic to methane.

This review considers the results of experimental and theoretical studies of the structures of methane complexes with neutral metal atoms, cations M^+ and molecular fragments ML_n . The effects of the charge and the electronic configuration of the central atom and the nature of the stabilising ligands L on the mode of methane coordination in the complexes are analysed. The calcu-

V D Makhaev Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 576 40 09. E-mail: vim@icp.ac.ru

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lated data on the structures of methane complexes are compared with the results of structural investigations of some classes of model compounds — borane complexes $M(\text{CO})_5 \cdot \text{BH}_3\text{L}$ ($M = \text{Cr}, \text{Mo}, \text{W}$) and tetrahydroborate complexes $\text{ML}_n(\text{BH}_4)_m$ in which the ligands are represented by the BH_4^- anions isoelectronic to methane and resembling methane in geometry. Some features determining the mode of methane coordination in the complexes are elucidated and suggestions concerning the dependence of the methane coordination mode on the electronic configuration of the central atom are made. The review covers papers published up to 2001 inclusively and some publications of 2002.

The following designations are used for the modes of methane coordination in the complexes. Compounds in which methane is linked to the central metal atom through one hydrogen bridge $[\text{MHCH}_3 \text{ (A)}, \text{ the } M-\text{H}_b-\text{C} \text{ angle is } \sim 180^\circ, \text{ the } \text{CH}_4 \text{ tetrahedron is coordinated by a vertex}]$ are designated as η^1 -complexes (Fig. 1). Compounds where methane is bound to the central atom by two $[\text{MH}_2\text{CH}_2 \text{ (B)}, \text{ the } \text{CH}_4 \text{ tetrahedron is coordinated by an edge}]$ or three $[\text{MH}_3\text{CH} \text{ (C)}, \text{ the } M-\text{C}-\text{H}_t \text{ angle is } \sim 180^\circ, \text{ the } \text{CH}_4 \text{ is coordinated by a face}]$ hydrogen bridges are designated as η^2 - and η^3 -complexes, respectively. Compounds with one bent hydrogen bridge $[\text{MHCH}_3 \text{ (D and E)}, \text{ the } M-\text{H}_b-\text{C} \text{ angle is much smaller than } 180^\circ]$ are referred to as η_2^1 - and η_3^1 -complexes. The complexes **D** and **E** are often designated in the literature by $\eta^2\text{-C,H}$; however, this designation does not provide a strict description of the structure, because these complexes can be formed upon distortion of either the η^2 - or η^3 -structure. Therefore, for more exact descriptions of the structures of these complexes, here we call them η_2^1 and η_3^1 .

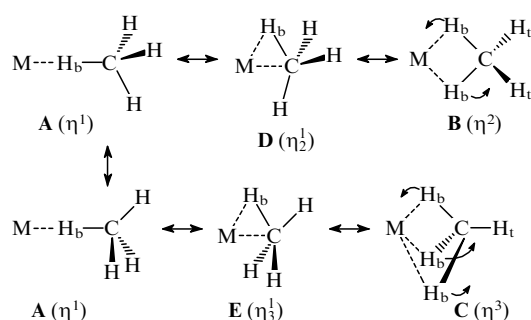


Figure 1. Types of methane coordination in the complexes; η^1 is mono-, η^2 is bi-, and η^3 is tridentate coordination of methane; η_2^1 and η_3^1 are intermediate modes of coordination; H_b and H_t are bridging and terminal hydrogen atoms, respectively.

The accepted notation for the quantum-chemical methods and the software used is given in the Supplement.

II. Methane complexes with neutral metal atoms

The data on the structures of methane complexes with neutral metal atoms are relatively scarce. The formation of the $\text{Co}(\text{CH}_4)$ complex was detected experimentally by IR spectroscopy upon irradiation of the CH_3CoH complex with light with $\lambda > 400 \text{ nm}$ in a low-temperature argon matrix. This reaction is reversible; on exposure to UV radiation, the $\text{Co}(\text{CH}_4)$ complex is converted again into CH_3CoH . After the formation of the $\text{Co}(\text{CH}_4)$ complex, the triply degenerate absorption band of methane $\nu_4(\text{f}_2)$ located at 1305.3 cm^{-1} was split into two peaks. This allowed the authors to suggest that this complex has C_{3v} symmetry. The most likely coordination of methane in this complex is tridentate — $\text{Co}(\eta^3\text{-CH}_4)$.²⁰

Similar complexes have also been obtained for iron atoms in a methane matrix.²¹ Molecular orbital calculations using the effective Hamiltonian proposed by Anderson (see Ref. 22 and references therein) have shown that Fe atoms in the ground state

($^5\text{D}, 3\text{d}^6 4\text{s}^2$) are able to form complexes with methane. A tridentate coordination of methane is most probable for these complexes. The energy of the $\text{Fe}-\text{C}$ bond is 11 kcal mol^{-1} and the $\text{Fe}-\text{C}$ distance is $3.4 \text{ \AA}$. The oxidative addition of methane to an iron atom is hampered due to the mutual repulsion of the closed electron shells of the methane $\text{C}-\text{H}$ bonds and the 4s electrons of iron atoms.²²

Experimental studies showed that none of the neutral atoms of 3d metals in the ground state reacts with alkanes in the gas phase at 300 K. In the case of 4d-metal atoms, only palladium atoms in the ground state ($^1\text{S}, 4\text{d}^{10}$) form complexes with higher alkanes with a binding energy of not less than 8 kcal mol^{-1} (see Ref. 23). However, a palladium complex with methane is not formed under these conditions, which points to a lower energy of the $\text{Pd}-\text{C}$ bond. The results of *ab initio* self-consistent field (SCF)²⁴ calculations of the interaction between a palladium atom and methane, which were carried out using the minimum basis set of gaussian orbitals (LCGO) before the relevant experiments, are at variance with experimental data.²³ According to calculations,²⁴ the palladium atom forms a methane complex with monodentate coordination of the methane ligand, $\text{Pd}(\eta^1\text{-CH}_4)$; the bond energy is $7\text{--}8 \text{ kcal mol}^{-1}$.

In a series of publications,^{25–30} Blomberg and coworkers studied theoretically the activation of the $\text{C}-\text{H}$ bonds in methane by 3d-, 4d- and 5d-metal atoms.† A modified coupled pair functional (MCPF) study of the reaction of methane with 4d metals ranging from yttrium to palladium showed²⁷ that only palladium in the ground state ($^1\text{S}, 4\text{d}^{10}$) is able to be complexed with methane to give a $\text{Pd}(\eta^2\text{-CH}_4)$ type complex. The stabilisation energy of this complex with respect to the initial reactants is 4 kcal mol^{-1} . Ruthenium and rhodium form complexes with methane only in the low-spin excited state ($^3\text{F}, 4\text{d}^7 5\text{s}^1$ and $^2\text{D}, 4\text{d}^9$, respectively), the stabilisation energies of these complexes relative to the excited metal atoms being 12 and 9 kcal mol^{-1} , respectively. It was noted²⁷ that the potential energy surface (PES) minima corresponding to metal complexes with methane can also be found for other 4d-metal atoms, but the metal...carbon distances in these complexes are very long (stabilisation energies do not exceed 2 kcal mol^{-1}). A MCPF study of the interaction of rhodium and niobium atoms with methane showed that rhodium in the low-spin excited state ($^2\text{D}, 4\text{d}^9$) is inserted almost without a barrier into a $\text{C}-\text{H}$ bond of methane to give the HRhCH_3 complex.³¹ The $\text{Rh}(\eta^2\text{-CH}_4)$ complex is formed as an intermediate. Unlike rhodium, niobium does not react with methane.²⁶

Experimental and theoretical investigations of the reactions of alkanes with transition metal atoms in the ground electronic state have shown that rhodium and palladium‡ are the only 4d metals able to react with ethane and higher alkanes at 300 K.²⁸

According to experimental results, among the transition 5d metals in the ground electronic state, only neutral platinum atoms can activate methane in the gas phase at 300 K.²⁹ The results of theoretical investigations [using the density functional theory (DFT) with Becke's exchange functional and the Lee–Yang–Parr correlation functional (B3LYP) with parametrised configuration interactions (PCI-80) and *ab initio* calculations]³⁰ of the activation of methane $\text{C}-\text{H}$ bonds by transition 3d-, 4d- and 5d-metal atoms are consistent with experimental data. The calculations showed that platinum and rhodium atoms are capable of activating the $\text{C}-\text{H}$ bonds in methane but only platinum can participate in the further formation of the $\text{Pt}=\text{CH}_2$ carbene, which is needed for experimental monitoring of the reaction.²⁹

† It is noteworthy that calculations of the $\text{M}-\text{C}$ bond energies for all metals were carried out using the geometric parameters optimised for the rhodium complex $\text{Rh}(\eta^2\text{-CH}_4)$, i.e., the influence of the electronic configuration of the central atom on the mode of coordination of the methane ligand was not taken into account.

‡ Palladium is unique due to its ability to form η^2 -complexes with linear alkanes (except for methane), while rhodium is able to dehydrate higher alkanes (but not methane).

Experimental and theoretical (MCPF technique) research of gas-phase reactions of iridium and platinum with n-alkanes C_nH_{2n+2} ($n = 3, 4$) demonstrated that the potential barrier to the reaction between a platinum atom and propane or butane does not exceed $1-2 \text{ kcal mol}^{-1}$, while iridium atoms are inert towards these alkanes.²⁹ Thus, the chemical behaviour of atomic iridium in the gas phase differs appreciably from the behaviour of iridium complexes in solutions; many of these complexes are able to react with alkanes.⁵

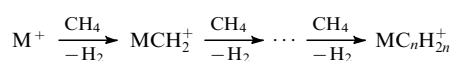
Density functional theory calculations in the PCI-80 approximation have shown³⁰ that the inertness of iridium atoms is due to the great promotion energy between the chemically inert ground state ($5d^7 6s^2$) and the excited state ($5d^8 6s^1$). In the excited state the iridium atom reacts with methane to give a molecular adduct with a bond energy of 2 kcal mol^{-1} . Attempts to calculate the geometric parameters of the complex formed by the iridium atom with methane by *ab initio* SCF methods in the MCPF approximation and by the second-order Møller–Plesset perturbation theory (MP2) have not met with success.

The platinum atom in the ground state ($5d^9 6s^1$) forms a weak complex with methane (the Pt–C distance is 3.61 Å , the bond energy is $2.1 \text{ kcal mol}^{-1}$).³⁰ The mode of coordination of methane in this complex was not indicated. In the case of the low-spin excited state of platinum ($1S, 5d^{10}$), MP2 calculations predict the formation of an η^2 -complex with a Pt–C distance of 2.38 Å and a binding energy of $19.1 \text{ kcal mol}^{-1}$. However, when the geometry of the singlet $Pt(\eta^2\text{-CH}_4)$ complex was optimised by more effective methods, no minimum was found on the PES.³⁰

The activation of methane by 5d-metal atoms (Re, Os, Ir and Pt) has been studied by *ab initio* methods using the relativistic effective core potentials (RECP) and taking into account electron correlation.³² It was found that rhenium atoms in the ground state ($6S, 5d^5 6s^2$) are highly inert with respect to methane, compared with other transition 5d metals, due to the presence of a half-filled 5d shell. Osmium in the ground state ($5D, 5d^6 6s^2$) is also inert toward methane; however, the energy barrier to the reaction is much lower for osmium than for rhenium. Iridium atoms in the excited state ($2P$), like platinum atoms in the ground ($3D, 5d^9 6s^1$) and low-spin ($1S, 5d^{10}$) states, are inserted into the C–H bond of methane to give $HMCH_3$ complexes.

III. Methane complexes with bare metal ions

It was found in 1979 that transition metal cations (Ti^+ , Fe^+ , Co^+ , Ni^+) are able to react with alkanes (butane and isobutane) in the gas phase.³³ This discovery has triggered intensive research into gas-phase reactions of transition metal cations M^+ with alkanes and the carbene complexes MCH_2^+ with hydrogen, which is still being continued. The purpose of the researches mentioned above is to elucidate the mechanism of activation of the H–H, C–H, and C–C bonds by metal cations. According to the obtained results, metal ions are markedly more reactive toward alkanes than neutral atoms. A typical gas-phase reaction of metal ions not stabilised by ligands is the dehydrogenation of alkanes C_nH_{2n+2} ($n \geq 2$). Methane dehydrogenation has been much less studied. None of the 3d transition metal ions in the ground state is able to perform exothermic dehydrogenation of methane. Of the 4d-metal ions, only Zr^+ exhibits capacity for methane dehydrogenation in the ground state. As regards 5d-metal ions, the fast successive reactions



have been observed for Ta^+ , W^+ , Os^+ , Ir^+ , and Pt^+ (iridium and platinum atoms are most reactive in this reaction); La^+ , Hf^+ , Re^+ and Au^+ ions did not dehydrogenate methane under similar conditions.³⁴ The reactivity of these ions depends on both the electronic configuration and the spin state.

Meanwhile, many ions of both transition and non-transition metals are able to form ion–molecular complexes $M(CH_4)_n^+$ with methane. The properties of these complexes, resulting from association of metal cations with one or more CH_4 molecules, have been studied experimentally using various methods, in particular, electron impact, photoionisation, photoelectron-photoion coincidence spectroscopy, standard or quadrupole mass spectrometry, *etc.* The $Mg(CH_4)^+$, $V(CH_4)^+$, $Fe(CH_4)^+$, $Co(CH_4)_n^+$ ($n = 1-4$), and $Pt(CH_4)_n^+$ ($n = 1, 2$) complexes have been studied experimentally. Under multicollision conditions at 300 K and a helium pressure of 0.75 mmHg, 3d-metal ions react with methane to form complexes with the composition $M(CH_4)_n^+$ [$M = Sc^+$ ($n = 1-3$), Ti^+ ($n = 1-5$), V^+ ($n = 1-4$), Cr^+ ($n = 1, 2$), Fe^+ ($n = 1-3$), Co^+ ($n = 1-3$), Ni^+ ($n = 1, 2$), Cu^+ ($n = 1, 2$), and Zn^+ ($n = 1$)], the structures of which have not been determined.³⁵ According to experimental results,³⁵ the energy of methane binding in these complexes exceeds 10 kcal mol^{-1} . An exception is the manganese ion, which does not form complexes with methane under these conditions.

The alkane complexes of alkali metal cations (sodium and potassium), which are similar in size to transition metal ions, have not been observed experimentally. This attests to an important role of d orbitals in the stabilisation of metal complexes of alkanes. The geometric parameters and bond energies of complexes formed by methane with lithium, sodium, magnesium, scandium, titanium, vanadium, chromium, iron, cobalt, copper, 4d metals, tantalum, iridium and platinum were calculated by quantum-chemical methods. Some of the results of experimental and theoretical investigations of the ion–molecular $M(CH_4)^+$ complexes are considered below.

1. Non-transition metal ions

The interaction of methane with the lithium cation has been studied theoretically.³⁶⁻³⁸ The geometry of the $Li(CH_4)^+$ complex was optimised by the restricted Hartree–Fock (RHF) method using the SKBJ effective core potential (relativistic compact effective core potential and the Stevens, Basch, Krauss and Jasien shared-exponent basis set). The complex $Li(\eta^3\text{-CH}_4)^+$ with C_{3v} symmetry was found to correspond to the minimum on the PES. The ion–ligand interaction in this complex was assumed to be mainly of the ion–dipole nature.³⁶

The potential energy surface of the $Li(CH_4)^+$ complex was studied within the framework of the *ab initio* Hartree–Fock method.³⁷ The tridentate coordination of methane in the $Li(\eta^3\text{-CH}_4)^+$ complex with a binding energy of $8.2 \text{ kcal mol}^{-1}$ was found to be energetically the most favourable. The researchers believe³⁷ that this binding energy is large enough to enable the existence of this ion in an isolated state in molecular beams or inert matrices. The potential barrier to the transition from the η^3 - to η^2 -complex is low ($0.5 \text{ kcal mol}^{-1}$), indicating structural non-rigidity of the $Li(CH_4)^+$ complex. Analysis of the Mulliken populations showed that the Li^+ cation perturbs only slightly the electron density of the CH_4 ligand. The electron density (expressed in fractions of the electron charge) on hydrogen atoms decreases upon coordination by 0.06 (H_b) and 0.13 e (H_i), and that on the C atom increases by 0.17 e. The overlap populations $Q(Li-H_b)$ and $Q(Li-C)$ are fairly low (0.03 and 0.16 e, respectively), pointing to weak covalent interaction of the Li^+ ion with the ligand. It should be noted that in the study cited,³⁷ the calculations were carried out in the approximation of a rigid tetrahedral CH_4 core with a fixed C–H distance (1.096 Å).

Charkin *et al.*³⁸ used the *ab initio* QCISD(T)/6-31G**//MP2/6-31G* + ZPE(MP2/6-31G*) calculation methods⁸ to represent

§ Here QCISD(T) means the single and double quadratic configuration interaction with an estimation of triple excitations by a perturbation method; 6-31G** is the Pople basis set extended by d- and p-polarisation functions with the 1s-AO being approximated by six and the 2s, 2p-AO, by four gaussian type functions grouped in the (3,1) form; ZPE is the zero-point energy.

fragments of the potential energy surfaces for the $\text{Li}(\text{CH}_4)^+$ and $\text{Na}(\text{CH}_4)^+$ ion–molecular complexes in the vicinity of formation of mono-, bi- and tridentate structures. It was found that the global minimum on the $\text{M}(\text{CH}_4)^+$ PES ($\text{M} = \text{Li}, \text{Na}$) corresponds to a tridentate structure, whereas a bidentate structure is matched by a maximum connecting the two nearest minima in the potential curve. The calculated energies for cation elimination from $\text{M}(\text{CH}_4)^+$ complexes ($\text{M} = \text{Li}, \text{Na}$) do not exceed 10–12 kcal mol⁻¹. However, they are sufficiently high to ensure the existence of these complexes in the isolated state or in inert matrices. The $\text{Li}(\eta^2\text{-CH}_4)^+$ and $\text{Li}(\eta^1\text{-CH}_4)^+$ complexes are 1.6 and 6.5 kcal mol⁻¹ less stable than $\text{Li}(\eta^3\text{-CH}_4)^+$, while the corresponding complexes $\text{Na}(\eta^2\text{-CH}_4)^+$ and $\text{Na}(\eta^1\text{-CH}_4)^+$ are 0.6 and 3.4 kcal mol⁻¹ less stable than $\text{Na}(\eta^3\text{-CH}_4)^+$.

For the $\text{Mg}(\text{CH}_4)^+$ complex, the geometric parameters and the energies of binding of the Mg^+ ion in the ground and excited electronic states to the methane ligand were calculated theoretically. The tridentate coordination of methane to form $\text{Mg}(\eta^3\text{-CH}_4)^+$ was found to be energetically the most favourable for the Mg^+ ion in the ground state ($^2\text{S}, 3\text{s}^1$); the same geometric configuration corresponds to a minimum on the system PES. The $\text{Mg}-\text{CH}_4$ binding energy in this complex is 4.0–7.6 kcal mol⁻¹ (see Ref. 39). The Mg^+ and CH_4 species in this complex are weakly bound by electrostatic forces. The methane ligand differs slightly from non-coordinated methane in geometric parameters, in particular, the $\text{H}-\text{C}-\text{H}$ angles change by about 0.5° and the $\text{C}-\text{H}$ distances, by less than 0.01 Å. Analysis showed that in the case of the Mg^+ ion, η^3 -coordination is preferred for methane over η^2 - or η^1 -coordination, as this decreases the repulsion between the 3s^1 electron of the magnesium ion and the $\text{C}-\text{H}$ bond electrons of the methane molecule. This results in a shorter $\text{M}-\text{C}$ bond and, hence, enhances the electrostatic interaction between the species. When the Mg^+ s electron passes to the $\text{p}\pi$ orbital of the complex, the methane ligand in $\text{Mg}(\text{CH}_4)^+$ retains the η^3 -coordination, while upon transition of the s electron to the $\text{p}\pi$ orbital, the coordination of the methane ligand changes to a bidentate one. The structure of the $\text{Mg}(\text{CH}_4)^+$ complex has been studied experimentally using photoelectron spectroscopy with a reflectron time-of-flight mass spectrometer.⁴⁰ The results of calculations³⁹ are in good agreement with the experimental data.

2. Transition metal ions

Mass-spectrometric studies of the interaction of the Sc^+ ion with alkanes in the gas phase have shown unique properties of this ion compared to other 3d-metal ions. With butane or higher alkanes, this ion forms $\text{Sc}(\text{C}_n\text{H}_{2n+2})_m^+$ complexes (presumably, dialkyl-scandium ions), which have not been detected for other 3d-metal ions.⁴¹ The reaction of Sc^+ with methane has been studied theoretically.^{42,43} The $\text{Sc}^+ + \text{CH}_4$ and $\text{ScCH}_2^+ + \text{H}_2$ reactions were investigated by the complete active space self-consistent field (CASSCF) method and by the multideterminant configuration interaction method with single and double excitations using the wave function obtained by CASSCF (MR-SDCI-CASSCF).⁴² The Sc^+ ion in the ground state ($^3\text{D}, 3\text{d}^1 4\text{s}^1$) reacts with methane to form the $\text{Sc}(\eta^3\text{-CH}_4)^+$ complex with a tridentate methane coordination and with an $\text{Sc}-\text{CH}_4$ binding energy of 15.1 kcal mol⁻¹. After the formation of this complex, the reaction is terminated due to the high energy barrier to its conversion into other isomeric complexes. In the case of the Sc^+ ion in the first excited state ($^1\text{D}, 3\text{d}^1 4\text{s}^1$), the bidentate coordination of methane is preferred. The stabilisation energy relative to the reactants is 13.3 kcal mol⁻¹ (the stabilisation energy with respect to the ground state of the Sc^+ ion is 5 kcal mol⁻¹).⁴² The reaction of methane with the Sc^+ cation was also studied by the density functional approach in the B3LYP approximation.⁴³ It was found that the Sc^+ cation both in the ground ($^3\text{D}, 3\text{d}^1 4\text{s}^1$) and the first excited state ($^1\text{D}, 3\text{d}^1 4\text{s}^1$) forms tridentate methane complexes $\text{Sc}(\eta^3\text{-CH}_4)^+$ due to the ion–dipole interaction. The $\text{Sc}-\text{CH}_4$ bond energies in these complexes are 15.7 and 8.4 kcal mol⁻¹, respectively (relative to the starting reactants).

A mass-spectrometric study⁴⁴ of the reaction of titanium ions with excess methane in the gas phase at 300 K has shown that under these conditions, the Ti^+ ion in the ground state ($^4\text{F}, 3\text{d}^2 4\text{s}^1$) is able to add up to three methane molecules. The binding energy for the first two methane molecules is ~17 kcal mol⁻¹, while that for the third molecule is 6.6 kcal mol⁻¹ (see Ref. 44). After the addition of two methane molecules, activation of $\text{C}-\text{H}$ bonds starts to compete with the addition reaction; in this case, the gas phase contains simultaneously the $\text{Ti}(\text{CH}_4)_3^+$, $(\text{CH}_4)_2\text{Ti}(\text{H})$, $(\text{CH}_3)^+$ and $(\text{CH}_4)_2\text{Ti}^+=\text{CH}_2$ ions. In the researchers' opinion,⁴⁴ the increase in the methane binding energy in the insertion products with respect to its binding energy in the corresponding $\text{Ti}(\text{CH}_4)_n^+$ complexes is the driving force of activation. The discovered reaction mechanism was called 'cluster-assisted σ -bond activation'.

The reaction of the excited titanium ion $\text{Ti}^+(^2\text{F}, 3\text{d}^2 4\text{s}^1)$ with CH_4 has been studied by the MP2/6-31G** method taking account of electron correlation and using the Hay–Wadt effective core potentials.⁴⁵ It was found that the first stage represents the formation of the intermediate $\text{Ti}(\text{CH}_4)^+$ complex, which is followed by hydrogen migration from methane to Ti^+ giving rise to an insertion product, HTiCH_3^+ . The calculation showed that the tridentate (η^3 , C_{3v}) coordination of methane with a binding energy of 73.1 kcal mol⁻¹ is most favourable for the $\text{Ti}^+(^2\text{F}, 3\text{d}^2 4\text{s}^1)$ ion. The $\text{Ti}(\eta^3\text{-CH}_4)^+$ complex corresponds to a deep energy minimum on the PES with respect to the starting reactants and to the transition state of the oxidative addition.⁴⁵

More recent calculations⁴⁶ by the DFT method in the B3LYP approximation also confirm the predominance of the tridentate coordination of methane to the excited $\text{Ti}^+(^2\text{F}, 3\text{d}^2 4\text{s}^1)$ ion; however, according to these results, the binding energy of methane to the titanium ion is only 21.81 kcal mol⁻¹ relative to the reactants (8.89 kcal mol⁻¹ with respect to the ground state of the Ti^+ ion). The reaction of methane with the Ti^+ ion in the ground state ($^4\text{F}, 3\text{d}^2 4\text{s}^1$) also yields the $\text{Ti}(\eta^3\text{-CH}_4)^+$ complex,⁴⁶ the $\text{Ti}-\text{CH}_4$ bond energy (22.21 kcal mol⁻¹) being roughly equal to that in a similar complex with the excited $\text{Ti}^+(^2\text{F}, 3\text{d}^2 4\text{s}^1)$ ion. These data are more consistent with the results of experimental studies⁴⁴ than the data obtained earlier.⁴⁵

Study of the gas-phase reaction between vanadium ions and methane by mass spectrometry⁴⁷ has shown that V^+ ions in the ground quintet state ($^5\text{D}, 3\text{d}^4$) do not react with methane. Transition of the V^+ ion into the triplet excited state ($^3\text{F}, 3\text{d}^3 4\text{s}^1$) results in a substantial increase in its reactivity. The weakly bound $\text{V}(\text{CH}_4)^+$ complex was prepared by ultrasonic expansion of the vanadium ion plasma generated by laser radiation with the use of helium containing 1% of methane as the carrier gas. The isolated $\text{V}(\text{CH}_4)^+$ ion was studied by resonance single-photon photodissociation spectroscopy.⁴⁸ The $3\text{d}^4 \rightarrow 3\text{d}^3 4\text{s}^1$ electron transition corresponding to the excitation of the central metal atom in the electrostatically bound $\text{V}(\text{CH}_4)^+$ complex was observed in this experiment. The binding energy between the V^+ ion in the ground state ($^5\text{D}, 3\text{d}^4$) and methane is ~15 kcal mol⁻¹. This differs little from the calculated Nb–C bond energy (11.8 kcal mol⁻¹) in the $\text{Nb}(\eta^2\text{-CH}_4)^+$ complex.⁴⁹ However, the researchers note that C_{2v} symmetry cannot be reliably ascribed to the $\text{V}(\text{CH}_4)^+$ complex in the ground state without full analysis of the rotation spectrum. The binding energy between the excited $\text{V}^+(3\text{d}^3 4\text{s}^1)$ ion and methane amounts to 8.3 kcal mol⁻¹. The decrease in the V^+-CH_4 binding energy taking place as vanadium passes from the ground state to the excited state is assumed⁴⁸ to be due to the mutual repulsion of the electron in the 4s shell of the excited ion and the electrons of the methane ligand.

The results of density functional calculations in the B3LYP approximation for the $\text{V}(\text{CH}_4)^+$ complex are consistent with the assumed bidentate coordination of methane by the V^+ ion in the ground state ($^5\text{D}, 3\text{d}^4$). The calculated energy of the bond between methane and V^+ in this complex (15.09 kcal mol⁻¹) is in good agreement with the experimental value (~15 kcal mol⁻¹). The

excited vanadium ion $V^+(^3F, 3d^3 4s^1)$ was found⁴⁶ to form a complex with tridentate coordination of the methane ligand.

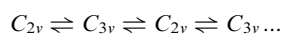
Ab initio quantum-chemical calculations with allowance for electron correlation (MCPF method) of the insertion of single-charged 4d-metal ions into a methane C–H bond have shown⁴⁹ that all these ions are capable of forming complexes with methane, the ion–ligand binding energy being lower for ions with an outer s shell or d^5 shell than for d^4 , d^7 , d^8 and d^9 ions.⁴⁹ It should be noted that these calculations were carried out for a fixed η^2 -geometry of methane complexes, *i.e.*, the influence of the electronic configuration of a particular ion on the geometry of the complex was neglected.⁴⁹ As far as we know, experimental data concerning the binding energies in the methane complexes with 4d-metal ions are missing.

The activation of the methane C–H bonds by the Ta^+ cation observed experimentally in the gas phase^{2, 50, 51} has been studied by the density functional approach in the B3LYP approximation.⁵² This process was found to consist of several steps. The first step is the formation of the $Ta(CH_4)^+$ complex with electrostatic binding; this is followed by Ta^+ insertion into the C–H bond to give the dihydride $H_2TaCH_2^+$. A slightly distorted η^3 -coordination of methane is preferred for the Ta^+ ion in the ground state ($^5F, 5d^3 6s^1$); the $Ta^+–CH_4$ binding energy is 12 kcal mol^{−1}. The interaction between Ta^+ and methane is mainly electrostatic. The methane ligand almost retains the geometry of the free molecule (the length of one C–H_b bridging bond is increased by 0.003 Å). The Ta^+ ion does not lie on the C–H_t axis but is shifted somewhat toward one of the H_b atoms (the Ta–C–H_{tb} angle equals 73.02°).⁵²

Recent results obtained by density functional calculations in the B3LYP approximation for the reaction of methane with the Cr^+ ion in the ground ($^6S, 3d^5$) and excited ($^4D, 3d^4 4s^1$) states attest to a tridentate methane coordination in the resulting complexes.⁴⁶ The binding energies between methane and chromium ions in the ground and excited states are equal to 13.1 and 29.31 kcal mol^{−1}, respectively, relative to the reactants.

The reaction of methane with the Fe^+ ion (in the gas phase) has been studied in more detail.^{53–56} The ion–ligand binding energy for the $Fe(CH_4)^+$ complex was determined experimentally and calculated theoretically. The collision-induced dissociation (CID) of $Fe(CH_4)_n^+$ ions ($n = 1–4$) was studied by mass spectrometry.⁵³ The dissociation energy of the $Fe(CH_4)^+$ complex was found to be 13.7 ± 0.8 kcal mol^{−1}. These results prompted the conclusion that the Fe^+ ion in $Fe(CH_4)^+$ has a sextet ground state ($^6D, 3d^6 4s^1$).⁵³ In a mass-spectrometric investigation⁵⁴ of the $FeCH_2^+ + D_2$ and $Fe^+(^6D, ^4F) + CD_4$ reactions, the bond dissociation energy was found to be $D_0(Fe^+–CH_4) = 13.62$ kcal mol^{−1}; this is consistent with the value $D_e(Fe^+–CH_4) = 13 \pm 1$ kcal mol^{−1}, determined by the MCPF calculations.⁵⁴

The CASSCF and MR-SDCI-CASSCF methods were employed to study the PES of the $FeCH_2^+ + H_2$ reaction; the formation of the ion–molecular $Fe(CH_4)^+$ complex was established.⁵⁵ The $Fe(CH_4)^+$ complex with a binding energy of ~ 16 kcal mol^{−1} is stable with respect to dissociation into $Fe^+(^6D, 3d^6 4s^1)$ and CH_4 . The back reaction, $Fe^+ + CH_4$, gives only one product, $Fe(CH_4)^+$, at moderate temperatures. The calculations showed that the structures with C_{2v} (η^2) and C_{3v} (η^3) symmetry for $Fe(CH_4)^+$ are almost degenerate (the energy difference between these two complexes is equal to 0.05–0.17 kcal mol^{−1}). Thus, $Fe(CH_4)^+$ can be considered to be a structurally non-rigid system in which the Fe^+ ion is almost free to migrate around the CH_4 molecule giving structures with the symmetry



The main forces that stabilise the $Fe(CH_4)^+$ complex are the dispersion interaction and the 'ion-induced dipole' interaction. Study of the back reaction $Fe^+ + CH_4$ demonstrated that Fe^+ in the ground state ($^6D, 3d^6 4s^1$) forms the ion–molecular $Fe(CH_4)^+$ complex in the sextet state ($^6A_2$) with a binding energy of

15.5 kcal mol^{−1}, which does not participate in subsequent transformations.

The structure in which methane is coordinated to Fe^+ by only one hydrogen atom (η^1) is energetically less favorable than the η^2 - or η^3 -structures.⁵⁵ More recent calculations⁵⁶ by the DFT method in the B3LYP approximation point to a η^2 -coordination of methane in the $Fe(CH_4)^+$ complex; however, the values for the $Fe^+–CH_4$ binding energy obtained in this study do not correspond to experimental results.

Of all the methane–bare metal ion systems studied in the gas phase, the $CH_4–Co^+$ system has been studied in most detail.^{57–62} The temperature-dependent equilibria of gas-phase reactions were investigated by mass spectrometry; the ion–ligand binding energies in the $Co(CH_4)_n^+$ complexes ($n = 1–4$) were determined. In the case of $Co(CH_4)^+$, the dissociation energy is equal to 22.9 ± 0.7 kcal mol^{−1} (see Ref. 57).

According to MCPF calculations with electron correlation,⁵⁸ methane is coordinated by the Co^+ ion through two or three hydrogen atoms, the complex with η^2 -coordination being 1.3 kcal mol^{−1} more stable than the complex with η^3 -coordination. The dissociation energy of the $Co(\eta^2-CH_4)^+$ complex found by these calculations is 21.4 kcal mol^{−1}. The Co^+ ion in this complex has a d^8 electron configuration. The researchers noted a substantial change in the methane geometry in the η^2 -complex compared to free methane, in particular, the C–H_b bond lengths increase by 0.016 Å and the Co–H_b–C angle increases by 10.3°. The C–H_t bond lengths change slightly. This change in the methane geometry diminishes the energy of the complex by 2.9 kcal mol^{−1}. In the η^3 -complex, the methane geometry changes to a lesser extent; consequently, the bond strength increases by only 1.1 kcal mol^{−1} (see Ref. 58). In the researchers' opinion,⁵⁸ the strength of the $Co^+–CH_4$ bond is mainly determined by the charge-induced polarisation. However, if the contribution of only this effect is taken into account, the η^3 -conformation should be somewhat more stable than the η^2 -conformation (18.2 and 17.7 kcal mol^{−1}, respectively). When other factors such as electron repulsion according to the Pauli principle, charge transfer from methane to Co^+ , and polarisation of metal non-bonding orbitals are also taken into account, the order of stability for these two conformations is reversed.⁵⁸

The mechanism of the reaction

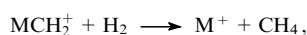


has been studied by the CASSCF and MR-SDCI-CASSCF methods.^{59, 60} It was found that cleavage of the H–H bond is the first to occur; this is followed by the formation of the ion–molecular $Co(CH_4)^+$ complex with a stabilisation energy of 19–22 kcal mol^{−1}. The back reaction $Co^+ + CH_4$ gives only one product, $Co(CH_4)^+$, at moderate temperatures. The researchers calculated the metal–ligand binding energies in the $Co(CH_4)^+$ complexes with C_{2v} and C_{3v} symmetry. The C–H_b and C–H_t bond lengths are nearly equal in the complexes with both types of symmetry, whereas the Co–H_b bond is much longer in the C_{3v} than in the C_{2v} structure. The calculations using the Hay–Wadt effective potential have shown that the two structures are nearly degenerate and it is difficult to choose which of them is more favourable. However, the calculations by the above-mentioned methods in the SKBJ approximation have shown that the C_{2v} structure is much more favourable (by 6.5 kcal mol^{−1}) than the C_{3v} -symmetric structure. The η^1 -structure in which Co^+ is coordinated to one hydrogen atom is 15–16 kcal mol^{−1} less favourable than η^2 - or η^3 -structures.^{59, 60}

The energies of successive elimination of the ligands from the $Co(CH_4)_n^+$ ($n = 1–4$) complexes have been determined both experimentally and theoretically.⁶¹ Study of the collision-induced dissociation of $Co(CH_4)_n^+$ complexes gave a dissociation energy of the Co–CH₄⁺ bond $D_0(Co–CH_4)^+ = 21.45 \pm 1.38$ kcal mol^{−1}, which is close to the value found previously.⁵⁷ These results are in good agreement with the results of *ab initio* calculations (MCPF method), which gave the value $D_e(Co–CH_4)^+ = 21.45$ kcal

mol^{-1} . According to calculations,⁶¹ the methane ligands in the $\text{Co}(\eta^2\text{-CH}_4)_n^+$ complexes ($n = 1-4$) are bound electrostatically to the Co^+ ion in the ground state ($^3\text{F}, 3\text{d}^8$). The structures with η^3 -coordination of the methane ligand are energetically somewhat less favourable.⁶¹

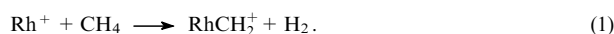
Study of the reactions



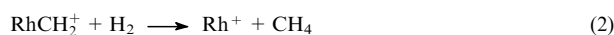
$\text{M} = \text{Co}, \text{Rh}$

by the density functional method with Becke's exchange potential and Perdew's correlation potential (B3P86)⁶² led to the conclusion that the reaction $\text{CoCH}_2^+ + \text{H}_2$ proceeds by a four-centre mechanism in the triplet state. In the complex formed upon the addition of hydrogen, methane is coordinated to cobalt in the bidentate manner. According to these calculations, the $\text{Co}(\eta^2\text{-CH}_4)^+$ complex corresponds to a global minimum on the PES, and its dissociation to give Co^+ and CH_4 requires $22.4 \text{ kcal mol}^{-1}$.

The reaction of Rh^+ with CH_4 was studied by guided-ion beams mass spectrometry (GIBMS).⁶³ This endothermic reaction was found to give ionic products, RhH^+ and RhCH_x^+ ($x = 0-3$). For low energies of the reactants, methane dehydrogenation is the predominant process



However, direct experimental data on the mechanism of the $\text{Rh}^+ + \text{CH}_4$ reaction are missing because the method used is unable to disclose mechanistic details. Therefore, considerable attention was devoted to quantum-chemical studies of methane activation by the Rh^+ ion.^{49, 60, 62, 64, 65} The PES of the reaction



was studied by the CASSCF and MR-SDCI-CASSCF methods.^{60, 64}

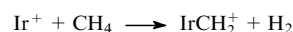
It was found that the first stage of the reaction gives the ion-molecular $(\text{H}_2)\text{RhCH}_2^+$ complex, which is then converted into HRhCH_3^+ upon cleavage of the $\text{H}-\text{H}$ bond. The latter complex rearranges into $\text{Rh}(\eta^2\text{-CH}_4)^+$, probably, without a barrier. This complex is more stable than the products of its dissociation, $\text{Rh}^+(^3\text{F})$ and CH_4 , by $16.8 \text{ kcal mol}^{-1}$. The $\text{Rh}(\text{CH}_4)^+$ structures with η^2 - and η^3 -coordination of methane differ little in energy but the C_{2v} -symmetric structure is more stable. The $\text{C}-\text{H}_\text{b}$ bond lengths in $\text{Rh}(\eta^2\text{-CH}_4)^+$ are longer than $\text{C}-\text{H}_\text{t}$ by $0.01-0.02 \text{ \AA}$.^{60, 64} Modified coupled pair functional calculations⁴⁹ also demonstrated that the η^2 -coordination of methane in the $\text{Rh}(\text{CH}_4)^+$ complex is most favourable (the $\text{Rh}-\text{CH}_4$ binding energy is $\sim 13 \text{ kcal mol}^{-1}$).⁴⁹

The potential energy surface of reaction (2) has been studied by the DFT approach in the B3P86 approximation.⁶² The Rh^+ cation occurs in the ground state $^3\text{F}, 4\text{d}^8$, and the initial steps of the $\text{RhCH}_2^+ + \text{H}_2$ reaction take place on a triplet potential surface. It was found that the HRhCH_3^+ intermediate formed in this reaction is unstable and rearranges without a barrier into $\text{Rh}(\eta^2\text{-CH}_4)^+$. The final complex corresponds to an absolute minimum on the PES with respect to any other critical point of the PES for both the triplet and singlet states of the Rh^+ ion. Dissociation of the $\text{Rh}(\eta^2\text{-CH}_4)^+$ complex to give Rh^+ and CH_4 requires $13.9 \text{ kcal mol}^{-1}$ (see Ref. 62). The researchers cited⁶² note that the results of PES calculations they obtained for this reaction are in good agreement with experimental data, unlike the results obtained in another study.⁶⁴

The potential energy surface for endothermic reaction (1) was studied by the density functional approach in the B3LYP approximation using the Hay-Wadt effective potential and by the MCPF method in the PCI-80 approximation.⁶⁵ The first stage gives the $\text{Rh}(\text{CH}_4)^+$ complex with electrostatic binding. The triplet state of this complex is more stable than the ground states of the reactants by 14.2 (PCI-80) or $11.5 \text{ kcal mol}^{-1}$ (B3LYP). The calculated⁶⁵ values for the $\text{Rh}-\text{CH}_4$ binding energy in $\text{Rh}(\text{CH}_4)^+$ are consistent with the results of calculations carried

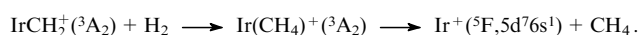
out by other researchers.^{62, 64} However, in Ref. 65 considering the $\text{Rh}(\text{CH}_4)^+$ molecular complex with C_s symmetry, methane was assumed to have a distorted η^3 -coordination, which was found to be more stable than the η^2 -coordination by $0.9 \text{ kcal mol}^{-1}$. Meanwhile, the latter was proposed as the coordination of choice in the other two studies.^{62, 64}

It has been noted above that the Ir^+ ion is most efficient, among transition metal ions, in the gas-phase methane dehydrogenation.³⁴ A theoretical investigation [Hartree-Fock method with singly and doubly excited configurations (HFSD)]⁶⁶ of the reaction profile for



has shown that the reaction of the Ir^+ ion in the ground state ($^5\text{F}, 5\text{d}^7 6\text{s}^1$) with methane yields initially an ion-molecular complex $\text{Ir}(\eta^2\text{-CH}_4)^+$ with weak binding. However, due to the intersection of PES for the triplet and quintet states, the spin state of iridium changes, which results in the formation of a triplet ion-molecular complex $\text{Ir}(\eta^2\text{-CH}_4)^+$ with stronger bonds ($^3\text{B}_2, \text{C}_{2v}$). The stabilisation energy of this complex with respect to the ground states of the reactants [$\text{Ir}^+(^5\text{F}, 5\text{d}^7 6\text{s}^1) + \text{CH}_4$] amounts to $20.4 \text{ kcal mol}^{-1}$. The energy of the triplet η^3 -complex ($^3\text{E}, \text{C}_{3v}$) is 4 kcal mol^{-1} higher than the energy of the η^2 -complex.⁶⁶

The CASSCF and MR-SDCI-CASSCF methods were used⁶⁰ to study the PES of the reaction



Unlike the exothermic reactions of the carbene complexes of cobalt and rhodium with hydrogen, this reaction with iridium is endothermic. The $\text{Ir}(\text{CH}_4)^+(^3\text{A}_2)$ complex is ~ 15.7 (26.4) kcal mol^{-1} more stable than the products of its dissociation, $\text{Ir}^+(^5\text{F}, 5\text{d}^7 6\text{s}^1)$ and CH_4 . The structures of $\text{Ir}(\text{CH}_4)^+$ with C_{2v} and C_{3v} symmetry are rather similar in energy. The back reaction $\text{Ir}^+ + \text{CH}_4$ yields initially the $\text{Ir}(\text{CH}_4)^+$ complex and then the HIrCH_3^+ methyl hydride complex and the $(\text{H})_2\text{IrCH}_2^+$ bis(hydrido)carbene complex.⁶⁰

The Pt^+ cation is only slightly inferior to Ir^+ regarding the efficiency of methane dehydrogenation.³⁴ Several studies dealing with reactions of methane with this cation have been reported.⁶⁷⁻⁷⁰ One publication presents a theoretical and experimental (guided ion beam tandem mass spectrometry, GIBTMS) study of the activation of methane by the Pt^+ ion.⁶⁷ The dehydrogenation of CH_4 by thermalised Pt^+ cations ($\text{Pt}^+ + \text{CH}_4 \longrightarrow \text{PtCH}_2^+ + \text{H}_2$) proceeds on a doublet PES of the ground state of the ion. The reaction is reversible under conditions of ion-cyclotron mass spectrometry (FTICR-MS). The insertion of the Pt^+ cation in the ground state ($^2\text{D}, 5\text{d}^9$) into the methane $\text{C}-\text{H}$ bond occurs *via* the formation of the $\text{Pt}(\eta^3\text{-CH}_4)^+$ complex, which is transformed with a negligibly low activation barrier ($1.3 \text{ kcal mol}^{-1}$) to give the methyl hydride HPtCH_3^+ complex. This complex corresponds to a global energy minimum on the PES. The $\text{Pt}(\eta^2\text{-CH}_4)^+$ and $\text{Pt}(\eta^3\text{-CH}_4)^+$ complexes are transition states; they are matched by saddle points on the reaction PES. According to calculations,⁶⁷ the ion-ligand binding energy in the $\text{Pt}(\eta^3\text{-CH}_4)^+$ complex is equal to $28.3 \text{ kcal mol}^{-1}$. In the researchers' opinion,⁶⁷ no structures of this type have been considered previously in theoretical investigations of $\text{M}(\text{CH}_4)^+$ complexes.

An experimental and theoretical study of the oxidation of methane by oxygen in the presence of the Pt^+ cation as the catalyst has been reported.⁶⁸ The first step of the process is the formation of electrostatically bound complex $\text{Pt}(\eta^3\text{-CH}_4)^+$ with C_s symmetry. The ion-ligand binding energy is equal to 19.2 (B3LYP) and $25.4 \text{ kcal mol}^{-1}$ (PCI-80). Calculations⁶⁸ using a fuller basis set than those reported in the publication discussed above⁶⁷ also showed the presence of a C_{2v} -symmetric structure very close in energy to the C_s structure. Unfortunately, no energetic or geometric parameters for the $\text{Pt}(\eta^2\text{-CH}_4)^+$ complex are given in the publication.⁶⁸

The reactions of argon complexes of platinum ions PtAr_m^+ ($m = 1-6$) with CH_4 and CD_4 were studied experimentally by the FTICR-MS method and theoretically by the density functional approach in the B3LYP approximation.⁶⁹ The PtAr_m^+ complexes ($m = 2-6$) enter into ligand exchange reactions in which up to four argon atoms can be replaced by methane molecules. Conversely, the bare Pt^+ ion and the PtAr^+ complex react with methane to give PtCH_2^+ . The intermediate formation of the $\text{Pt}(\text{CH}_4)^+$ complexes in the $\text{Pt}^+ + \text{CH}_4$ and $\text{PtAr}^+ + \text{CH}_4$ reactions is confirmed by peaks of these complexes observed experimentally in the mass spectra. It was noted⁶⁹ that the results of calculations of the geometric and energetic parameters of the $\text{Pt}(\text{CH}_4)^+$ complexes with predominating 'ion-induced dipole' interaction depend appreciably on the basis set chosen. As expected, the geometric parameters of these complexes calculated using polarisation functions and without these functions are substantially different.⁶⁹

The results of a combined experimental (GIBMS) and theoretical (DFT/B3LYP) investigation of the $\text{Pt}^+ + \text{CH}_4$ and $\text{PtCH}_2^+ + \text{H}_2$ reactions and collision-induced dissociation of $\text{Pt}(\text{CH}_4)^+$ upon the reaction with xenon have been reported.⁷⁰ For the $\text{Pt}^+ + \text{CH}_4$ system, it was found that the only process observed at low temperatures is effective exothermic dehydrogenation of methane giving rise to $\text{PtCH}_2^+ + \text{H}_2$. The reaction starts with the formation of the $\text{Pt}(\text{CH}_4)^+$ complex due to the 'ion-induced dipole' interaction. The depth of the potential well for the $\text{Pt}(\text{CH}_4)^+$ adduct with respect to the reactants is $\sim 20 \text{ kcal mol}^{-1}$ (0.9 eV). The geometric parameters of the $\text{Pt}(\text{CH}_4)^+$ complex were not reported.

A number of publications⁷¹⁻⁷⁴ report a theoretical study of the methane adduct with the Cu^+ cation with the filled d-electron shell. This adduct is of interest because it involves interaction of two species having filled electron shells, namely, the Cu^+ ion with a formal d^{10} configuration and a fully saturated hydrocarbon (CH_4). The *ab initio* SCF method with different basis sets was used⁷¹ to calculate the geometry and the relative energetic characteristics for various structures of $\text{Cu}(\text{CH}_4)^+$. This complex was shown to be stable against unimolecular decomposition. It was suggested that it can exist in the isolated state in inert matrices. At the given theoretical level, the tridentate coordination of the CH_4 molecule, characterised by a $\text{Cu}-\text{CH}_4$ binding energy of $9.8 \text{ kcal mol}^{-1}$, was shown to be the most favourable for the $\text{Cu}(\text{CH}_4)^+$ ion. The complexes with bi- and monodentate types of coordination of methane are higher in energy than the η^3 -complex

by 3.8 and 5 kcal mol^{-1} , respectively. At moderately high temperatures, the Cu^+ cation can migrate quasi-freely around the methane molecule.⁷¹

The electronic structure and the geometric parameters of the $\text{Cu}(\text{CH}_4)^+$ adduct were also calculated by the SCF method in the approximation of linear combination of gaussian orbitals (LCGO-SCF) and by the MP2 method.⁷² The $\text{Cu}(\text{CH}_4)^+$ complex was found to be stable with respect to the reactants. The metal-ligand binding is mainly due to electrostatic interactions. The geometry optimisation for $\text{Cu}(\text{CH}_4)^+$ resulted in a C_{3v} -symmetric structure with a rotation axis. In the $\text{Cu}(\eta^3\text{-CH}_4)^+$ complex, the Cu, C and H_i atoms are located on the rotation axis, while the other three hydrogen atoms are arranged to form an 'umbrella' pointing towards the copper ion. The dissociation energy of this complex is $9.3 \text{ kcal mol}^{-1}$ (SCF) or $16.6 \text{ kcal mol}^{-1}$ (MP2).⁷²

The full optimisation of the complex geometry at the SCF level with the use of analytical methods to calculate the first and second derivatives (the GRADSCF method) has also led to an η^3 -structure.⁷³ It was noted that metal-ligand binding in $\text{Cu}(\text{CH}_4)^+$ is mainly electrostatic; therefore, it is not surprising that the geometric structure of the methane ligand differs little from the structure of free methane. The C-H distances in methane change by not more than $0.01 \text{ \AA}$ upon complexation. Other geometric parameters of the complex were not reported. The energy of the $\text{Cu}-\text{CH}_4$ bond for this structure determined by MCPF calculations is equal to $14.8 \text{ kcal mol}^{-1}$. It was suggested⁷³ that this value is understated by $\sim 5 \text{ kcal mol}^{-1}$ due to the limited basis set and incomplete allowance made for the correlation interaction.

In another study,⁷⁴ where the geometry of $\text{Cu}(\text{CH}_4)^+$ was optimised by the MP2 method with fuller basis sets, a structure with bidentate coordination was found to be most stable; in particular, more stable than the η^3 -structure by $0.3-1.2 \text{ kcal mol}^{-1}$. Comparison of these results⁷⁴ with the results of earlier calculations⁷¹⁻⁷³ provides the conclusion that with the extension of the basis set and more perfect allowance for the electron correlation for the Cu^+ (d^{10}) ion, the η^2 -coordination of methane to Cu^+ would prove to be preferred. The researchers believe that the electrostatic interaction promotes η^3 -coordination to the Cu^+ ion, whereas the dative interaction is favourable for the formation of the η^2 -complex.⁷⁴

The dissociation energies of the $\text{M}(\text{CH}_4)^+$ complexes determined experimentally and the calculated geometric parameters

Table 1. Results of experimental and theoretical studies of the $\text{M}(\text{CH}_4)^+$ complexes.

Complex	Electronic state and term of the ion	Symmetry	Bond lengths / $\text{\AA}$			The M-C-H _b angle /deg	E_{bd}^a / kcal mol^{-1}	Calculation techniques (programs); investigation methods	Ref.
			M...C	M-H _b	C-H _b (C-H _i)				
$\text{Li}(\eta^3\text{-CH}_4)^+$	$^1\text{S}, 1s^2$	C_{3v}	2.25	—	—	—	—	RHF/SKBJ (GAMESS)	36
$\text{Li}(\eta^3\text{-CH}_4)^+$	$^1\text{S}, 1s^2$	C_{3v}	2.33	[2.27]	1.096	—	8.2	<i>ab initio</i> Hartree-Fock method	37
$\text{Li}(\eta^3\text{-CH}_4)^+$	$^1\text{S}, 1s^2$	C_{3v}	2.195	2.165	1.098	—	$< 10-12$	} QCISD(T)/MP2 (GAUSSIAN92, 94) photoelectron spectroscopy; SCF, MP2 (GAUSSIAN90); MCPF (MOLECULE-SWEDEN)	38, 39, 40
$\text{Na}(\eta^3\text{-CH}_4)^+$	$^1\text{S}, 2p^6$	C_{3v}	2.631	2.541	1.095	—	$< 10-12$		
$\text{Mg}(\eta^3\text{-CH}_4)^+$ (see b)	$^2\text{S}, 3s^1$	C_{3v}	2.65	—	—	—	4.0 (SCF)		
			2.54	—	—	—	7.6 (MP2)		
$\text{Sc}(\eta^3\text{-CH}_4)^+$	$^3\text{D}, 3d^1 4s^1$	C_{3v}	2.785	[2.691]	1.087	73.72	15.1	} CASSCF (GAMESS, MOLPRO), MR-SDCI-CASSCF (MOLPRO)	42
$\text{Sc}(\eta^2\text{-CH}_4)^+$	$^1\text{D}, 3d^1 4s^1$	C_{2v}	4.281	[3.776]	1.085	55.59	13.1		
$\text{Sc}(\eta^3\text{-CH}_4)^+$	$^3\text{D}, 3d^1 4s^1$	C_{3v}	2.025	—	—	—	15.7	} DFT/B3LYP (GAUSSIAN94/DFT) MP2/6-31G** (GAUSSIAN92W)	43, 45
$\text{Sc}(\eta^3\text{-CH}_4)^+$	$^1\text{D}, 3d^1 4s^1$	C_{3v}	2.411	—	—	—	8.4 (3.8 rel. to ^3D)		
$\text{Ti}(\eta^3\text{-CH}_4)^+$	$^2\text{F}, 3d^2 4s^1$	C_{3v}	2.751	[2.526]	1.093	74.1	73.1		

Table 1 (continued).

Complex	Electronic state and term of the ion	Symmetry	Bond lengths /Å			The M—C—H _b angle /deg	E_{bd}^{a} /kcal mol ⁻¹	Calculation techniques (programs); investigation methods	Ref.
			M...C	M—H _b	C—H _b (C—H _i)				
Ti(η^3 -CH ₄) ⁺	² F, 3d ² 4s ¹	C _{3v}	2.354	—	—	75.0	21.81	DFT/B3LYP (GAUSSIAN94/DFT)	46
Ti(η^3 -CH ₄) ⁺	⁴ F, 3d ² 4s ¹	C _{3v}	2.350	—	—	74.0	22.21		
V(CH ₄) ⁺	⁵ D, 3d ⁴	—	—	—	—	—	(15.0)(for ⁵ D, 3d ⁴)	resonance single-photon photodissociation spectroscopy	48
	⁵ P ₂ , 3d ³ 4s ¹	—	—	—	—	—	(8.3)(for ⁵ P ₂ , 3d ³ 4s ¹)		
V(η^2 -CH ₄) ⁺	⁵ D, 3d ⁴	C _{2v}	2.485	—	—	59.0	15.09	DFT/B3LYP (GAUSSIAN94/DFT)	46
V(η^3 -CH ₄) ⁺	³ F, 3d ³ 4s ¹	C _{3v}	2.259	—	—	88.6	16.68		
Nb(η^2 -CH ₄) ⁺ (see ^b)	⁵ D, 4d ⁴	C _{2v}	2.65	—	—	—	11.8	SCF/MCPF (GAMESS)	49
Ta(η^3 -CH ₄) ⁺ (see ^b)	⁵ F, 5d ³ 6s ¹	C _s	3.199	[2.924]	1.096 (1.093)	73.02	12	DFT/B3LYP (GAUSSIAN94)	52
Cr(η^3 -CH ₄) ⁺	⁶ S, 3d ⁵	C _{3v}	2.361	—	—	75.8	13.1	DFT/B3LYP (GAUSSIAN94/DFT)	46
Cr(η^3 -CH ₄) ⁺	⁴ D, 3d ⁴ 4s ¹	C _{3v}	2.296	—	—	75.5	29.31		
Fe(CH ₄) ⁺ , Fe(CH ₄) _n ⁺ (n = 1–4)	⁶ D, 3d ⁶ 4s ¹	—	—	—	—	—	(13.7 ± 0.8)	mass spectrometry	53
Fe(CH ₄) ⁺	—	—	—	—	—	—	(13.6 ± 0.9)	mass spectrometry	54
Fe(η^2 -CH ₄) ⁺	⁶ D, 3d ⁶ 4s ¹	C _{2v}	3.433	[2.871]	1.088 (1.080)	56.4	15.5	CASSCF (GAMESS), MR-SDCI-CASSCF (MOLPRO)	55
Fe(η^3 -CH ₄) ⁺	⁶ D, 3d ⁶ 4s ¹	C _{3v}	3.12	[2.88]	1.086 (1.081)	74.72 {180 (Fe—C—H _i)}	~ 15.5		
Fe(η^2 -CH ₄) ⁺	⁴ F, 3d ⁷	C _{2v}	2.373	—	—	58	[24.5]	DFT/B3LYP (GAUSSIAN94)	56
Fe(η^2 -CH ₄) ⁺	⁶ D, 3d ⁶ 4s ¹	C _{2v}	2.780	—	—	58	[5.9]		
Co(CH ₄) ⁺ , Co(CH ₄) _n ⁺ (n = 1–3)	—	—	—	—	—	—	(22.9 ± 0.7)	mass spectrometry	57
Co(η^2 -CH ₄) ⁺	³ F, 3d ⁸	C _{2v}	2.24	1.94	[1.109]	[~ 60]	21.4	MCPF (GVB, MOLECULE-SWEDEN)	58
Co(η^3 -CH ₄) ⁺	³ F, 3d ⁸	C _{3v}	2.11	2.11	—	—	20.1		
Co(η^2 -CH ₄) ⁺	³ F, 3d ⁸	C _{2v}	2.608	2.229	1.093 (1.078)	57.9	19–22	CASSCF (GAMESS),	59, 60
Co(η^3 -CH ₄) ⁺	³ F, 3d ⁸	C _{3v}	2.370	2.313	1.092 (1.078)	73.6	15.5–22.3	MR-SDCI-CASSCF (MOLPRO)	
Co(η^2 -CH ₄) ⁺ (see ^b)	³ F, 3d ⁸	C _{2v}	2.24	—	—	—	(21.4 ± 1.4) 17.3	mass spectrometry, MCPF (GVB, MOLECULE-SWEDEN)	61
Co(η^2 -CH ₄) ⁺	³ F, 3d ⁸	C _{2v}	2.034	1.810	1.152 (1.101)	62.1	22.4	DFT/B3P86 (Dgauss)	62
Rh(η^2 -CH ₄) ⁺	³ F, 4d ⁸	C _{2v}	2.829	2.427	1.092 (1.078)	57.65	16.8	CASSCF (GAMESS), MR-SDCI-CASSCF (MOLPRO)	60, 64
Rh(η^3 -CH ₄) ⁺	³ F, 4d ⁸	C _{3v}	2.515	2.440	1.085 (1.076)	73.52	13.8–13.9		
Rh(η^2 -CH ₄) ⁺	³ F, 4d ⁸	C _{2v}	2.65	—	—	—	13	SCF/MCPF (GAMESS);	49
Rh(η^2 -CH ₄) ⁺	³ F, 4d ⁸	C _{2v}	2.347	2.083	1.132 (1.101)	62.6	13.9	GRADSCF, DFT/B3P86 (Dgauss)	62
Rh(η_3^1 -CH ₄) ⁺	—	C _s	2.536	[< 2.33]	1.132 (1.098)	—	11.5 (B3LYP) 14.2 (MCPF)	DFT/B3LYP, MCPF (STOCKHOLM)	65
Ir(η^2 -CH ₄) ⁺	see text	C _{2v}	2.47	[2.016]	—	59.15 {112.3 (H ₁ —C—H _i)}	20.4	HFSD, MCPF (GVB, MOLECULE-SWEDEN)	66
Ir(η^2 -CH ₄) ⁺	see text	C _{2v}	2.754	2.370	1.095 (1.079)	58.33	6.0; 18.2	CASSCF (GAMESS), MR-SDCI-CASSCF (MOLPRO)	60
Ir(η^3 -CH ₄) ⁺	see text	C _{3v}	2.794	2.705	1.087 (1.084)	74.44	—		
Pt(η_3^1 -CH ₄) ⁺	² D, 5d ⁹	C _s	2.258	1.700	1.229	[53.25]	28.3	DFT/B3LYP (GAUSSIAN92)	67
Pt(η_3^1 -CH ₄) ⁺	—	C _s	2.36	1.83	1.19	[53.24]	25.4 (PCI-80) 19.2 (B3LYP)	mass spectrometry, MCPF (STOCKHOLM),	68
Pt(η^2 -CH ₄) ⁺	—	C _{2v}	—	—	—	—	—	DFT/B3LYP (GAUSSIAN94)	

Table 1 (continued).

Complex	Electronic state and term of the ion	Symmetry	Bond lengths /Å			The M—C—H _b angle /deg	<i>E</i> _{bd} ^a /kcal mol ⁻¹	Calculation techniques (programs); investigation methods	Ref.
			M...C	M—H _b	C—H _b (C—H _i)				
Pt(η ¹ -CH ₄) ⁺	—	—	2.28	1.71	1.22	[52.71]	30.12	mass spectrometry, DFT/B3LYP (GAUSSIAN94)	69
Pt(CH ₄) ⁺	—	—	—	—	—	—	(19.67–21.06)	mass spectrometry, DFT/B3LYP (GAUSSIAN98)	70
Cu(η ³ -CH ₄) ⁺ (see ^b)	¹ S,3d ¹⁰	C _{3v}	2.44	[2.37]	1.10 (1.09)	73.5	9.8	SCF (GAUSSIAN80)	71
Cu(η ³ -CH ₄) ⁺ (see ^b)	¹ S,3d ¹⁰	C _{3v}	4.489	[4.186]	1.077 (1.065)	74.36	9.3 (SCF) } 16.6 (MP2) }	SCF-CI, MP2	72
Cu(η ³ -CH ₄) ⁺ (see ^b)	¹ S,3d ¹⁰	C _{3v}	—	—	—	—	14.8 (MCPF)	MCPF, GRADSCF (MOLECULE-SWEDEN)	73
Cu(η ² -CH ₄) ⁺	¹ S,3d ¹⁰	C _{2v}	[2.41]	1.944	1.108	58.9	16.8–21.43	MP2, CCSD(T) (GAUSSIAN90)	74

Note. The values in brackets are the distances and the angles calculated by the author of the review using data from the cited publications.

^a The methane—cation bond energy in the complex. The values in parentheses are experimental data. ^b The complex is formed due to weak electrostatic interactions. The CH₄ ligand is slightly distorted with respect to non-coordinated methane.

Li — η ³	Be											B
Na — η ³	Mg — η ³											Al
K	Ca	Sc — η ³	Ti — η ³	V — η ² , η ³	Cr — η ³	Mn	Fe η ³ (Fe ⁰ d ⁶ s ²) η ² ~ η ³	Co η ³ (Co ⁰ d ⁷ s ²) η ²	Ni	Cu — η ²	Zn	Ga
Rb	Sr	Y	Zr	Nb — η ²	Mo	Tc	Ru	Rh η ² (Rh ⁰ d ⁹) η ² , η ³	Pd η ² (Pd ⁰ d ¹⁰) η ²	Ag	Cd	In
Cs	Ba	Lu	Hf	Ta — η ³	W	Re	Os	Ir — η ²	Pt η ² (Pt ⁰ d ¹⁰) η ³ ~ η ²	Au	Hg	Tl

Figure 2. Dependence of the modes of coordination of the CH₄ ligands in the complexes M⁰(CH₄) and M⁺(CH₄) on the nature of the complexing metal (the upper line gives the data for complexes of neutral atoms and the lower line, for cation complexes).

and M—CH₄ binding energies are summarised in Table 1. The dependence of the mode of coordination of CH₄ ligands on the nature of the complexing metal in the M(CH₄)⁰ and M(CH₄)⁺ complexes is shown in Fig. 2.

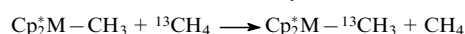
IV. Methane complexes with the molecular fragments ML_n

Complexes of many transition metals are able to react with saturated hydrocarbons under certain conditions in solutions, thus activating the C—H bonds. The activation of alkanes can follow different mechanisms. Complexes containing metals in high oxidation states with a d⁰ electron configuration tend to undergo cycloaddition of alkanes to a single or multiple metal—ligand bond (σ-bond metathesis and 1,2-addition, respectively). Transition metal complexes with a dⁿ electron configuration of the metal are prone to enter into electrophilic substitution or oxidative addition of alkane to the central atom of the complex.^{2–12} The activation of alkanes by complexes of platinum group metals, especially rhodium and iridium, has been studied most comprehensively. Presumably, complexes with alkane molecules as ligands are formed as intermediates in these reactions.^{13–18}

Apart from experimental studies, considerable attention has been devoted to the theoretical investigation of the mechanisms of these reactions, in particular, by quantum-chemical methods.

1. Complexes with the d⁰ electron configuration of the complex-forming ion

It was found experimentally that organometallic compounds of early transition metals (lanthanides, actinides) in higher oxidation states are able to activate the C—H bonds in alkanes according to the mechanism of σ-bond metathesis. The first example of this type of reaction was described by Patricia Watson in 1983.⁷⁵

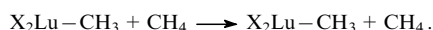
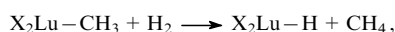


M = Y, Lu; Cp* = η⁵-C₅Me₅.

Subsequently, other similar systems have been found and studied in detail.^{11,76–79} Metathesis of σ-bonds is highly selective with respect to the sterically least hindered C—H bonds at the primary carbon atom. The selectivity is so high that it is possible to use cyclohexane as an inert solvent to study these reactions.^{5,7}

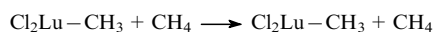
A number of publications^{80–82} have been devoted to quantum-chemical investigations of the mechanism of σ-bond metathesis. The activation of the H—H and C—H bonds in the

$X_2LuCH_3 + H_2$ and $X_2LuCH_3 + CH_4$ systems was studied by the density functional approach with different potentials.⁸⁰



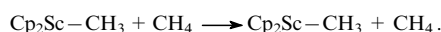
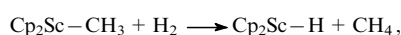
In this study, the Cp_2^*Lu fragment of the $Cp_2^*LuCH_3$ complex used in experiments, was modelled by the Cl_2Lu species. It was found that both reactions involve the formation of a highly ordered four-centre transition state with a negative activation entropy. The weakly bound methane adduct $Cl_2LuH(\eta_3^1-CH_4)$ with a binding energy of $1.96 \text{ kcal mol}^{-1}$ with respect to the final products, Cl_2LuH and CH_4 , is formed as the intermediate compound in hydrogenolysis.

The exchange reaction



has a high activation barrier and proceeds *via* the adduct $Cl_2Lu(CH_3)(\eta_1^1-CH_4)$, which is $4.64 \text{ kcal mol}^{-1}$ less stable than the initial reactants (Cl_2LuCH_3 and CH_4). The methane fragments in the η_3^1 and η_2^1 adducts are distorted only slightly compared to free methane.

The density functional approach in the B3P86 approximation has been used⁸¹ to study the energy profiles of hydrogenolysis and methyl-group exchange for the Cp_2ScCH_3 complex.



After the initial formation of the Cp_2ScCH_3 adduct with H_2 , the energetic profile of hydrogenolysis leads, *via* a transition state, to the $Cp_2ScH(\eta_3^1-CH_4)$ adduct. The methane ligand in this complex has a distorted tridentate coordination. The bridging C–H_b bonds (1.14 and 1.11 Å) are elongated compared to the C–H bonds in free methane. The binding energy of methane in the $Cp_2ScH(\eta_3^1-CH_4)$ complex is $4.78 \text{ kcal mol}^{-1}$ relative to the products (Cp_2ScH and CH_4). The exchange by methyl groups proceeds *via* the adduct $Cp_2Sc(CH_3)(\eta^2-CH_4)$ with a binding energy of $5.97 \text{ kcal mol}^{-1}$. Comparison of the hydrogenolysis and methyl exchange processes for scandium and lutetium complexes shows that the replacement of hydrogen in X_2M-Y ($M = Sc, Lu$; $X = Cp, Cl$; $Y = H, CH_3$) by a bulkier CH_3 group entails a change in the mode of coordination of the methane ligand from the tridentate (or distorted tridentate) coordination found in the $X_2MH(CH_4)$ complex to a bidentate one in the $X_2M(CH_3)(CH_4)$ complex. This replacement also results in a longer M–CH₄ bond, apparently, due to steric factors (the geometric parameters of the complexes were optimised without non-local corrections).

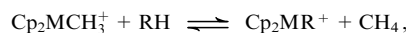
The activation of methane by model compounds Cl_2LnZ ($Z = H, CH_3$) has been studied for the whole lanthanide row⁸² by the density functional method using the hybrid B3PW91 functional. These compounds were assumed to be rather good models for bis(pentamethylcyclopentadienyl) complexes Cp_2^*LnZ . The obtained results appear to cast doubt on the possibility of intermediate formation of the $Cp_2^*LnZ(CH_4)$ complexes in these reactions. The researchers believe that the process of methane activation can be represented in this case as proton transfer between two anionic groups coordinated to Ln atoms.

It is well-known that Ziegler–Natta catalysts and metallocene catalysts for polymerisation of α -olefins can react with methane and that methane can be used to terminate the growth of polymer chains to control the molecular mass of polymers.⁸³ To elucidate the mechanism of methane activation by metallocene catalysts, the PES for model reactions between methane and $Cp_2M(CH_3)^+$ cations ($M = Ti, Zr$) (σ -bond metathesis) have been studied in detail by the density functional method in the generalised gradient approximation (GGA) using the Perdew, Burke and Ernzerhof (PBE) density functional.^{84,85} The calculations showed that the first stage gives the intermediate σ -complex $Cp_2M(CH_3)$.

$(\eta^2-CH_4)^+$. The complexation energy for the zirconium cation is $9.4 \text{ kcal mol}^{-1}$ and that for the titanium cation is $4.2 \text{ kcal mol}^{-1}$. It was noted that the free energies of complexation (ΔG_{298}) at room temperature are positive with respect to the initial components due to a great entropy contribution; they are $1.5 \text{ kcal mol}^{-1}$ for zirconium and $8.3 \text{ kcal mol}^{-1}$ for titanium.

The reactions of $Cp_2MCH_3^+$ cations with H_2 result directly in the $Cp_2MH(\eta^2-CH_4)^+$ σ -complexes without an activation barrier. The back reaction $Cp_2MH^+ + CH_4$ also includes the intermediate formation of $Cp_2MH(\eta^2-CH_4)^+$ in which the electrons of two C–H_b bridging bonds are involved in binding of the CH_4 molecule to the central metal atom.

Density functional theory calculations in the PBE approximation for the model reaction



$M = Ti(IV), Zr(IV)$; $R = Me, Et, Pr^n, Pr^i$

showed that the reaction of $Cp_2MCH_3^+$ with alkanes proceeds *via* the stage of formation of $Cp_2M(RH)(CH_3)^+$ complexes, which are subsequently isomerised into $Cp_2MR(CH_4)^+$.⁸⁶ The energy of the M–CH₄ bond in the $Cp_2MR(CH_4)^+$ complexes decreases on passing from $R = Me$ to $R = Et, Pr^n$ or Pr^i . This sequence of variation of the bond energy was attributed to the influence of steric factors. In the case of isopropyl ligands, the minima corresponding to the $Cp_2MPri(CH_4)^+$ complexes ($M = Ti, Zr$) could not be found on the PES, as these complexes undergo barrier-free dissociation to give methane and $Cp_2M(Pr^i)^+$. In zirconium complexes, methane is coordinated according to the η^2 mode; in the case of the titanium ion, which is smaller in diameter, according to the η_2^1 mode ($R = Pr^n, Pr^i$), apparently, also due to steric factors. The geometric parameters of methane ligands in these complexes were not reported.⁸⁶

Yet another type of complexes formed by high-valence transition metals able to activate the C–H bonds in alkanes includes compounds with metal–ligand multiple bonds. It has been found experimentally that the imido complexes $L_nM=NR$ formed by transition d^0 metals ($M = Ti, Zr, Ta, V, W$) are able to activate various hydrocarbons including methane.^{87–94} The reaction results in alkane ($R'H$) addition to the highly polarised $M^{\delta+}=N^{\delta-}$ double bond of the complex giving rise to $L_nM(R')(NHR)$. The addition of alkanes to the $M^{\delta+}=N^{\delta-}$ multiple bonds, like the metathesis of σ -bonds, is distinguished by a high degree of selectivity with respect to the primary C–H bonds. It was suggested that high polarity of the metal–imide ligand bond is important for this reaction, as it promotes the subsequent cleavage of the activated C–H bond in the alkane.⁸⁷ Data obtained by isotope labelling are consistent with the intermediate formation of alkane complexes assumed for these reactions.^{91,93,94}

A series of publications have been devoted to theoretical investigation of the mechanism of methane addition to the $M=NR$ multiple bonds.^{36,95–100}

The activation of methane by the imido complexes $H_2M=NH$ ($M = Ti, Zr, Hf$) has been studied *ab initio* (RHF, MP2) methods.⁹⁵ Methane is coordinated by the metal in the η^3 mode to give the $H_2M(=NH)(\eta^3-CH_4)$ charge transfer complex. The hydrogen atoms bound to the metal occur in an eclipsed conformation relative to the $H_2M=NH$ complex. In this complex, the activated C–H bond lies in the same plane as the $M=N$ bond. The geometric parameters of fragments in the $H_2M(=NH)(\eta^3-CH_4)$ complexes are virtually identical to those calculated for free reactants. The calculation results support the hypothesis of an important role of the highly polar $M=N$ bond in this reaction and demonstrate that the formation of the alkane complex increases the polarity of the $C^{\delta-}-H^{\delta+}$ bond. In the free methane molecule, the charge on the carbon atom is $-0.24 e$, while that on the hydrogen atoms is $+0.06 e$. On complexation, the polarity of the C–H bonds increases and the charge on carbon becomes equal to $-0.48 \pm 0.02 e$, and that on hydrogen is $+0.15 \pm 0.01 e$. Due to the reaction, the negatively charged

methyl group is transferred to the central metal atom and the positively charged hydrogen atom migrates to the imide nitrogen atom carrying a negative charge. Thus, the overall process can be regarded as proton transfer between two anionic centres. The calculated energy barriers to the elimination of methane from the $H_2M(CH_3)(NH_2)$ complexes ($M = Ti, Zr, Hf$) are in good agreement with the values found experimentally regarding both the absolute magnitude and the pattern of variation of the magnitude depending on the nature of the central atom.

The structures of methane complexes with monoimides of Group IV metals, bisimides of Group V metals, and trisimides of Group VI metals with a d^0 electron configuration and the $M-CH_4$ binding energies in these compounds have been determined by RHF and MP2 calculations.⁹⁶ It was found that methane adducts with pyramidal bisimides $(NH_2)M(=NH)_2$ ($M = Nb, Ta$) and trisimides $M(=NH)_3$ ($M = Mo, W$) are characterised by rather high bond enthalpies (11–16 kcal mol⁻¹), comparable to those for dihydrogen complexes (Kubas complexes). Meanwhile, the enthalpy of binding of the methane ligand to Group IV metal monoimides is much lower. The coordination of methane is accompanied by the transfer of 0.1–0.3 e from methane to the central metal atom, which results in elongation and polarisation of the $C^{\delta-}-H^{\delta+}$ bond. These data are indicative of the important role of the methane adduct in the subsequent cleavage of the C–H bond.

The charges on the central metal atoms (Z) in the starting imido complexes have been calculated.⁹⁶ According to this calculation, the enthalpy of the $M-CH_4$ bond in Group IV–VI metal imido complexes varies in proportion to the variation of the Z/r^2 ratio, where r is the $M-C$ distance (Table 2). In our opinion, this correlation implies a predominant contribution of electrostatic interaction to the formation of the methane–imido complex bond. In the case of imido complexes of metals with a d^2 electron configuration, no correlation of this type is found; they cannot form adducts with methane due to repulsion between the free electron pair in the metal d orbital and the electrons of the C–H σ -bond.

Table 2. Dependence of the stabilisation enthalpy of methane complexes with metal imides on the charge on the central metal atom and the $M-C$ distance (from the data of Ref. 96).

Complex	Electronic state of M	$M-C$ / Å	$Z(M)^a$	Z/r^2	H_{add} (see ^b)
$Ti(OH)_2(=NH)(\eta^1_2-CH_4)$	d^0	2.84	+1.36	0.169	6.6
$Ti(NH_2)_2(=NH)(\eta^1_2-CH_4)$	d^0	3.10	+1.08	0.112	4.4
$Zr(NH_2)_2(=NH)(\eta^1_2-CH_4)$	d^0	3.05	+1.62	0.174	6.3
$Nb(NH_2)(=NH)_2(\eta^2-CH_4)$	d^0	2.84	+1.48	0.183	11.1
$Ta(NH_2)(=NH)_2(\eta^2-CH_4)$	d^0	2.79	+1.55	0.199	13.6
$Mo(=NH)_3(\eta^1_2-CH_4)$	d^0	2.77	+1.2	0.19	13.7
$W(=NH)_3(\eta^1_2-CH_4)$	d^0	2.72	+1.48	0.224	15.6
$W(OH)_2(=NH)(CH_4)$	d^2	—	+1.54	—	<0
$Os(=NH)_3(CH_4)$	d^2	—	+1.19	—	<0

^a Calculated (Mulliken) charges on the metal atoms in the reactants.

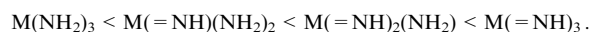
^b In kcal mol⁻¹.

The mechanism of methane activation by Group V metal bisimido complexes has been studied.⁹⁸ Methane adducts with the $(NH_2)M(=NH)_2$ complexes ($M = V, Nb, Ta$) have C_s symmetry; one C–H bond of the methane ligand is arranged above the bisector of the $N=M-N$ angle. The geometric parameters of the fragments in the adducts differ little from those of free molecules. In the Group V metal adducts, methane is considered to be coordinated by an edge, because the $M-H_b$ distances for the two bridging hydrogen atoms are nearly equivalent. The complexes formed by Group V metals, $M(NH_2)(=NH)_2(\eta^2-CH_4)$, differ in the mode of methane coordination from similar complexes derived from Group IV and VI metals, which should rather

be regarded as monodentate complexes with a bent $M-H-C$ bridge, $M(NH_2)_2(=NH)(\eta^1_2-CH_4)$ ($M = Ti, Zr, Hf$) and $M(=NH)_3(\eta^1_2-CH_4)$ ($M = Mo, W$), because in this case, the lengths of the $M-H_b$ bonds for two bridging H atoms markedly (by more than 0.2 Å) differ from each other.

The activation of methane by the trisimido complexes formed by d^0 metals, $M(=NH)_3$ ($M = Mo, W$), $Ta(=NH)_3^-$, $M(=NH)_3^+$ ($M = Tc, Re$), and d^2 metals, $Tc(=NH)_3^-$, $Os(=NH)_3$, has been studied by RHF calculations with the effective core potential and by molecular mechanics.³⁶ It was found that the energy of methane binding to imido complexes is more sensitive to the type of electronic configuration of the central atom (d^0 or d^2) than to the nature of the metal or the charge of the complex. According to calculations, methane reacts with d^0 -metal complexes irrespective of their charge (neutral, anionic, or cationic) but does not react with d^2 -metal imides.

In the complexes formed by d^0 metals, the energy of binding of methane to the metal increases on passing from anionic to neutral and cationic complexes in the series $Ta(=NH)_3^- < W(=NH)_3 < Re(=NH)_3^+$, being equal to 8.3, 15.6 and 26.3 kcal mol⁻¹, respectively. The methane binding energy increases on passing from Group III metal amides to Group IV metal monoimides, Group V metal bisimides, and Group VI metal trisimides



It was suggested that complexes of alkanes with $M(=NAr)_3^+$ ($M = Tc, Re$) can be sufficiently stable to be studied experimentally.

The changes in the geometry of the reactants upon complexation are insignificant. The angle between the C–H_b bridging bonds somewhat increases, from 109.5° (in free methane) to 113° [in the anionic complex of tantalum $Ta(=NH)_3^-$] and to 119° [in the cationic complex of rhenium $Re(=H)_3^+$]. The lengths of uncoordinated C–H bonds are similar to the C–H bond lengths in free methane. The length of the C–H_b bridging bond increases with an increase in the $M-CH_4$ binding energy from 1.10 (in the anionic tantalum complex) to 1.14 Å (in the cationic rhenium complex).^{36,98}

The above theoretical data dealing with the activation of methane C–H bonds by two types of complexes based on metal ions in high oxidation states with a formal d^0 electron configuration (cyclopentadienyl complexes of Group III, IV metals and Group IV–VI metal imides) show that methane is coordinated in these compounds *via* either a face (η^3 and η^1_3 modes of coordination) or an edge (η^2 and η^1_2 modes of coordination). The mode of methane coordination is appreciably affected by steric (the size of stabilising ligands) and electronic factors (high polarity of the metal–ligand bond). The activation of methane C–H bonds by complexes of this type can be represented as proton transfer between two anionic centres in the coordination sphere of a highly charged d^0 metal.

2. Complexes with a d^n electron configuration of the complexing ion

A much larger number of papers have been devoted to methane activation by complexes formed by transition metals with d^n electron configurations. Sixteen-electron molybdenum and tungsten metallocenes Cp_2M (d^4 configuration) are well-known to be highly reactive intermediates which readily enter into oxidative addition reactions to give 18-electron derivatives. In particular, these complexes are able to activate the C–H bonds of alkanes. The reactions of methane with metallocene derivatives of molybdenum and tungsten have been studied by the density functional method in the B3P86 and B3LYP/LANL2DZ approximations.^{101–103}

Study of the intramolecular hydrogen exchange in the $Cp_2W(CH_3)H$ and $[CH_2(C_5H_4)_2]W(CH_3)H$ complexes showed that in both cases, hydrogen exchange proceeds *via* the intermediate formation of the methane complex with η^1_2 -coordination of

methane. In these complexes, two C–H bonds of the methane ligand pointing toward the tungsten atom are located in the equatorial plane of the metallocene fragment.¹⁰¹

Density functional theory calculations in the B3LYP approximation were used to study the oxidative addition of methane to molybdenum and tungsten 16-electron $[n]$ -metallocenophanes.¹⁰² According to the results of calculations, these $[n]$ -metallocenophanes react with methane to form σ -complexes with a binding energy of 1.3–7.6 kcal mol^{−1}. In these σ -complexes, methane is bound to the central metal atom according to the η_2^1 type, the bridging C–H_b bonds being located in the equatorial plane of the metallocene fragment.¹⁰²

Poli and coworkers¹⁰³ have studied the addition of methane to various types of metallocenes formed by Group VI metals, namely, Cp₂M, [CH₂(C₃H₄)₂]M, and Cp₂⁺M (M = Mo, W), by density functional theory calculations in the B3LYP/LANL2DZ approximation. It was found that these compounds in the singlet excited state form asymmetric η^1 -complexes with methane, in which the M–H_b–C hydrogen bridge is situated in the equatorial plane of the metallocene fragment. The C–H_b bridging bond is much longer than the other C–H bonds of the methane ligand, whose average length is 1.088 Å. This elongation is more pronounced in tungsten complexes (1.138–1.156 Å) than in molybdenum complexes (1.122–1.126 Å), indicating that the M–CH₄ interaction is stronger in the case of tungsten. The W...H_b distance is 0.1 Å shorter than Mo...H_b. The binding energy of methane in cyclopentadienyl and *ansa*-metallocene complexes is equal to 3.4–6 kcal mol^{−1} relative to the excited (singlet) state of the corresponding metallocenes. The reaction of Cp₂⁺M with methane is energetically unfavourable even for the singlet state of these complexes due to the influence of steric factors.¹⁰³

To elucidate the reason for the experimentally observed difference between the reactivities of the Cp*W(NO)(CH₂Bu)₂ and Cp*Mo(NO)(CH₂Bu)₂ complexes towards alkanes,¹⁰⁴ the reactions of model compounds CpM(NO)(=CH₂) (M = W, Mo) were studied by density functional theory calculations in the B3LYP/LANL2DZ approximation.¹⁰⁵ It was found that the reaction of methane with the model compound CpW(NO)(=CH₂) is more exothermic and has a lower activation barrier than the reaction with CpMo(NO)(=CH₂). The calculations attest to the formation of intermediate CpM(NO)(=CH₂)(CH₄) complexes for both molybdenum and tungsten. The methane ligands in both complexes are coordinated according to the η_2^1 pattern, one M...H_b bridging bond being 0.4 Å shorter than the other. One of the C–H_b bonds in the methane ligand is somewhat elongated (1.119 Å for Mo and 1.12 Å for W) compared to the other C–H bonds (each ≤ 1.10 Å). In addition, the H–C–H angle between the two hydrogen atoms directed toward the metal is also increased to 116.5° for Mo and to 117.2° for W. The energy of methane binding in the complexes is 6.5 (for Mo) and 7.7 kcal mol^{−1} (for W). The CpM(NO)(=CH₂)(CH₄) complexes can participate in two competing processes, namely, activation of the C–H bonds to give CpM(NO)(CH₃)₂ and dissociation with the loss of methane. The calculations showed that for the tungsten complex, the heights of the energy barriers to both reactions are almost equal, whereas in the case of the molybdenum complex, the formation of CpM(NO)(CH₃)₂ is energetically rather unfavourable.¹⁰⁵

Fast time-resolved infrared spectroscopy (TRIS) has been used to study the reactions of a number of alkanes and fluoroalkanes with the 16-electron species W(CO)₅ in the gas phase.¹⁰⁶ It was found that W(CO)₅ is reversibly complexed with unsubstituted alkanes, except for CH₄. The binding energies of alkanes in the complexes are in the range 7–11 kcal mol^{−1}; they increase with an increase in the alkane size. Since no complex with CH₄ was detected experimentally, it was concluded¹⁰⁶ that the binding energy in this complex is less than 5 kcal mol^{−1}.

For comparison with experimental data, the energies of binding of alkanes to W(CO)₅ were found by *ab initio* calculations using various basis sets and methods for taking into account the

electron correlation.¹⁰⁷ The Hartree–Fock (HF) optimisation of the geometric parameters of the W(CO)₅(RH) complexes showed that the η_2^1 -coordination is energetically the most favourable for methane, although two transition states with η_3^1 and η^2 modes of coordination do not differ much from it in energy. When the geometry of W(CO)₅(CH₄) was optimised by the MP2 methods, all three structures were found to correspond to energy minima, the energy difference between them being less than 1 kcal mol^{−1} and the order of their stability being dependent on the basis set and the calculation method used. Excellent agreement with experimental data was attained only when the MP2 binding energies in the largest basis set were corrected for the basis set superposition error (BSSE), the zero point energy (ZPE), and the temperature; the difference between the results of MP2 and QCISD calculations was also taken into account.¹⁰⁷

In a recent publication,¹⁸ the alkane complex CpRe(CO)₂·(C₅H₁₀-cyclo) was observed directly by NMR spectroscopy in a solution at −80 °C. According to NMR data, the cyclopentane ligand in this complex is bound to rhenium according to the η^2 or η_2^1 pattern.¹⁸ Unfortunately, to the best of our knowledge, no theoretical calculations of a similar rhenium complex with methane have been reported.

The oxidative addition of methane to model 14-electron complexes, *cis*- and *trans*-[OsCl₂(PH₃)₂], was studied theoretically by the RHF method with subsequent correction for electron correlation by the MP2 and the density functional theory techniques. It was concluded that isomeric σ -complexes can be formed, namely, *cis*- and *trans*-[OsCl₂(PH₃)₂(η^2 -CH₄)].¹⁰⁸ According to the calculations, the complex of methane with *cis*-[OsCl₂(PH₃)₂] is much more stable than that with *trans*-[OsCl₂(PH₃)₂]. Oxidative addition giving rise to OsCl₂(PH₃)₂(CH₃)(H) was found to be energetically favourable for the *trans*-[OsCl₂(PH₃)₂(η^2 -CH₄)] complex.

The coordination of methane by the Cp₂M complexes (M = Ti–Ni) was studied by semiempirical SCF MO LCAO calculations in the INDO (intermediate neglect of differential overlap) valence approximation using the unrestricted Hartree–Fock (UHF) formalism.¹⁰⁹ The results of calculations attest to the possible formation of weak complexes of methane with these metallocenes. In the researchers' opinion,¹⁰⁹ the coordination of a methane molecule by titanium, vanadium, manganese or nickel derivatives is likely to be accompanied by oxidative addition resulting in Cp₂M(H)(CH₃). In all of these complexes, methane is coordinated according to the η_2^1 pattern. It should be noted that the calculation method used leads to an unusually great value for the length of the C–H_b bridging bond (1.2–1.35 Å) in these complexes compared to the values obtained by other researchers (1.11–1.16 Å). The unusually high bond energies of methane in the complexes with ferrocene, cobaltocene and nickelocene (14–21 kcal mol^{−1}) also raise doubts.

A number of papers are devoted to the theoretical investigation of carbonylation of alkanes with carbonyl chloride rhodium complexes Rh(PR₃)₂Cl(CO), which was discovered experimentally and studied by Sakakura and Tanaka.¹¹⁰ An *ab initio* investigation of the PES for the oxidative addition of methane to the model 14-electron RhCl(PH₃)₂ complex has shown¹¹¹ that the reaction proceeds *via* the formation of the *trans*-[RhCl(PH₃)₂(η^2 -CH₄)] complex and a three-centre transition state. According to these calculations, the bond energy of methane in RhCl(PH₃)₂(η^2 -CH₄) is 16.7–17.2 kcal mol^{−1}. However, a repeated (MP2) study of this system carried out by the same researchers¹¹² gave somewhat different results. The authors noted that C–H-bond activation proceeds *via* the *trans*-[RhCl(PH₃)₂(η_2^1 -CH₄)] complex with C_s symmetry rather than *via* the *trans*-[RhCl(PH₃)₂(η^2 -CH₄)] complex, as they had established previously. One Rh...H_b distance in the η_2^1 complex is much shorter than the other (by 0.4 Å). Both C–H_b bridging bonds are elongated relative to the C–H bonds in free methane, although to different extents. The energy of methane binding in this complex is 13.7 kcal mol^{−1}. The energy of the structure with C_{2v} symmetry is

higher by 0.1 kcal mol⁻¹ than the energy of the *C_s*-symmetric structure. The former is not an equilibrium structure but a transition state between two *C_s* structures. The Rh–C distances are nearly equal for both structures (~2.53 Å). The C–H_b bond length in the *C_{2v}* structure is 1.119 Å. According to more recent density functional theory calculations,¹¹³ the activation of methane by the RhCl(PH₃)₂ complex proceeds *via* a η²-adduct with *C_{2v}* symmetry, RhCl(PH₃)₂(η²-CH₄). The stabilisation energy of the *cis*-isomer with respect to the reactants is 6.4 kcal mol⁻¹, while that of the *trans*-isomer is 13.9 kcal mol⁻¹. Comparison of the results of two publications^{112, 113} concerning the structures of the RhCl(PH₃)₂(CH₄) complex determined using different calculation techniques attests to a higher stability of the *trans*-isomer [the bond energies are similar, 13.7 (Ref. 112) and 13.9 kcal mol⁻¹ (Ref. 113)] relative to the *cis*-isomer. However, the modes of methane coordination found in the two studies are dissimilar.

The intermediate complexes formed in the reactions of methane with rhodium compounds, RhCl(CO), RhH(CO) and RhH(NH₃), have been studied theoretically.¹¹⁴ The presence of a ground or low-lying singlet state of the central metal atom was found to favour the formation of a stable methane complex, while the presence of a ground or low-lying triplet state contributes to the decrease in the energy barrier to oxidative addition. The geometric parameters of methane complexes were found by SCF and MP2 calculations. In these complexes, methane was assumed to have a distorted η³-coordination¹¹⁴ with one of the three Rh–H_b bonds being substantially shorter than the other bonds. This difference increases in the sequence RhCl(CO)(CH₄)–RhH(CO)(CH₄)–RhH(NH₃)(CH₄).

Numerous experimental data have been obtained indicating that the 16-electron intermediates Cp*ML (M = Rh, Ir; L = PR₃, CO) are able to activate C–H bonds in alkanes according to the oxidative addition mechanism (see a review¹¹⁵ and references therein). This initiated several theoretical studies dealing with methane interaction with the CpMX fragments (M = Co, Rh, Ir; X = CO, CH₂, PH₃, SH₂).^{116–119} Ziegler *et al.*¹¹⁶ used the density functional method to find out that a σ-adduct of methane with CpMX (M = Rh, Ir; X = CO, PH₃) is formed in an early step. The energy of formation of the adduct varies from 5.7–6.9 kcal mol⁻¹ for rhodium complexes to 12.2–14.1 kcal mol⁻¹ for iridium complexes. In the CpRh(CO)(CH₄) complex, methane is coordinated to rhodium in the η¹ mode (the Rh–H_b–C angle is close to 180°). The C–H_b bond (1.15 Å) is somewhat longer than the C–H_t bonds (1.09 Å).¹¹⁶

Song and Hall¹¹⁷ studied the oxidative addition of methane to CpRh(CO) by the RHF and MP2 methods. The reaction PES was found to contain two local energy minima, one corresponding to the CpRh(CO)(CH₄) complex and the other, to the oxidative addition product, CpRh(CO)(CH₃)(H). The methane binding energy in CpRh(CO)(CH₄) is 2.2 (RHF) or 14.8 kcal mol⁻¹ (MP2). The experimental value for the binding energy of alkanes in such complexes was estimated to be ~10 kcal mol⁻¹ (see Ref. 120). According to Song and Hall,¹¹⁷ the methane ligand in the CpRh(CO)(CH₄) intermediate is coordinated in the η¹ mode (the Rh–H_b–C fragment is markedly bent, the corresponding angle being 114.9°). The C–H_b bond is somewhat elongated (1.128 Å) with respect to the C–H bonds in free methane.¹¹⁷

Musaev and Morokuma,¹¹⁸ who studied the PES of the CpRh(CO) + CH₄ reaction by the MP2 method with the effective Hay–Wadt potential for the Rh atom and with different basis sets, have found that the first step of the reaction gives CpRh(CO)(η¹-CH₄) (the Rh–H_b–C angle is 179.3°) with a stabilisation energy of 7.7 kcal mol⁻¹ with respect to the reactants. The formation energies of the structures with two or three bridging hydrogen atoms are only 1 kcal mol⁻¹ higher than the energy of the monodentate structure but they do not correspond to local minima on the PES and, hence, they rearrange spontaneously to a monodentate complex. The C–H_b bridging bond in the methane ligand is 0.02 Å longer than the C–H_t bonds. The

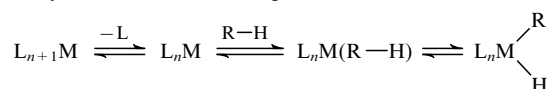
charge on the bridging hydrogen atom changes under the influence of the electronically unsaturated rhodium atom from +0.12 e in free CH₄ to –0.13 e in CpRh(CO)(η¹-CH₄).

More recently,¹¹⁹ the reactions of the 16-electron complexes CpM(CO) (M = Ru⁺, Os⁺, Rh, Ir, Pd⁺, Pt⁺) with methane have been studied by the MP2, MP4SDTQ (fourth-order Møller–Plesset perturbation theory with single, double, triple and quadruple excitations) and by the density functional method in the B3LYP approximation. Each of these complexes was found to form the compounds CpM(CO)(CH₄) with η²- or slightly distorted η²-coordination of methane. The equilibrium geometries of the intermediate methane complexes were determined without any symmetry restrictions by the MP2 method with the LANL1DZ basis set and by the density functional method in the B3LYP approximation. It was found that the central atoms with a high electron density (Ru⁺, Os⁺) or with a large atomic mass (Pd⁺, Pt⁺) readily enter into oxidative addition reactions with methane, while electronically unsaturated light central metal atoms tend to undergo reductive elimination reactions to give C–H bonds.¹¹⁹ The results of calculations attest to η¹-coordination of CH₄ in the CpRh(CO)(CH₄) complex and they are in better agreement with the data obtained by Song and Hall¹¹⁷ than with Ziegler's¹¹⁶ and Musaev and Morokuma's results.¹¹⁸

The binding energies of methane in the complexes with CpML (M = Co, Rh, Ir; L = CO, CH₂, SH₂, PH₃) have been determined in terms of the perturbation theory in the PCI-80 approximation and by the density functional method in the B3LYPB approximation.^{121, 122}

The mechanism of activation of methane C–H bonds by coordinatively unsaturated rhodium and iridium complexes CpM(PH₃)(CH₃)⁺ has been studied by the MP2 method with the LANL2DZ basis set and the QCISD method.¹²³ The iridium complex tends to undergo oxidative addition, whereas in the case of rhodium, σ-bond metathesis with a four-centre transition state is a more probable mechanism. The CpM(PH₃)(CH₃)(η¹-CH₄)⁺ complexes (the M–CH₄ binding energy is 9.5 kcal mol⁻¹ for Rh and 7.09 kcal mol⁻¹ for Ir) are formed intermediately in these reactions.

A number of studies^{124–127} have been devoted to experimental and theoretical investigations of the reactions of alkanes with pyrazolylborate rhodium complexes.



Experimental data^{124, 125} indicate that alkane σ-complexes are involved in the reductive elimination of alkanes from the pyrazolylborate rhodium complexes Tp'Rh(L)(R)(H) [Tp' is tris(3,5-dimethylpyrazolyl)borate, L = CNCH₂Bu⁺; R = CH₃, CH₂D, CD₃]. The results of a study of the photoinitiated activation of alkanes by the Tp'Rh(CO)₂ complexes by fast time-resolved infrared spectroscopy point to successive formation of two different complexes along the pathway to the oxidative addition product, Tp'Rh(CO)(R)(H).¹²⁶ To elucidate the nature of these complexes, density functional theory calculations in the B3P86 and LANL2DZ approximations were carried out for the PES of the reaction between the model TpRh(CO) compound [Tp is tris(pyrazolyl)borate] and methane.¹²⁷ Two minima corresponding to the (η³-Tp)Rh(CO)(η¹-CH₄) and (η²-Tp)Rh(CO)(η¹-CH₄) complexes were found on the PES. Parameters of the methane–rhodium bonds (bond length and energy) in these complexes are substantially different, which is consistent with the results of experimental studies.

Generally, different calculation methods give different results concerning the mode of coordination of the methane ligand in rhodium complexes. Structures with one linear (η¹-coordination) or bent (η²- or η³-coordination) Rh–H_b–C bridge or with two bridges (η²-coordination) are presumably formed.

Parallel supercomputer calculations have been performed to study the methane activation by 14-electron $\text{Ir}(\text{PH}_3)_2\text{X}$ fragments ($\text{X} = \text{H}, \text{Cl}$).¹²⁸ This study demonstrated that the formation of σ -complexes with an η^2 -coordination of methane is energetically the most favourable for $\text{Ir}(\text{PH}_3)_2\text{H}$. The geometric parameters of the products were determined by the RHF method. The energy of the complex with η^2 -coordinated methane is only $0.1 \text{ kcal mol}^{-1}$ lower than the energy of the transition state with η^2 -coordination. In the author's opinion, the $\text{Ir}(\text{PH}_3)_2(\text{H})(\text{CH}_4)$ methane adduct should exhibit structural non-rigidity at ambient temperatures. The replacement of hydrogen by chlorine in $\text{Ir}(\text{PH}_3)_2\text{X}$ results in a substantial decrease in the $\text{Ir}\cdots\text{C}$ and $\text{Ir}\cdots\text{H}$ distances and an increase in the stabilisation energy of the $\text{Ir}(\text{PH}_3)_2\text{Cl}(\eta^1\text{-CH}_4)$ complex.

Strout *et al.*¹²⁹ carried out a density functional theory study (B3LYP approximations) of the mechanism of the low-temperature activation of C–H bonds in alkanes by the cationic iridium complex $\text{Cp}^*\text{Ir}(\text{PMe}_3)(\text{CH}_3)^+$ in perfluoropyridine. Earlier, this reaction was found experimentally.¹³⁰ This reaction is formally similar to the metathesis of σ -bonds typical of electron-deficient complexes of early transition metals. Therefore, it was suggested in the experimental study¹³⁰ that this reaction was a new example of σ -bond metathesis involving a complex of a late transition metal. Since the two possible mechanisms (oxidative addition or σ -bond metathesis) cannot be distinguished experimentally, it was of interest to perform a theoretical study of this system. Quantum-chemical calculations for the model $\text{CpIr}(\text{PH}_3)(\text{CH}_3)^+ - \text{CH}_4$ system showed the intermediate formation of the $\text{CpIr}(\text{PH}_3) \cdot (\text{CH}_3)(\eta^1\text{-CH}_4)^+$ complex in which methane is weakly bound to iridium by the bent $\text{Ir}-\text{H}_b-\text{C}$ bridge (the $\text{Ir}-\text{H}_b-\text{C}$ angle is 134°). The results of density functional theory calculations of the coordination mode of methane in this complex¹²⁹ are consistent with the results obtained by the MP2 method with the LAND2DZ basis set.¹²³ According to the calculations, the low-temperature reaction of $\text{CpIr}(\text{PH}_3)(\text{CH}_3)^+$ with CH_4 occurs as oxidative addition of methane to the central metal atom. The pathway involving a four-centre transition state (metathesis of σ -bonds) is energetically unfavourable.

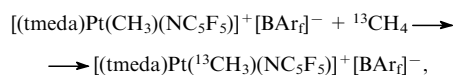
Thus, the results obtained by various methods point to the η^2 -coordination of the methane ligand as energetically the most favourable for all the iridium complexes studied, namely, $\text{CpIr}(\text{CO})(\text{CH}_4)$, $\text{Ir}(\text{PH}_3)_2(\text{H})(\text{CH}_4)$, $\text{Ir}(\text{PH}_3)_2\text{Cl}(\text{CH}_4)$ and $\text{CpIr}(\text{PH}_3)(\text{CH}_3)(\text{CH}_4)^+$.

Density functional theory calculations have been carried out¹³¹ to study the mechanism of the recently discovered dehydrogenation of alkanes by the $[\eta^3\text{-C}_6\text{H}_3(\text{CH}_2\text{P}^i\text{Bu}^t)_2\text{-1,3}]\text{IrH}_2$ complex.¹³² It was shown that the formation of a σ -complex with methane is endothermic in this case.¹³¹

The energy characteristics and the mechanism of oxidative addition of methane to the zerovalent 14-electron $\text{Ni}(\text{PH}_3)_2$ fragment has been studied by the RHF method.¹³³ It was shown that the formation of the $\text{Ni}(\text{PH}_3)_2(\text{CH}_4)$ σ -complex is energetically favourable and that the pseudo-tetrahedral η^2 -coordination of the methane ligand with two hydrogen atoms pointing towards the nickel atom is the most stable.

The MP2 and the density functional (B3LYP) approaches were used to study the PES for two model systems — CH_4 –*trans*- $[\text{PdCl}_2(\text{PH}_3)_2]$ and CH_4 –*trans*- $[\text{PtCl}_2(\text{PH}_3)_2]$.¹³⁴ According to the results,¹³⁴ the palladium and, especially, platinum complexes $\text{MCl}_2(\text{PH}_3)_2$ ($\text{M} = \text{Pd}, \text{Pt}$) are more active in stepwise methane activation according to the oxidative addition pattern with preliminary forced abstraction of the phosphine ligand than in the metathesis of the C–H and M–Cl bonds. The 14-electron $\text{MCl}_2(\text{PH}_3)$ fragments resulting from the removal of one phosphine ligand react with methane to give the σ -complexes $\text{MCl}_2(\text{PH}_3)(\eta^2\text{-CH}_4)$.

The elementary steps of the recently described¹³⁵ activation of methane by a cationic platinum(II) complex with a bidentate N-donor ligand $[N,N,N',N']$ -tetramethylethylenediamine (tmeda)]



have been studied by the density functional technique in the B3P86 approximation.¹³⁶ The theoretical results are consistent with the mechanism comprising the formation of a σ -complex and subsequent oxidative addition. In the model σ -complex $[(\text{en})\text{Pt}(\text{CH}_3)(\text{CH}_4)]^+$ (en is ethylenediamine), methane is bound according to the η^2 type. The C–H_b bridging bond is elongated by $0.08 \text{ \AA}$ compared to the C–H bonds in free methane. The energy of the $\text{Pt}-\text{CH}_4$ bond amounts to $21.9 \text{ kcal mol}^{-1}$. In order to compare the calculated bond energy with that obtained experimentally (for the reaction in solution), the energy of methane solvation by the solvent has to be subtracted from the calculated value.

Calculations by the MP4SDQ method for the reaction of $(\text{PH}_3)_2\text{Pt}$ with CH_4 indicate the formation of the $(\text{PH}_3)_2\text{Pt}(\eta^2\text{-CH}_4)$ complex having C_{2v} symmetry and a very small stabilisation energy ($0.6 \text{ kcal mol}^{-1}$).¹³⁷ In line with the small stabilisation energy, the geometric parameters of the methane fragment in this complex change only slightly with respect to those in free methane.

The reductive elimination of methane from a model complex of divalent platinum, $(\text{PH}_3)_2\text{Pt}(\text{H})(\text{CH}_3)$, has been investigated by the density functional approach in the B3LYP approximation.¹³⁸ Unlike the results cited above,¹³⁷ the results of these calculations showed that the process includes the formation of the $(\text{PH}_3)_2\text{Pt}(\eta^1\text{-CH}_4)$ σ -complex with a straight bridge (the $\text{Pt}-\text{H}_b-\text{C}$ angle is close to 180°). The length of the C–H_b bond directed towards the metal is virtually the same as the lengths of the other three C–H_i bonds. The stabilisation energy of this complex with respect to free reactants is close to zero.

The reductive elimination of methane from the $(\text{PH}_3)_2\text{Pt}(\text{H}) \cdot (\text{CH}_3)$ complex gives the σ -complex $(\text{PH}_3)_2\text{Pt}(\eta^2\text{-CH}_4)$ as an intermediate in which two C–H bonds of the methane ligand undergo equally strong interactions with the platinum atom (the corresponding $\text{Pt}-\text{H}$ bonds are 2.065 and $2.066 \text{ \AA}$). Both these bonds are almost $1 \text{ \AA}$ shorter than the $\text{Pt}-\text{H}$ agostic bond in $(\text{PH}_3)_2\text{Pt}(\eta^1\text{-CH}_4)$, which is indicative of a stronger binding of methane in this complex. Indeed, the enthalpy of methane binding in $(\text{PH}_3)_2\text{Pt}(\eta^2\text{-CH}_4)$ is $10.8 \text{ kcal mol}^{-1}$, whereas this value for $(\text{PH}_3)_2\text{Pt}(\eta^1\text{-CH}_4)$ is negligibly small. The reductive elimination of methane from *trans*- $[(\text{PH}_3)_2\text{PtCl}_2(\text{H})(\text{CH}_3)]$ proceeds *via* the complex *trans*- $[(\text{PH}_3)_2\text{PtCl}_2(\eta^2\text{-CH}_4)]$ (C_{2v} symmetry) in which the enthalpy of methane binding is equal to $3.6 \text{ kcal mol}^{-1}$.

The reductive elimination of methane from the cationic *cis*- $[(\text{PH}_3)_2\text{PtCl}(\text{H})(\text{CH}_3)]^+$ complex yields *cis*- $[(\text{PH}_3)_2\text{PtCl}(\eta^2\text{-CH}_4)]^+$ in which the lengths of the two $\text{Pt}-\text{H}_b$ bonds are different. The enthalpy of methane binding in *cis*- $[(\text{PH}_3)_2\text{PtCl}(\eta^2\text{-CH}_4)]^+$ is $9.5 \text{ kcal mol}^{-1}$, which is much higher than that in *cis*- $[(\text{PH}_3)_2\text{PtCl}_2(\eta^2\text{-CH}_4)]$. Apparently, the stronger binding of methane in $(\text{PH}_3)_2\text{PtCl}(\eta^2\text{-CH}_4)^+$ is due to the fact that methane is attached to the positively charged $(\text{PH}_3)_2\text{PtCl}^+$ fragment, unlike the neutral $(\text{PH}_3)_2\text{PtCl}_2$ fragment in the other complex.¹³⁸

The results of calculations of geometric parameters of the $\text{ML}_n(\text{CH}_4)$ complexes and the binding energies of the methane ligand in these complexes are listed in Table 3, and the modes of coordination of the CH_4 ligand in these complexes, depending on the nature of the complexing ion, are shown in Fig. 3.

The results of calculations considered above demonstrate that in methane complexes with ML_n molecular fragments whose central atoms have a d^n electron configuration, the methane ligand is typically coordinated along the edge (η^2 and η^1_2 modes of coordination). The η^2 -coordination where one bridging bond is much shorter than the other is found most often. A somewhat less frequently encountered mode of methane coordination to the metal is η^2 -coordination due to two bridging hydrogen atoms, which results in elongation of the C–H_b bonds compared to those

Table 3. Data of calculation of the geometric structure and the bond energy for the $ML_n(CH_4)$ complexes containing stabilising ligands.

Complex	Bond lengths /Å			The M—C—H _b angle /deg	E_{bd}^a /kcal mol ⁻¹	Calculation techniques (programs)	Ref.
	M...C	M—H _b	C—H _b				
Cl ₂ LuH(η^1_3 -CH ₄)	2.535	—	1.118	—	1.96	DFT (A-MOL)	80
Cl ₂ Lu(CH ₃)(η^1_2 -CH ₄)	2.625	2.277	1.117	[59.75]	-4.64		
Cp ₂ ScH(η^1_3 -CH ₄)	2.51	2.31; 2.50	1.14; 1.11	[66.7; 76.7]	[4.78]	DFT/B3P86 (A-MOL)	81
Cp ₂ Sc(CH ₃)(η^2 -CH ₄)	2.72	2.34; 2.36	1.11; 1.11	[58.5; 59.5]	[5.97]		
Cp ₂ TiH(η^2 -CH ₄) ⁺	2.53	2.09; 2.24	1.12; 1.11	55; 62	0.8	DFT/PBE, GGA (Laikov)	84
Cp ₂ ZrH(η^2 -CH ₄) ⁺	2.70	2.27; 2.39	1.12; 1.11	56; 62	12.0		
Cp ₂ Ti(CH ₃)(η^2 -CH ₄) ⁺	2.66	2.23; 2.31	1.11	56; 60	4.2	DFT/PBE, GGA (Laikov)	85
Cp ₂ Zr(CH ₃)(η^2 -CH ₄) ⁺	2.77	2.40; 2.37	1.11	59; 58	9.4		
Cp ₂ TiEt(η^2 -CH ₄) ⁺	—	—	—	—	2.0	DFT/PBE, GGA (Laikov)	86
Cp ₂ ZrEt(η^2 -CH ₄) ⁺	—	—	—	—	7.3		
Cp ₂ TiPr ⁿ (η^1_2 -CH ₄) ⁺	—	2.19; 2.33	—	—	2.5		
Cp ₂ ZrPr ⁿ (η^2 -CH ₄) ⁺	—	2.42; 2.37	—	—	7.8		
Cp ₂ TiPr ⁱ (η^1_2 -CH ₄) ⁺	—	2.13; 2.41	—	—	-4		
Cp ₂ ZrPr ⁱ (η^2 -CH ₄) ⁺	—	2.34; 2.39	—	—	2		
H ₂ Ti(=NH)(η^3 -CH ₄)	2.63	—	—	—	8.9	RHF/MP2, SKBJ (GAMESS)	95
H ₂ Zr(=NH)(η^3 -CH ₄)	2.80	—	—	—	8.7		
H ₂ Hf(=NH)(η^3 -CH ₄)	2.79	—	—	—	9.3		
Ti(OH) ₂ (=NH)(η^1_2 -CH ₄)	2.84	2.32; 2.60	1.11; 1.10	—	6.6	RHF/MP2 (GAMESS)	96
Ti(NH ₂) ₂ (=NH)(η^1_2 -CH ₄)	3.10	2.52; 2.79	1.10; 1.10	[56.5]	4.4		
Zr(NH ₂) ₂ (=NH)(η^1_2 -CH ₄)	3.05	2.55; 2.69	1.10; 1.10	[57]	6.3		
Nb(NH ₂)(=NH) ₂ (η^2 -CH ₄)	2.84	2.44; 2.43	1.10; 1.10	[57.5]	11.1		
Ta(NH ₂)(=NH) ₂ (η^2 -CH ₄)	2.79	2.37; 2.41	1.11; 1.11	[58]	13.6		
Mo(=NH) ₃ (η^1_2 -CH ₄)	2.77	2.25; 2.51	1.11; 1.10	[58]	13.7		
W(=NH) ₃ (η^1_2 -CH ₄)	2.72	2.22; 2.46	1.12; 1.10	[58.5]	15.6	RHF/MP2 (GAMESS)	98
Hf(NH ₂) ₂ (=NH)(η^1_2 -CH ₄)	—	—	—	—	8.6		
V(NH ₂)(=NH) ₂ (η^2 -CH ₄)	2.76	2.31; 2.39	1.104; 1.10	—	13.2		
Ta(=NH) ₃ (η^1_2 -CH ₄) ⁻	3.03	2.51; [2.67]	1.10	[52; 61]	8.3 ^b	RHF/MP2, SKBJ (GAMESS)	36
Tc(=NH) ₃ (η^1_2 -CH ₄) ⁺	2.66	2.06; [2.51]	1.13	[46.8; 70]	25.7 ^b		
Re(=NH) ₃ (η^1_2 -CH ₄) ⁺	2.64	2.05; [2.46]	1.14	[47.5; 68.5]	26.3 ^b		
Cp ₂ Ti(η^1_2 -CH ₄)	3.32	—	1.32	—	2	MO LCAO SCF/INDO	109
Cp ₂ V(η^1_2 -CH ₄)	2.84	—	1.35	—	6		
Cp ₂ Cr(η^1_2 -CH ₄)	2.66	—	1.35	—	7 ^b		
¹ [Cp ₂ W(η^1_2 -CH ₄)]	2.925	2.224; 2.804	1.14; 1.099	[42.6; 72.8]	—	DFT/B3P86 (ADF)	101
¹ [CH ₂ (C ₅ H ₄) ₂ W(η^1_2 -CH ₄)]	2.895	2.196; 2.786	1.144; 1.096	[42.7; 73.3]	—		
¹ [Cp ₂ Mo(η^1_2 -CH ₄)]	2.940	2.185	1.122	38.96	2.55	DFT/B3LYP, LANL2DZ (GAUSSIAN94)	102
¹ [S(CH ₂ C ₅ H ₄) ₂ Mo(η^1_2 -CH ₄)]	2.975	2.202	1.120	37.96	1.86		
¹ [(CH ₂ C ₅ H ₄) ₂ Mo(η^1_2 -CH ₄)]	2.937	2.203	1.121	40.24	3.48		
¹ [CH ₂ (C ₅ H ₄) ₂ Mo(η^1_2 -CH ₄)]	2.891	2.178	1.123	41.31	4.52	DFT/B3LYP, LANL2DZ (GAUSSIAN94)	102
¹ [Cp ₂ W(η^1_2 -CH ₄)]	2.884	2.093	1.138	37.16	4.70		
¹ [S(CH ₂ C ₅ H ₄) ₂ W(η^1_2 -CH ₄)]	2.944	2.128	1.133	35.64	7.57		
¹ [(CH ₂ C ₅ H ₄) ₂ W(η^1_2 -CH ₄)]	2.901	2.111	1.137	37.24	1.61		
¹ [CH ₂ (C ₅ H ₄) ₂ W(η^1_2 -CH ₄)]	2.827	2.057	1.143	38.35	1.28		
¹ [Cp ₂ Mo(η^1_2 -CH ₄)]	2.842	2.215	1.122	[46]	3.56	DFT/B3LYP, LANL2DZ (GAUSSIAN98, Jaguar 4.0)	103
¹ [CH ₂ (C ₅ H ₄) ₂ Mo(η^1_2 -CH ₄)]	2.867	2.162	1.126	[41.8]	4.47		
¹ [Cp ₂ *Mo(η^1_2 -CH ₄)]	2.981	2.200	1.122	[37.5]	-2.17		
¹ [Cp ₂ W(η^1_2 -CH ₄)]	2.752	2.120	1.138	[45.7]	3.42		
¹ [CH ₂ (C ₅ H ₄) ₂ W(η^1_2 -CH ₄)]	2.729	2.022	1.156	[41.9]	6.14		
¹ [Cp ₂ *W(η^1_2 -CH ₄)]	(2.797)	(2.040)	(1.150)	[39.2]	-7.3		
CpMo(NO)(=CH ₂)(η^1_2 -CH ₄)	2.76	2.17; [2.58]	1.119; 1.10	[47.6]	6.5	DFT/B3LYP, LANL2DZ (GAUSSIAN94)	105
CpW(NO)(=CH ₂)(η^1_2 -CH ₄)	2.74	2.14; [2.67]	1.12; 1.10	[44.75]	7.7		
W(CO) ₅ (η^1_2 -CH ₄)	2.804	2.096	1.147	[42]	7.07–8.88	HF, MP2–MP4 (GAUSSIAN92,94; GAMESS-UK)	107
W(CO) ₅ (η^2 -CH ₄)	2.764	2.350	1.129	[57]	6.09–8.51		
Cp ₂ Fe(η^1_2 -CH ₄)	2.44	—	1.20	—	14 ^b	MO LCAO SCF/INDO	109
CpRu(CO)(η^2 -CH ₄) ⁻	2.617	[2.315]	1.108	62.07	6.87 (B3LYP)	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
	2.533	[2.143]	1.129	57.21	13.2 (MP2)		
CpOs(CO)(η^2 -CH ₄) ⁻	2.558	[2.155]	1.127	56.65	10.1 (B3LYP)	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
	2.253	[2.164]	1.135	57.39	19.4 (MP2)		
<i>cis</i> -[(PH ₃) ₂ Cl ₂ Os(η^2 -CH ₄)]	2.62	[2.24]	1.118	58.3	12 (MP2)	RHF, MP2, DFT/B3LYP (GAUSSIAN92)	108
	2.81	[2.39]	1.103	56.6	— (DFT)		
<i>trans</i> -[(PH ₃) ₂ Cl ₂ Os(η^2 -CH ₄)]	2.55	[2.19]	1.118	58.7	4 (MP2)		
	2.50	[2.16]	1.112	59.6	— (DFT)		

Table 3 (continued).

Complex	Bond lengths / Å			The M—C—H _b angle /deg	<i>E</i> _{bd} ^a /kcal mol ^{−1}	Calculation techniques (programs)	Ref.
	M...C	M—H _b	C—H _b				
Cp ₂ Co(η ¹ -CH ₄)	3.40	—	1.23	—	16 ^b	MO LCAO SCF/INDO	109
RhCl(PH ₃) ₂ (η ² -CH ₄) (C _{2v})	2.395	2.046	1.094	[58.4]	16.7–17.2	RHF/MP2, MP4SDTQ (GAUSSIAN82, MELD)	111
RhCl(PH ₃) ₂ (η ¹ -CH ₄) (C _s)	2.533	1.994; 2.356	1.136; 1.105	[47; 68.1]	13.7	MP2–MP4, QCISD (GAUSSIAN90)	112
<i>trans</i> -[RhCl(PH ₃) ₂ (η ² -CH ₄)] (C _{2v})	2.427	2.038	1.127	56.6	13.9	DFT/B3P86 (ADF)	113
<i>cis</i> -[RhCl(PH ₃) ₂ (η ² -CH ₄)] (C _{2v})	2.562	2.167	1.113	56.9	6.4		
RhCl(CO)(η ¹ -CH ₄)	2.58	2.20; 2.66	1.115; 1.104	[57.9]	3.4 (MP2)	SCF (GAMESS); MCPF (STOCKHOLM); MP2 (GAUSSIAN92)	114
	2.87	2.37; 2.94	1.089; 1.083	[52.5]	−3.8 (SCF)		
RhH(CO)(η ¹ -CH ₄)	2.47	2.12; 2.55	1.122; 1.105	[58.9]	10.8 (MP2)	SCF (GAMESS); MCPF (STOCKHOLM); MP2 (GAUSSIAN92)	114
	2.80	2.24; 2.90	1.093; 1.083	[49.0]	8.6 (SCF)		
RhH(NH ₃)(η ¹ -CH ₄)	2.49	1.88; 2.71	1.138; 1.102	[46.0]	14.5 (MP2)	SCF (GAMESS); MCPF (STOCKHOLM); MP2 (GAUSSIAN92)	114
	2.91	2.26; 3.05	1.090; 1.082	[44.2]	7.1 (SCF)		
CpRh(CO)(η ¹ -CH ₄)	3.16	2.01	1.15	(180)	6.9	HFS-LCAO (A -MOL)	116
CpRh(CO)(η ¹ -CH ₄)	2.494	1.799	1.128	[40.8]	2.2 (RHF)	RHF (GAMESS), MP2 (GAUSSIAN90)	117
				(114.9)	14.8 (MP2)		
CpRh(CO)(η ¹ -CH ₄)	3.003	1.893	1.110	[0.45]	7.7	MP2	118
				(179.3)		(GAUSSIAN92/DFT)	
CpRh(CO)(η ¹ -CH ₄)	2.676	[2.058]	1.122	[45.85]	6.37 (B3LYP)	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
				[(111.1)]			
	2.542	[1.969]	1.135	[47.86]	13.6 (MP2)		
				[(106.9)]			
η ³ -TpRh(CO)(η ¹ -CH ₄)	3.538	2.436	1.103	[2]	1.70	DFT/B3P86, LANL2DZ, (GAUSSIAN94)	127
				(177.6)			
η ² -TpRh(CO)(η ¹ -CH ₄)	2.450	1.902	1.139	[48.7]	9.39		
				(104.6)			
CpRh(PH ₃)(CH ₃)(η ¹ -CH ₄) ⁺	2.689	2.014; 2.598	1.128	42.88	12 (MP2)	MP2/LANL2DZ, QCISD (GAUSSIAN94)	123
					9.5 (QCISD)		
Ir(PH ₃) ₂ H(η ¹ -CH ₄)	2.95	2.25	1.10	[41.6]	6.8	RHF/MP2, SKBJ (GAMESS)	128
				(119)			
Ir(PH ₃) ₂ H(η ² -CH ₄)	—	—	—	—	6.7		
Ir(PH ₃) ₂ Cl(η ¹ -CH ₄)	2.67	1.97	1.13	[41.4]	15.6		
				(116)			
CpIr(PH ₃)(CH ₃)(η ¹ -CH ₄) ⁺	2.905	2.007	1.129	[29.9]	1	DFT/B3LYP (GAUSSIAN94)	129
				[(133.8)]			
CpIr(PH ₃)(CH ₃)(η ¹ -CH ₄) ⁺	2.653	1.909; 2.699	1.152	39.43	10 (MP2)	MP2/LANL2DZ, QCISD (GAUSSIAN94)	123
					7.09 (QCISD)		
CpIr(CO)(η ¹ -CH ₄)	2.588	[1.891]	1.160	41.94	9.64 (B3LYP)	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
	2.609	[1.945]	1.114	42.79	16.4 (MP2)		
Cp ₂ Ni(η ¹ -CH ₄)	3.28	—	1.25	—	21 ^b	MO LCAO SCF/INDO	109
(PH ₃) ₂ Ni(η ² -CH ₄)	2.49	2.07	—	[55.2]	3.5	SCF-SDCI (GAMESS)	133
CpPd(CO)(η ² -CH ₄) ⁺	2.641	[2.211]	1.112	55.53	9.96 (B3LYP)	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
	2.527	[2.133]	1.118	56.91	12.2 (MP2)		
<i>trans</i> -[(PH ₃)Cl ₂ Pd(η ² -CH ₄)]	2.55	2.17	—	[57.6]	8.8 (MP2)	MP2, DFT/B3LYP, GAUSSIAN94	134
<i>trans</i> -[(PH ₃)Cl ₂ Pt(η ² -CH ₄)]	2.66	2.37	—	[63]	— (HF)		
	2.51	2.14	—	[58]	8.6 (B3LYP)		
	2.47	2.10	—	[58]	11.9 (MP2)		
(En)PtCH ₃ (η ¹ -CH ₄) ⁺	2.36	1.73	1.18	[44.5]	21.9	DFT/B3P86 (ADF)	136
				(29)			
(PH ₃) ₂ Pt(η ² -CH ₄)	4.644	—	—	—	0.6 (HF)	HF; MO/MP4SDQ (GAUSSIAN82)	137
					0.4 (MP4)		
(PH ₃) ₂ Pt(η ¹ -CH ₄)	4.4	3.308	1.095	0	~0	DFT/B3LYP, CCSD(T) (GAUSSIAN98)	138
				(180)			
(PH ₃)Pt(η ² -CH ₄)	2.43	2.065; 2.066	1.119; 1.118	[58]	10.8	DFT/B3LYP, CCSD(T) (GAUSSIAN98)	138
<i>trans</i> -[(PH ₃)Cl ₂ Pt(η ² -CH ₄)]	2.562	2.188; 2.188	1.108; 1.108	[58]	3.6		
<i>cis</i> -[(PH ₃) ₂ ClPt(η ² -CH ₄)] ⁺	2.543	2.082; 2.296	1.121; 1.105	[53.5; 64.6]	9.5	MP2, MP4SDTQ, DFT/B3LYP (GAUSSIAN94)	119
CpPt(CO)(η ² -CH ₄) ⁺	2.674	[2.019]	1.137	44.11	10.9 (B3LYP)		
	2.611	[1.928]	1.116	41.78	17.4 (MP2)		

Note. The values in brackets have been calculated by the author of the review using data from the cited publications.

^a The M—CH₄ bond energy in the complex. ^b The enthalpy of formation of the complex.

Li	Be											B
Na	Mg											Al
K	Ca	Sc η_3^1, η^2	Ti $\eta_2^1, \eta_3^1, \eta^2, \eta^3$	V η_2^1, η^2	Cr η_2^1	Mn	Fe η_2^1	Co η_2^1	Ni η_2^1, η^2	Cu	Zn	Ga
Rb	Sr	Y	Zr η_2^1, η^2, η^3	Nb η_2^1, η^2	Mo η_2^1	Tc η_2^1	Ru η_2^1	Rh $\eta_2^1, \eta_3^1, \eta^1, \eta^2$	Pd η^2	Ag	Cd	In
Cs	Ba	Lu η_3^1, η^2	Hf η^3	Ta η_2^1, η^2	W η_2^1	Re η_2^1	Os η^2	Ir η_2^1, η_2	Pt η_2^1, η^1, η^2	Au	Hg	Tl

Figure 3. Dependence of the modes of coordination of the CH_4 ligands in the complexes $\text{ML}_n(\text{CH}_4)$ on the nature of the complexing ion.

in free methane. Examples of methane coordination along a face (η^3 and η_3^1) by d^n -ion complexes are rare; this mode of coordination was mentioned only in one study.¹¹⁴ The η^1 -coordination of methane (by a tetrahedron vertex) is equally unusual.^{116, 118}

V. Some structural features of methane complexes

The data considered above demonstrate that the results of quantum-chemical calculations of methane complexes with neutral metal atoms, metal ions and molecular fragments ML_n predict a diversity of modes of methane coordination in these complexes and small energy differences between various structures, which is typical of structurally non-rigid compounds. In complexes with neutral atoms or metal ions without stabilising ligands, η^2 and η^3 modes of coordination are energetically preferred for methane. No complexes with linear η^1 -coordination have been found for these species. In rare cases, calculations predict the η_3^1 -coordination of methane as the most stable [for example, in $\text{Rh}(\eta_3^1\text{-CH}_4)^+$ and $\text{Pt}(\eta_3^1\text{-CH}_4)^+$];^{65, 67} however, the use of other calculation methods or higher-level theories shows that for Rh^+ and Pt^+ complexes, too, η^2 -coordination is the most stable.^{62, 68}

Complexes with η^3 -coordination of methane are mainly typical of non-transition metal ions M^+ and for transition metal ions of the beginning of the row (Li^+ , Mg^+ , Sc^+ , Ti^+ , Cr^+ , Ta^+), while transition metal ions of the end of the row (Co^+ , Rh^+ , Ir^+ , Cu^+) tend to form complexes with η^2 -coordination of methane. The $\text{Fe}(\text{CH}_4)^+$ structures with C_{2v} (η^2) and C_{3v} (η^3) symmetry are nearly degenerate, the energy difference between them being 0.05–0.17 kcal mol^{−1} (see Ref. 55).

The results of calculations of the geometric structure of $\text{Mg}(\text{CH}_4)^+$ and $\text{V}(\text{CH}_4)^+$ show that it depends appreciably on the electronic state of the central atom.^{39, 46} The energy of binding of the methane ligand to the metal increases on passing from non-transition to transition metals. For neutral metal atoms in the ground state, the energy of methane binding in the complexes is relatively low, as a rule, less than 4 kcal mol^{−1} (see, for example, Ref. 29). Of transition metal ions in the ground state, the lowest binding energy of the methane ligand was found for Mn^+ and Zn^+ (~10 kcal mol^{−1}),³⁵ while the highest energy was found for the Pt^+ ion (~30 kcal mol^{−1}).⁶⁹

Some discussion has been devoted to the dependence of the mode of methane coordination on the nature of the complexing ion. According to Yoshizawa,⁵⁶ η^2 -coordination is most probable for low-spin states of ions and η^3 -coordination is most likely for high-spin ions. Bauschlicher and coworkers,⁷⁴ while considering the structure of the $\text{Cu}(\text{CH}_4)^+$ complex, suggested that electrostatic interaction is favourable for the formation of a η^3 -structure, and dative interaction promotes η^2 -coordination.

Other modes of coordination are typical of methane complexes with ML_n molecular fragments. Only a few examples of complexes where η^3 -coordination of methane should be preferred according to calculations are known [derivatives of d^0 ions:

Cl_2LuH ,⁸⁰ $\text{H}_2\text{M}=\text{NH}$ ($\text{M} = \text{Ti}, \text{Zr}, \text{Hf}$)⁹⁵]. Complexes with η_3^1 -coordination of the methane ligand are also represented by single examples [RhHCl , $\text{RhH}(\text{CO})$, $\text{RhH}(\text{NH}_3)$]¹¹⁴. It is noteworthy that η_3^1 -coordination of methane has not been found for platinum complexes containing stabilising ligands, whereas this mode of coordination has been reported⁶⁷ to be preferred for complexes of the Pt^+ ion without ligands. In most cases, calculations point to monodentate methane coordination with a bent $\text{M}-\text{H}-\text{C}$ bridge (η_2^1 -coordination) as the most energetically favourable for complexes with ML_n molecular fragments. η^2 -Coordination is also often found for these complexes (however, not as often as η_2^1). In both cases, methane is coordinated to the metal by the tetrahedron edge. The difference between these modes of coordination is that in the case of η_2^1 -coordination, two bridging $\text{M}-\text{H}_b$ bonds have markedly different lengths. The energy of methane binding is much lower in complexes containing stabilising ligands than in complexes with bare ions; in most cases, the former does not exceed 10 kcal mol^{−1}.

It is obvious that this difference in the structures and binding energies between complexes with bare ions and with ML_n molecular fragments is due to the stabilising ligands. In particular, a substantial influence of steric factors on the structure of methane complexes has been noted in an early publication¹³⁹ devoted to this problem and in a number of subsequent studies.^{81, 86}

It should be noted that the results of calculations of the geometric structures of methane complexes obtained by different researchers differ markedly from one another. Quantum-chemical calculations point to an insignificant energy difference between complexes that differ only in the mode of methane coordination. Therefore, determination of the most stable structure is ambiguous and depends on both the system under study (the complex) and the calculation methods and basis sets used.¹⁰⁷ This ambiguity is observed both for complexes containing stabilising ligands and for complexes formed by bare ions.

Currently it is impossible to verify experimentally the calculation results for methane complexes, because, unlike complexes formed by molecular N_2 or H_2 , which have been isolated in the crystalline state, no metal complexes with an alkane molecule as a ligand have been isolated so far. In view of the ambiguity of calculation results and the impossibility of their experimental verification, it would be useful to compare the results of calculations of the structures of methane complexes with experimental data for some existing systems that resemble methane complexes in electronic and geometric structures.

Several systems have been proposed to model various steps of alkane activation. For example, structural data for alkyl complexes with intramolecular $\text{C}-\text{H}\cdots\text{M}$ agostic bonds were used by Crabtree *et al.*¹⁴⁰ to model the trajectory of addition of the $\text{C}-\text{H}$ bond to the central atom. However, this model does not allow one to identify the mode of methane coordination in the complexes.

Recently, adducts of metal carbonyls with phosphine and amine boranes, $\text{M}(\text{CO})_4\cdot\text{H}_3\text{BL}$ ($\text{M} = \text{Cr}, \text{Mo}, \text{W}$; $\text{L} = \text{PMe}_3$,

PPh_3 , NMe_3), have been considered as structural models of methane complexes.^{141, 142} Presumably, these complexes are fairly important as model systems because H_3BL molecules are isoelectronic to methane and, like methane, they are electrically neutral. According to X-ray diffraction data, the borane ligand in the considered complexes is attached to the metal according to the η^3 pattern through one bent hydrogen bridge.¹⁴¹ This mode of coordination is apparently due to steric reasons because it allows the bulky substituent L in the borane ligand to be located far from the $\text{M}(\text{CO})_4$ fragment. According to NMR data, the three hydrogen atoms of the borane ligands are equivalent in solutions; this is indicative of structural non-rigidity of the complexes on the NMR time scale. Examples of η^2 -complexes formed by boranes are also known.¹⁴³

The η^1 -coordination of phosphine or amine boranes to Group VI metal carbonyls, found experimentally, is not quite consistent with the results of calculations for $\text{M}(\text{CO})_5 \cdot \text{CH}_4$, according to which the η^2 -coordination of methane is preferred for these complexes from the energy standpoint.¹⁰⁷ The data presented in this review demonstrate (see Tables 1 and 3) that η^1 -coordination is unusual for methane and seldom corresponds to an energy minimum. Apparently, this difference between the two systems being compared is due to steric factors, in particular, the presence of bulky substituents L in phosphine or amine boranes and the absence of such groups in the methane molecule. Unfortunately, the scope of applicability of this model is limited due to the limited selection of stabilising ligands (mainly, these are carbonyl or phosphine ligands) and complexing ions (Group VI–VIII metals). The number of structurally studied complexes of this type is small. Therefore, this model does not permit a systematic investigation of the dependence of the structure of complexes on the nature of the ligands and the complexing metal. It is also evident that due to steric factors, these complexes are not quite suitable for the modelling of methane complexes.

It has been assumed repeatedly that tetrahydroborates of various metals, whose structures have been studied rather extensively, could serve as structural models of methane complexes.^{144, 145} Indeed, the BH_4^- anion is isoelectronic to the methane molecule. The BH_4^- and CH_4 species are very similar in size and geometry (tetrahedron), which is rather important in view of the considerable influence of the steric factor on the mode of coordination of these ligands. The BH_4^- anion forms a rather large number of complexes, sufficiently stable to be studied experimentally, with metal ions of almost all Groups (with diverse modes of ligand coordination). However, the use of these compounds as models for comparison with methane complexes was precluded by the lack of knowledge of particular factors determining the structural and dynamic properties of tetrahydroborates themselves.

Recently, some previously unknown features of the structures of tetrahydroborate complexes have been elucidated.¹⁴⁶ It was shown that tetrahydroborate complexes can be subdivided into two large groups which differ appreciably in the structural (the mode of coordination of the tetrahydroborate ligand) and dynamic (structural rigidity or non-rigidity) properties.¹⁴⁶ The main factor determining the difference between the structures and dynamic properties of tetrahydroborate complexes is the difference between the electronic configurations of the central metal atom.

Derivatives of transition metals in high oxidation states [as a rule, these are Group III and IV metals having no outer d electrons — d^0 -electron configuration or d^1 -configuration in the case of Ti(III) complexes] and alkali and alkaline earth metals tend to form structurally non-rigid complexes with tridentate BH_4 ligands. Other modes of coordination (η^2 and η^1) in these complexes usually arise due to the presence of stabilising ligands (e.g., as a result of steric hindrance), i.e., they are forced.¹⁴⁷

Tetrahydroborate complexes of monovalent metals with the s^1 configuration have not been isolated in a pure state and no structural data for these compounds are available. However,

gas-phase studies have shown that the tetrahydroborate ligand in the monovalent calcium complex $\text{Ca}(\text{BH}_4)$ is coordinated according to the η^3 type (C_{3v} symmetry).¹⁴⁸ These data are consistent with the results of *ab initio* calculations.¹⁴⁹

Tetrahydroborate η^3 -complexes with d^2 – d^{10} central metal atoms are unknown. Even in the absence of steric hindrance, the BH_4 ligand in these complexes is coordinated according to the η^2 type (in a few cases, according to the η^1 type).

The data presented in this review demonstrate that a similar pattern of dependence of the structure of complexes on the electronic configuration of the central atom is also observed for methane complexes with neutral metal atoms and bare metal ions. Indeed, according to quantum-chemical calculations, a tridentate methane coordination is assumed for $\text{Li}^+(1s^2)$, $\text{Na}^+(2p^6)$, $\text{Mg}^+(3s^1)$, $\text{Sc}^+(3d^1 4s^1)$, $\text{Ti}^+(3d^2 4s^1)$, $\text{V}^+(3d^3 4s^1)$, $\text{Ta}^+(5d^3 6s^1)$, $\text{Cr}^+(4d, 3d^3 4s^1)$, $\text{Fe}^+(3d^6 4s^1)$, $\text{Fe}^0(3d^6 4s^2)$ and $\text{Co}^0(3d^7 4s^2)$ ions having no d electrons in the outer shell. In the case of d^n ions ($n = 2$ – 10) and neutral atoms with a d^n -type shell — $\text{Nb}^+(5d, 4d^4)$, $\text{Co}^+(3f, 3d^8)$, $\text{Rh}^+(3f, 4d^8)$, $\text{Ir}^+(3f, 5d^8)$, $\text{Cu}^+(1s, 3d^{10})$, $\text{Rh}^0(2d, 4d^9)$, $\text{Pd}^0(1s, 4d^{10})$ and $\text{Pt}^0(1s, 5d^{10})$ — a bidentate methane coordination predominates. Due to the scarcity of experimental data and the results of calculations of methane complexes with multicharged M^{n+} ions, it is impossible to draw any general conclusions concerning their structure. However, the dependence of the mode of methane coordination on the electronic configuration of the complexing ion, observed for single-charged ions M^+ , might also hold for multicharged ions M^{n+} .

Similar regularities, that is, the tendency for the formation of η^3 -complexes for d^0 ions and $\eta^2(\eta^1)$ -complexes for d^n -ion derivatives, are also observed for complexes containing stabilising ligands. However, in this case, the mode of methane coordination is determined not only by the electronic configuration of the central metal atom but also by the electronic and steric properties of the ligands. Thus the bidentate coordination of the methane ligand in the complexes formed by d^0 ions, in particular, $\text{Cp}_2\text{Sc}(\text{CH}_3)(\eta^2\text{-CH}_4)^{81}$ and $\text{Cp}_2\text{MR}(\eta^2\text{-CH}_4)^+$ ($\text{M} = \text{Ti}, \text{Zr}$; $\text{R} = \text{CH}_3, \text{C}_2\text{H}_5, \text{C}_3\text{H}_7$),⁸⁶ corresponds to the coordination of the BH_4 groups in similar tetrahydroborates, namely, $\text{Cp}_2\text{Sc}(\eta^2\text{-BH}_4)$, $\text{Cp}_2\text{Ti}(\eta^2\text{-BH}_4)$ and $\text{Cp}_2\text{Zr}(\eta^2\text{-BH}_4)_2$, where this mode of coordination is due to the influence of steric factors.¹⁴⁷

There are only a few exceptions to this regularity. The results of calculations predict a tridentate coordination of methane to the Cr^+ ion in the ground ($6s, 3d^5$) state⁴⁶ and η^3 -coordination to the $\text{Pt}^+(2d, 5d^9)$ ion,⁶⁷ instead of the expected η^2 -coordination. Currently, it is impossible to find out whether this discrepancy in the calculation results is caused by the difference in the coordination properties of methane and the tetrahydroborate anion or is related to inaccuracy of the calculation techniques. An extension of the basis set and the use of higher-level theory for these calculations might bring the calculated data in correspondence with those we predict in terms of the tetrahydroborate model, as was the case for the $\text{Cu}^+(1s, 3d^{10})$ ion.

Unfortunately, direct comparison of the structure of methane complexes with similar tetrahydroborate complexes can seldom be carried out. The prevalence of monodentate coordination for methane complexes can be explained by the lower strength of the bond between the methane ligand and the metal compared to that in the case of tetrahydroborate; this makes methane more susceptible to the influence of the ligands.

In our opinion, the analogy found in the dependences of the mode of coordination of methane and the tetrahydroborate anion on the electronic configuration of the central atom for these two types of complexes is not accidental. This is due, apparently, to high accuracy of modern quantum-chemical calculations, which often allow one to predict properly the relative stabilities of various conformations of methane complexes, and to the existence of some common features in the structures of complexes formed by tetrahedral species, BH_4^- and CH_4 .

Probably, the discovered dependence of the structure of the BH_4^- and CH_4 complexes on the nature of the central metal atom is related to the difference between the coordination properties of d^0 and d^n ions, well-known in coordination chemistry.¹⁵⁰ The d^0 -metal ions tend to undergo ion–ion or ion–dipole electrostatic interactions with formation of weak complexes, while d^n -metal ions are more prone to covalent interactions to give strong metal–ligand bonds. Thus, these two types of complexes differ in the nature of the metal–ligand interaction. The results of studies of the electronic structure of the methane ligand in complexes formed by d^0 and d^n ions are in line with this assumption.

In d^0 -ion complexes $[\text{Cl}_2\text{LuH}]$,⁸⁰ $[\text{Cl}_2\text{LnZ}]$ ($Z = \text{H}, \text{CH}_3$),⁸² $\text{H}_2\text{M} = \text{NH}$ ($\text{M} = \text{Ti}, \text{Zr}, \text{Hf}$)⁹⁵, methane coordination is accompanied by an increase in the negative charge on the carbon atom and the positive charge on the bridging hydrogen atoms ($\text{C}^{\delta-} - \text{H}_b^{\delta+}$). Therefore, metathesis of σ -bonds in the series of lanthanide complexes and methane addition to imide complexes can be interpreted as hydrogen transfer between two anionic CH_3 groups in the coordination sphere of the positively charged central atom.^{82, 96} When methane reacts with $\text{CpRh}(\text{CO})$, polarisation of the $\text{C}-\text{H}$ bonds switches to the opposite one: $\text{C}^{\delta+} - \text{H}_b^{\delta-}$ (see Ref. 118). Unfortunately, data on $\text{C}-\text{H}$ bond polarisation in other d^n -ion complexes are missing, but one can assume that polarisation of the methane $\text{C}-\text{H}$ bonds in these complexes would be similar to that found in $\text{CpRh}(\text{CO})(\text{CH}_4)$. Apparently, the difference in the polarisation of $\text{C}-\text{H}$ bonds of the methane ligand is responsible for the different mechanisms of activation of these bonds by d^0 - and d^n -ion complexes, namely, proton transfer between two carbanions for d^0 -ion complexes and oxidative addition of the hydride ion and the carbocation for d^n complexes.

The observed dependence of the ligand denticity on the nature of the complexing ion can be explained qualitatively in the following way. In the case of spherically symmetrical ions with an $s(s^1, s^2)$ or s^2p^6 outer electronic shell where the ion–ion or ion–dipole interaction predominates, the highest bond energy is provided by the shortest distance between the components, which is attained in the case of η^3 -coordination. As noted above, this entails only a slight change in the geometric parameters of the methane ligand. In the case of d^n ions, the predominant contribution is made by directional covalent interaction with one or two $\text{E}-\text{H}$ bonds of the EH_4 species ($\text{E} = \text{B}, \text{C}$), resulting in η^2 - or η^2_2 -coordination, higher bond energy and more pronounced distortion of the ligand geometry.

It should be noted that the differences between the properties of d^0 and d^n transition metal complexes can also be followed in systems with intramolecular $\text{M}\cdots\text{H}-\text{C}$ agostic bonds. Indeed, the figure, reported previously,¹⁴⁰ which describes the dependence of the $\text{M}\cdots\text{H}-\text{C}$ angle (α) in complexes with an agostic bond on the radius r_{bp} ($r_{\text{bp}} = d_{\text{bp}} - r_{\text{M}}$, where d_{bp} is the distance from the metal to the electron pair of the $\text{C}-\text{H}$ agostic bond, r_{M} is the covalent radius of the metal, and bp is the bonding pair), shows that any point for d^0 complexes lies below the curve characteristic of d^n complexes (Fig. 4).

Thus, of all the structural models of methane complexes considered above, the tetrahydroborate model describes most adequately the available results of structural studies of methane complexes. In terms of this model, one is not only able to make assumptions concerning the influence of the electronic configuration of the central atom on the mode of coordination of the methane ligand but can also attack the problem of the possible difference between structural properties of $\text{M}\cdots\text{C}-\text{H}$ agostic bonds in d^0 and d^n transition metal complexes.

One may hope that further studies of the structure of tetrahydroborate complexes would throw light on some structural features of methane complexes. For instance, information concerning monodentate tetrahydroborate complexes, little studied at present, could be useful for the understanding of factors that determine the prevalence of η^2_1 methane coordination in the complexes containing stabilising ligands. Systematic research

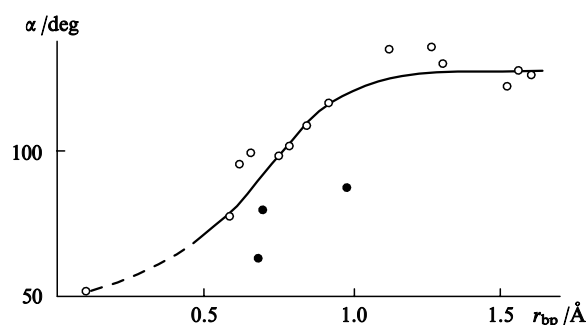


Figure 4. Dependence of the $\text{M}\cdots\text{H}-\text{C}$ angle in complexes with agostic bonds on the radius r_{bp} (according to Ref. 140).

The light dots are the $\text{M}\cdots\text{H}-\text{C}$ angles in d^n -complexes and the dark dots correspond to d^0 -complexes.

into structurally rigid tetrahydroborates could be helpful in the search for compounds that would hold methane most firmly in the coordination sphere.

* * *

The considered experimental and theoretical data on the structures of complexes containing methane as a ligand and comparison of these data with the structural information concerning tetrahydroborate complexes provide the following conclusions:

— methane as a ligand is characterised by diverse modes of coordination to central metal atoms. The mode of coordination of the methane ligand depends appreciably on the electronic configuration of the central metal atom and the nature of stabilising ligands;

— neutral atoms M^0 and bare ions M^+ tend to form $\text{M}(\eta^2\text{-CH}_4)^+$ or $\text{M}(\eta^3\text{-CH}_4)^+$ complexes. The geometry of these complexes is determined by the electronic configuration of the central atom: ions and neutral atoms with either s or s^2p^6 outer shell form complexes with tridentate coordination of methane. In the case of d^n ions ($n = 2-10$), bidentate methane coordination predominates. Apparently, similar regularities are to be expected for multicharged M^{n+} ions;

— for ML_n fragments containing stabilising L ligands, calculations point to a similar dependence of the structure of methane complexes on the electronic configuration of the central atom (η^3 -complexes are formed for derivatives of d^0 ions and are not formed for complexes of d^n ions). However, the presence of stabilising ligands results in η^2 and η^2_1 modes of methane coordination becoming more energetically favourable for these complexes, apparently, due to the electronic and steric influence of the ligands. Factors determining the preference of the η^2_1 methane coordination over η^2 -coordination have not yet been elucidated.

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VI. Supplement

Below we present the accepted abbreviations for calculation techniques and software

SCF — self-consistent field method;

LCGO — linear combination of gaussian orbitals;

MCPF — modified coupled pair functional method;

DFT — density functional theory;

PCI-80 — parametrised configuration interaction method with an 80% parameter (in the general case, PCI-X);¹⁵¹

RECP — relativistic effective core potential;

B3LYP — Becke's gradient-corrected three-parameter non-local exchange functional^{152, 153} and Lee–Yang–Parr gradient-corrected non-local correlation functional;¹⁵⁴

B3P86 — Becke's gradient-corrected three-parameter non-local exchange functional combined with Perdew's gradient-corrected correlation functional;¹⁵⁵

B3PW91 — the same with the Perdew *et al.* correlation functional;¹⁵⁶

RHF — restricted Hartree–Fock method;

UHF — unrestricted Hartree–Fock method;

HFSD — Hartree–Fock method with singly and doubly excited configurations;

SKBJ — relativistic compact effective core potential and the Stevens, Basch, Krauss and Jasien shared-exponent basis set;¹⁵⁷

DZVP — a basis set proposed by Wimmer and coworkers;¹⁵⁸

6-31G — Pople basis set with the 1s-AO being approximated by six and the 2s,2p-AO, by four gaussian functions grouped in (3,1); 6-31G** — the 6-31G basis set extended by d- and p-polarisation functions;

6-31G+ — the 6-31G basis set extended by diffusive functions;

QCI — quadratic configuration interaction method;

QCISD — single and double quadratic configuration interaction method;

QCISD(T) — the same with an estimation of triple excitations by a perturbation method;

MP2(3,4) — second- (third-, fourth) order Møller–Plesset perturbation theory;

MP4SDTQ — fourth-order Møller–Plesset perturbation theory with single, double, triple and quadruple excitations;

CASSCF — complete active space self-consistent field method;

MR-SDCI-CASSCF — multideterminant configuration interaction method with single and double excitations using the wave function obtained by CASSCF;

GRADSCF — a vectorised SCF method with the first and second derivatives;

SCF-CI — self-consistent field configuration interaction method;

SCF-SDCI — self-consistent field with single and double configuration interactions;

CCSD(T) — coupled-cluster theory with singles and doubles and non-iterative estimation of triple excitations;

GGA — generalised gradient approximation;¹⁵⁹

PBE — Perdew, Burke and Ernzerhof density functional;¹⁵⁹

INDO — intermediate neglect of differential overlap;

SBK — relativistic compact effective potential and the Stevens, Basch and Krauss basis set;¹⁶⁰

LANL1DZ, LANL2DZ — effective core potentials and basis sets developed by Hay and Wadt at the Los-Alamos National Laboratory;^{161–163}

GVB (General Valence Bond) — a quantum-chemical program package developed at the California Institute of Technology under the direction of W A Goddard III;

GAMESS (General Atomic and Molecular Electronic Structure System) — a quantum-chemical program package (M Dupuis, D Spangler, J Wendolowski. NRCC Software Catalog. Vol. 1, Program No. QG01);¹⁶⁴

GAMESS-UK — a quantum-chemical program package (F M Guest, P Fantucci, R J Harison, J Kendrick, J H Van Lenthe, K Schoeffel, P Sherwood. CFS Ltd., Darenbury, UK, 1993);

GAUSSIAN80–98 — various versions of a quantum-chemical program package developed by the GAUSSIAN corporation (Gaussian Inc., Pittsburgh, PA, 1998);

MOLECULE-SWEDEN — a quantum-chemical program package (J Almlof, C W Bauschlicher Jr., M R A Blomberg, D P Chong, A Heiberg, S R Langhoff, P-A Malmqvist, A P Rendell, B O Roos, P E M Siegbahn, P R Taylor);

MOLPRO — a quantum-chemical program package developed at the Sussex University;^{165–168}

Dgauss — a quantum-chemical program package;¹⁶⁹

STOCKHOLM — a quantum-chemical program package for general purposes (P E M Siegbahn, M R A Blomberg, L G M Petersson, B O Roos, J Almlof);

A-MOL — a program system developed by Baerends *et al.*¹⁷⁰ and vectorised by Ravenek;¹⁷¹

Laikov — is the program package developed by Laikov;¹⁷²

ADF — the Amsterdam density functional program system;¹⁷³

Jaguar 4.0 — a quantum-chemical program package of the Schrödinger corporation (Schrödinger Inc., Portland, Oregon, 1991–2000);

MELD — a quantum-chemical program package (E R Davidson, L E McMurchie, S T Elbert, S R Langhoff, D Rawlings, D Feller. Computer Centre Library Program No 030).

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Nitro derivatives of 1,3,5-triazine: synthesis and properties

A V Shastin, T I Godovikova, B L Korsunskii

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Abstract. The published data on nitro derivatives of 1,3,5-triazine, belonging to the class of high-energy substances, have been systematised for the first time. The properties of *C*-nitrotriazines, nitraminotriazines and nitroalkyltriazines are considered. The data on the synthesis of previously unknown trisubstituted 1,3,5-triazines containing various functional groups including trinitromethyl groups are generalised. The bibliography includes 69 references.

I. Introduction

1,3,5-Triazines are known for about 200 years.¹ They are used as herbicides, pesticides, coupling reagents in the peptide synthesis, modifiers, antioxidants, thermal stabilisers, antipyrenes, bleaching agents, dyes and base compounds for combinatorial libraries.^{1–6} Melamine–formaldehyde resins have found broad application.⁷ It was shown that 1,3,5-triazines encounter in some natural objects, such as meteorites and algae.^{8,9} However, despite the great body of the published data on substituted 1,3,5-triazines,^{1,7,9,10} information on nitro-, nitramino- and nitro(poly-nitro)methyl 1,3,5-triazine derivatives is scattered in the literature.

The aim of the present review is to generalise and systematise the published data on nitro derivatives of 1,3,5-triazines which present special interest as high-energy compounds. Some of these compounds have been synthesised as explosives or components of explosive mixtures; therefore, special emphasis in their description is given to their explosive properties and sensitivity to shock, friction, etc.

II. Nitro-1,3,5-triazines

There are several approaches to the synthesis of nitro-1,3,5-triazines, viz.:

- (1) electrophilic nitration of the triazine ring;
- (2) nucleophilic substitution of the nitrite ion for the halogen atom or other good leaving groups (nucleophilic nitration);
- (3) oxidation of amino, nitroso, hydroxyamino or azido groups;
- (4) cyclotrimerisation of nitriles containing a nitro group;
- (5) nitration of heterocyclic organometallic compounds.

1. Electrophilic nitration

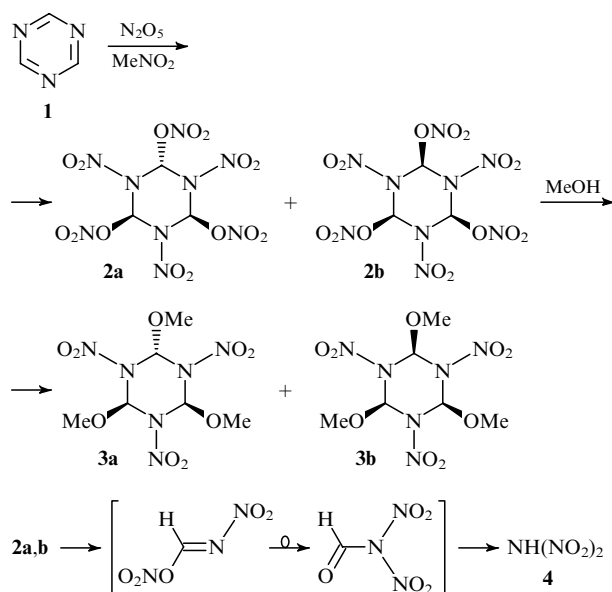
Electrophilic nitration of 1,3,5-triazine (**1**) has been described relatively recently.¹¹ In contrast to nitration of aromatic compounds, that of heteroaromatic compounds containing several nitrogen atoms is significantly inhibited due to the acceptor effect of the nitrogen atoms present in the ring (the nitration rate decreases 10⁶-fold upon substitution of C=N for one C=C fragment).¹² Moreover, nitration in acidic media creates additional difficulties due to easier protonation of nitrogen-containing heterocycles in comparison with aromatic rings, which also reduces the nitration rate. In general, direct nitration of six-membered azines is used only if the heterocycle contains some activating groups (e.g., amino or hydroxy groups) or *N*-oxide groups. However, no more than two nitro groups can be incorporated simultaneously irrespective of the nature of the heterocycle.¹³ Nitration of unsubstituted triazines with nitric anhydride (Scheme 1) occurs as a conjugate addition of nitronium nitrate to the N=C bond, which affords isomeric *N*-nitronitroxyhexahydro-1,3,5-triazines, viz., 1,3,5-trinitro-*cis*-2,4,6-trinitroxyhexahydrotriazine (**2a**) and 1,3,5-trinitro-*trans*-2,4,6-trinitroxyhexahydrotriazine (**2b**).¹¹ In this case, nitration proceeds similarly to the known halogenation reactions of the triazine ring and affords perhalogenohexahydrotriazines.¹⁴ The structures of the compounds obtained were established¹¹ based on the analysis of the NMR spectra of the reaction mixture and the composition of their methanolysis products **3a** and **3b** (yields 14% and 10%, respectively). Nitronitroxyhexahydro-1,3,5-triazines **2a,b** themselves could not be isolated because of their low stability (according to the NMR spectroscopic data, they are rather stable at temperatures below 0 °C and decompose at nearly the same rates at 20 °C). Presumably,¹¹ dinitramide (**4**) is the final decomposition product of these compounds (see Scheme 1). This is formed as a result of retro-[2+2+2]cycloaddition of hexahydrotriazines **2a,b** and formation of transient imidoyl nitrate which is further rearranged into *N,N*-dinitroformamide to give dinitramide **4**. The reaction products **3a,b** represent methoxy-substituted analogues of hexogen.

A V Shastin, B L Korsunskii Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-096) 514 32 44. Tel. (7-096) 522 33 01. E-mail: shastin@icp.ac.ru (A V Shastin). Tel. (7-095) 939 71 10. E-mail: kors@polymer.chph.ras.ru, kor@icp.ac.ru
T I Godovikova N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 134 03 76, (7-095) 938 36 27. E-mail: orakitn@ioc.ac.ru

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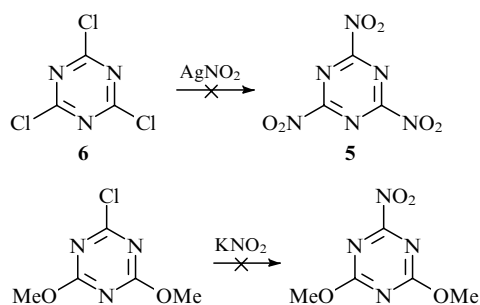
Uspekhi Khimii 72 (3) 311–320 (2003); translated by R L Birnova

Scheme 1



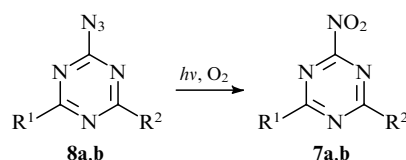
2. Nucleophilic nitration

Nucleophilic nitration is not virtually applied to aromatic compounds because of the high mobility of the aromatic nitro group and the ambident nature of the nitrite ion.¹⁵ Nevertheless, alkali metal nitrites were used as efficient nucleophiles for the replacement of halogen atoms in 1-halogeno-4-nitro-, 1-halogeno-4,6-dinitro- and 1-chloro-2,4,6-trinitrobenzenes under conditions of phase transfer catalysis (solid phase – liquid) in the presence of 18-crown-6 ether.¹⁶ Nucleophilic nitration of some halogen-substituted pyridazinones also gives acceptable yields.¹⁷ It is not therefore surprising that nucleophilic nitration of cyanuric chloride (6) with silver nitrite was the first, albeit unsuccessful, attempt to synthesise 2,4,6-trinitro-1,3,5-triazine (5).¹⁸ A similar reaction of 4,6-dimethoxy-2-chloro-1,3,5-triazine with potassium nitrite was unsuccessful also.¹⁹

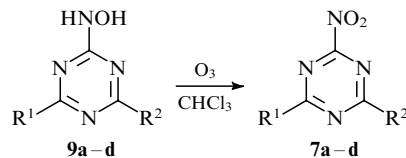


3. Oxidation of nitrogen-containing groups

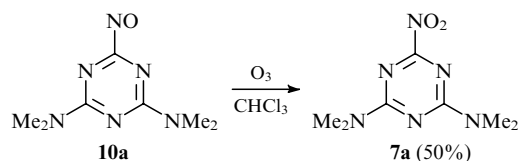
Oxidation of exocyclic nitrogen-containing groups is a convenient method for the synthesis of nitroazines.¹³ Few mononitro-1,3,5-triazines 7 were prepared by photochemical oxidation of azido-1,3,5-triazines 8 in the presence of oxygen²⁰ (similar to oxidation of azidopyrimidines²¹) or by ozonisation of the corresponding hydroxyaminotriazines 9 or nitrosotriazines 10, e.g., the bisdimethylamino-substituted derivative 10a.^{22,23} The yields of mononitrotriazines 7 are 15%–50%. Photooxidation includes the formation of a transient triplet nitrene. Ozonisation is very sensitive to the electronic properties of the substituents in the triazine ring; thus the reaction is only successful if one or two dialkylamino groups are present in the ring.



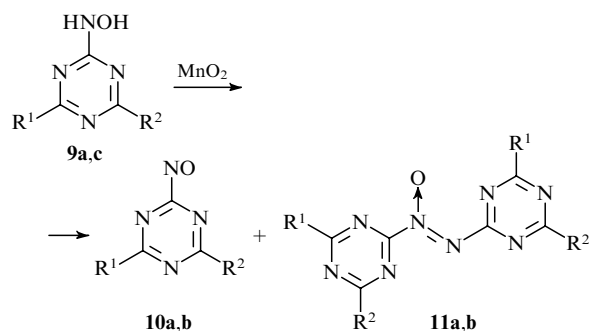
a: $\text{R}^1 = \text{R}^2 = \text{NMe}_2$ (29%); b: $\text{R}^1 = \text{OMe}$, $\text{R}^2 = \text{NMe}_2$ (15%).



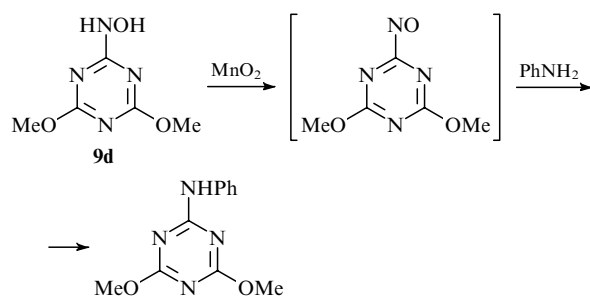
a: $\text{R}^1 = \text{R}^2 = \text{NMe}_2$ (28%); b: $\text{R}^1 = \text{OMe}$, $\text{R}^2 = \text{NMe}_2$ (30%); c: $\text{R}^1 = \text{R}^2 = \text{N}(\text{CH}_2)_5$ (50%); d: $\text{R}^1 = \text{R}^2 = \text{OMe}$ (0%).



However, this method cannot be used for the introduction of several nitro groups into the triazine ring. The oxidation of hydroxyaminotriazines 9a,c with manganese oxide in chloroform gives only nitrosotriazines 10a,b and their condensation products with the starting hydroxylamines 11a,b.²⁴ The oxidation of 2-hydroxyamino-4,6-dimethoxy-1,3,5-triazine (9d) under identical conditions resulted in the formation of solutions with the greenish colour typical of nitrosoazines, but the attempts to isolate the corresponding triazine or to identify its adduct with aniline failed. 2-Anilino-4,6-dimethoxy-1,3,5-triazine formed as a result of substitution of aniline for a mobile nitroso group was the only compound identified.²⁴

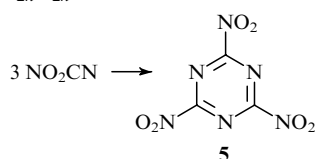


Compounds	R^1, R^2	Yield of 10 (%)	Yield of 11 (%)
9a, 10a, 11a	NMe_2	35	0
9c, 10b, 11b	$\text{N}(\text{CH}_2)_5$	30	30



4. Cyclotrimerisation

The trimerisation of hypothetical nitrocyanogen into 2,4,6-trinitro-1,3,5-triazine (**5**) is discussed in a study²⁵ devoted to the energy characteristics of trinitrotriazine as a representative of a novel class of high-energy compounds of the general formula $C_nN_{2n}O_{2n}$.



This scheme looks rather attractive: according to the calculations [*ab initio* calculations with optimisation of geometrical parameters using the HF/6-31G* and MBPT(2)/6-31G* basis sets and the ACES II software], the trimerisation of hypothetical nitrocyanogen can be energetically favourable: $\Delta E = -70.2 \text{ kcal mol}^{-1}$ as calculated by MBPT(2). However, it has been shown²⁶ that the reaction of HCN with NO_2BF_4 in nitromethane, tetrahydrothiophene 1,1-dioxide or in the absence of a solvent is not accompanied by trimerisation of the intermediate, structurally similar and less sterically hindered neutral $\text{CN}-\text{NO}_2$.

In the calculated trinitrotriazine structure with the symmetry C_3 corresponding to the minimum energy, the aromatic triazine ring is planar and the nitro groups are rotated 40° to the ring plane. Such a spatial arrangement of the nitro groups compensates for their conjugation with the ring and the mutual repulsion of the negatively charged oxygen atoms and the nitrogen atoms of the triazine ring (the minimum value corresponds to the angle 90°). The length of the C–N bond in the triazine ring is equal to 1.331 Å, the NCN angle is equal to 128.4° (according to the electron diffraction spectroscopy data, the length of the C–N bond in unsubstituted 1,3,5-triazine is 1.338 Å, while the NCN angle is equal to 126.2°). The standard enthalpy of formation (ΔH_f°), the heat of explosive degradation (ΔE_r) and specific impulse (I_{sp}) of compound **5** were calculated to be equal to $\Delta H_f^\circ = 46 \text{ kcal mol}^{-1}$, $\Delta E_r = 304 \text{ kcal mol}^{-1}$, I_{sp} is 269 s at ambient pressure and 294 s in vacuum. These characteristics are similar to the corresponding values for hexogen, but the calculated density (ρ_0) of trinitrotriazine **5** is higher (1.82 and 2.1 g cm^{-3} for hexogen and compound **5**, respectively).²⁷ Korkin and Bartlett²⁵ expect to prepare trinitrotriazine **5** using an original scheme which includes trimerisation of nitrocyanogen. The following characteristics of compound **5** have been calculated²⁸ (for comparison, the corresponding parameters for hexanitrobenzene are given in parentheses): detonation rate (D), 9530 (9413) m s^{-1} ; $\Delta H_f^\circ = 18$ (36) kcal mol^{-1} , $\rho_0 = 1.973$ (1.973) g cm^{-3} .

5. Nitration of organometallic compounds

Nitration of 1,3,5-triazine stannyl derivatives is yet another, hitherto non-explored method for the synthesis of nitro-substituted triazines. Recently, this approach has been used in the synthesis of 2-nitro derivatives from 2-trimethylstannylated benzo[*b*]furan, benzo[*b*]thiophene, substituted indoles and 2-, 3- and 4-trimethylstannylpyridines under the action of tetranitromethane or dinitrogen tetroxide (in the case of 3- and 4-trimethylstannylpyridines, the yields did not exceed 2%).²⁹

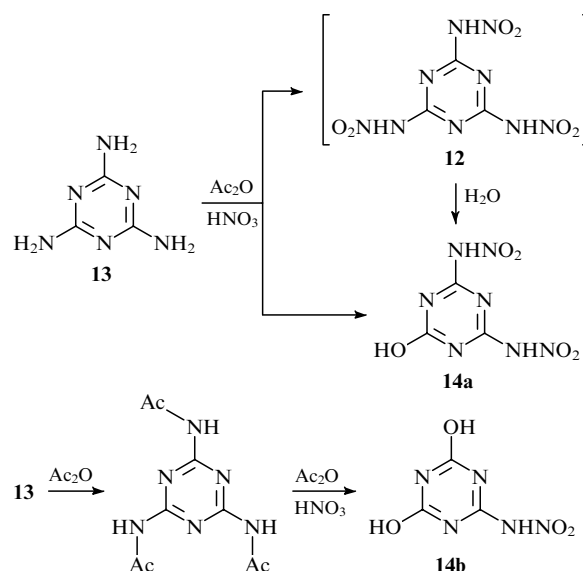
Thus, 2,4,6-trinitro-1,3,5-triazine, a heterocyclic analogue of one of the most potent explosives, *viz.*, hexanitrobenzene,³⁰ could not be prepared so far.

III. Nitramino-1,3,5-triazines

Both substituted and unsubstituted nitramines based on heterocyclic compounds are usually prepared by nitration of the corresponding amines, sometimes with preliminary protection of the NH_2 group. Primary and secondary (*i.e.*, containing the NHNO_2 and NRNO_2 groups, respectively) nitramines of the 1,3,5-triazine series are documented. Numerous attempts at the

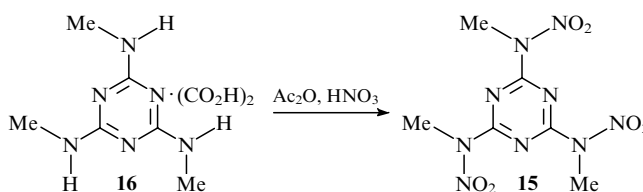
synthesis of 2,4,6-tris(nitramino)-1,3,5-triazine (**12**), which is the first member of this series, failed.^{31,32}

It was shown³³ that nitration of melamine (**13**) gives dinitroammeline (**14a**) in 44%–52% yield. Presumably, the transient compound **12** formed in this reaction is hydrolysed to dinitroammeline with the loss of a nitramino group, which is typical of nitramino derivatives of six-membered heterocycles.³² It is of note that nitration of triacetylmelamine at higher temperatures yields nitroammelide (**14b**). The feasibility of dinitroammeline as a high-energy compound is being investigated.^{33,34} Dinitroammeline rapidly decomposes on heating to 228°C , while nitroammelide decomposes at 248°C and slowly sublimates at 200°C (1 Torr).



Melamine salts with nitramide and nitric acid are considered to be promising candidates for high-energy compounds.³⁵

The data on substituted nitraminotriazines, *i.e.*, triazines containing secondary nitramino groups as substituents, are more numerous. Thus the synthesis and properties of 2,4,6-tris(methylnitramino)-1,3,5-triazine (**15**) have been described.³⁶ This compound is prepared by nitration of a complex of 2,4,6-tris(methylamino)-1,3,5-triazine with oxalic acid (**16**) with acetyl nitrate (40°C , 5 h) (the yield of the product **15** is 72%).

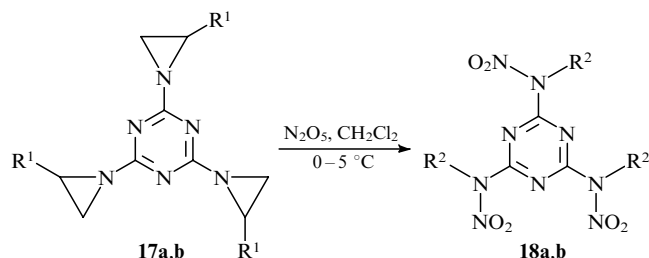


According to derivatography data, triazine **15** decomposes at 210°C . This compound has the following characteristics (for comparison, some parameters of tetryl are given in parentheses): single crystal density (ρ_m), 1.67 g cm^{-3} , $\Delta H_f^\circ = 275.1$ (33.9) kJ mol^{-1} , friction sensitivity > 36 (36), impact sensitivity, 12.5 (6.5–12.5),[†] detonation rate, 7228 m s^{-1} at the charge density of $\rho = 1.53 \text{ g cm}^{-3}$ (7575 m s^{-1} at $\rho = 1.71 \text{ g cm}^{-3}$).³⁶

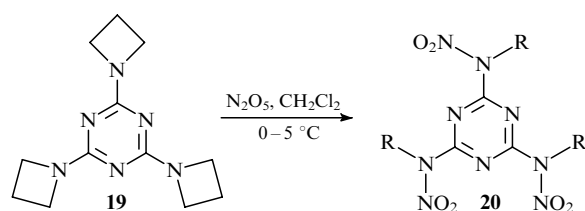
The nitration of such melamine derivatives as 2,4,6-triaziridino-1,3,5-triazine (**17a**) and 2,4,6-tris(methylaziridino)-1,3,5-

[†] There are many ways for expressing the sensitivity of explosives. As a rule, this is determined as a ratio of the number of explosions of a standard amount of a substance for a given number of trials to the total number of trials at a given mass and load fall height. In this case, they represent relative values.³⁶ In the Russian literature, the sensitivity is traditionally expressed on a per cent basis; the mass and load fall height separated by an oblique stroke are given in parentheses: $x\%$ ($M \text{ kg}/N \text{ cm}$).

triazine (**17b**) with N_2O_5 in dichloromethane at $0-5^\circ\text{C}$ (the molar ratio **17**: N_2O_5 is 1.0:3.3) afforded nitramines **18a,b** (yields 95% and 78%, respectively).³⁷ The nitration of 2,4,6-triazetidino-1,3,5-triazine (**19**) under analogous conditions yields a mixture of products which contains nitramine nitrate **20** (60%) and non-identified compounds.³⁸



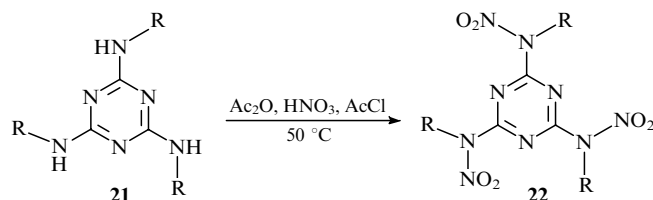
$\text{R}^1 = \text{H}$ (**a**), Me (**b**); $\text{R}^2 = \text{CH}_2\text{CHR}^1\text{ONO}_2$.



$\text{R} = (\text{CH}_2)_3\text{ONO}_2$.

Some characteristics of triazine **18a** (its commercial name is 'Tris-X') have been reported:³⁹ m.p. = $68-69^\circ\text{C}$, $\rho_m = 1.73\text{ g cm}^{-3}$ (data from X-ray diffraction analysis), impact sensitivity, 57, detonation rate, 8700 m s^{-1} . The latter value suggests that compound **18a** is a high-energy low-melting explosive despite its relatively low density.

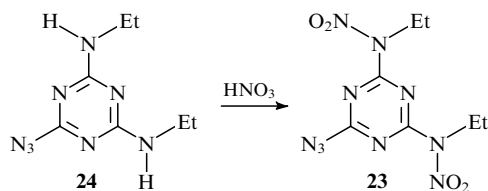
2,4,6-Tris(picrylnitramino)-1,3,5-triazine (**21**) gave 2,4,6-tris(picrylnitramino)-1,3,5-triazine (**22**) in 95% yield.⁴⁰



$\text{R} = 2,4,6-(\text{NO}_2)_3\text{C}_6\text{H}_2$.

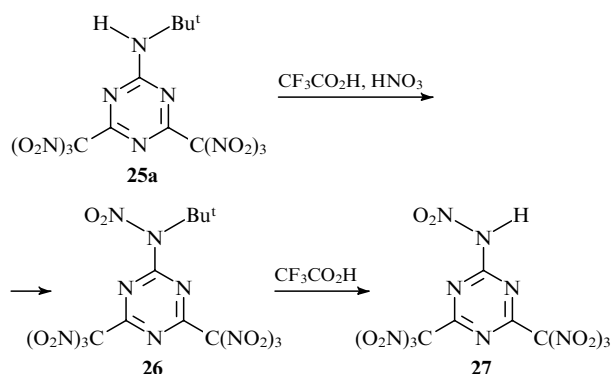
Unlike nitramines **18a,b**, which dissociate at $177-197^\circ\text{C}$, compound **22** is unstable: this slowly decomposes at 0°C and rapidly decomposes at 100°C .³⁹

Synthesis of 2-azido-4,6-bis(ethylnitramino)-1,3,5-triazine (**23**) from 2-azido-4,6-bis(ethylamino)-1,3,5-triazine (**24**) has been described.⁴¹ The characteristics of compound **23** obtained in 20% yield are as follows: m.p. = $40-41^\circ\text{C}$, $\rho_m = 1.375\text{ g cm}^{-3}$, $\Delta H_f = 540.2\text{ kJ mol}^{-1}$, initial decomposition temperature, 207°C . Presumably,⁴¹ elimination of nitrogen from the azido group is the initial step in the decomposition of azidotriazine **23**.

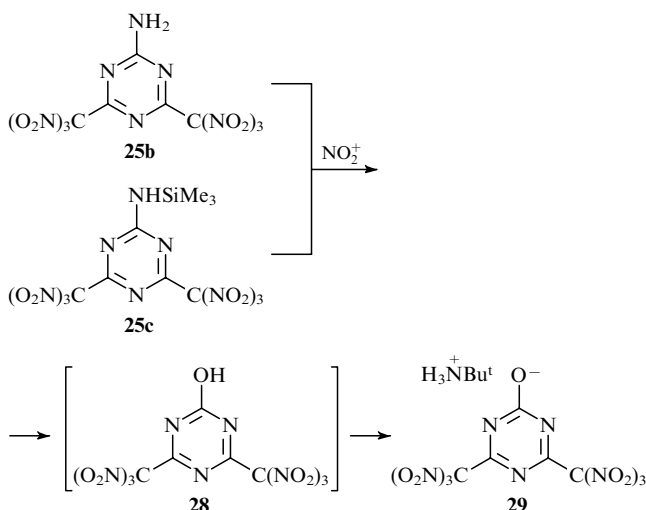


The use of *tert*-butyl protection in the nitration of bistrinitromethyl-substituted triazine **25a** and subsequent removal of the protective group in the *tert*-butylnitraminotriazine **26** formed with

trifluoroacetic acid has enabled the preparation of nitraminotriazine **27**,⁴² which possesses low thermal stability.



Attempts at direct nitration of unprotected aminotriazine **25b** and introduction of the trimethylsilyl protective group (compound **25c**) were ineffective: the amino group of triazine underwent oxidative hydroxylation. 2-Hydroxy-4,6-bis(trinitromethyl)-1,3,5-triazine (**28**) formed in this reaction was isolated and characterised as *tert*-butylammonium salt **29** (for the synthesis of trinitromethyl-substituted aminotriazines see Section IV.1).

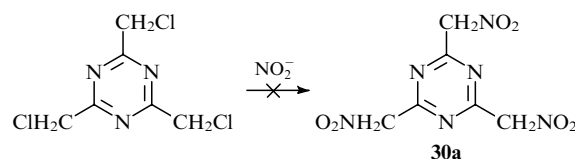


IV. Nitromethyl-, dinitromethyl- and trinitromethyl-1,3,5-triazine derivatives

The synthesis of these 1,3,5-triazine derivatives includes nucleophilic substitution, nitration, destructive nitration and cyclotrimmerisation.

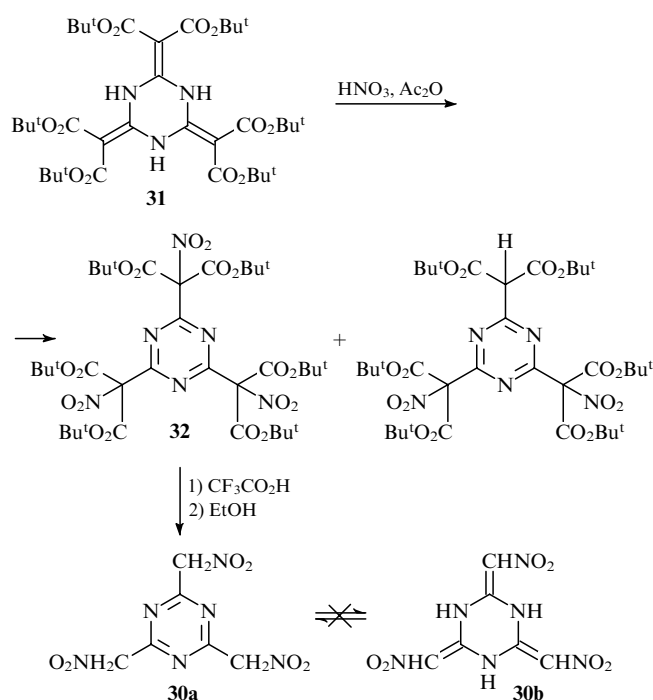
1. Nitromethyl derivatives

The attempts to synthesise 2,4,6-tris(nitromethyl)-1,3,5-triazine (**30a**), the first representative of nitromethyl-substituted 1,3,5-triazines, by nucleophilic substitution of the chlorine atom in 2,4,6-tris(chloromethyl)-1,3,5-triazine were unsuccessful.⁴³

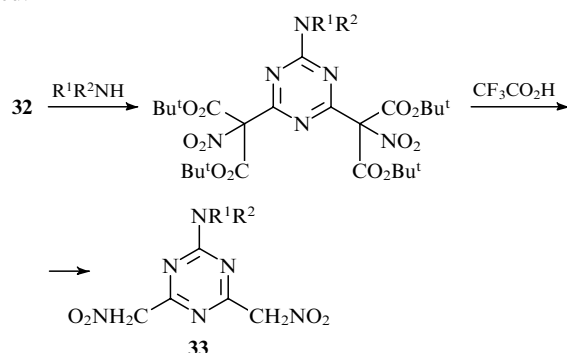


Compound **30a** could be synthesised⁴³ starting from 2,4,6-tris[di(*tert*-butoxycarbonyl)methylidene]hexahydro-1,3,5-triazine (**31**). 2,4,6-Tris(nitromethyl)-1,3,5-triazine (**30a**) represents a solid yellow-coloured substance (decomposition temperature is 155°C). According to NMR spectroscopic data (acetone- d_6), it

exists in solution exclusively in a nitromethyl form (the potential tautomer **30b** was not found).⁴³

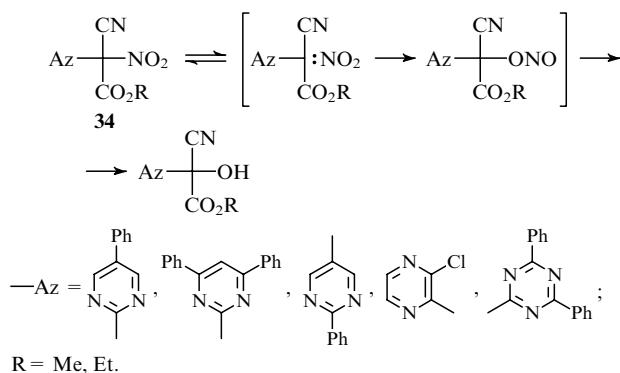


A convenient method for the synthesis of substituted 2-amino-4,6-bis(nitromethyl)-1,3,5-triazines **33** based on 2,4,6-tris[di(*tert*-butoxycarbonyl)nitromethyl]-1,3,5-triazine (**32**) has been developed.^{44, 45}



$R^1, R^2 = \text{H, Alk.}$

As can be seen from the scheme, the bulky di(*tert*-butoxycarbonyl)nitromethyl group in triazine **32** acts as a pseudo-halogen. It is noteworthy that reactions involving compounds of the type **34** (triazine, pyrimidine and pyrazine derivatives) are documented,⁴⁶ where the nitro group plays the role of a leaving group. Such a



$R = \text{Me, Et.}$

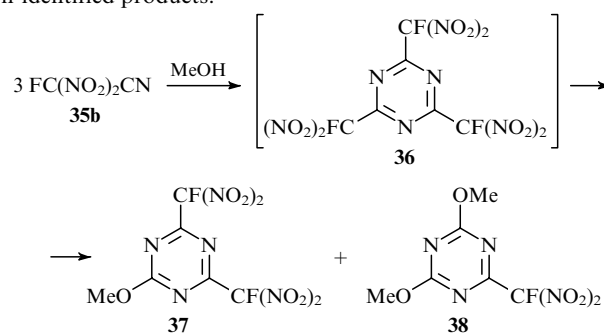
substitution proceeds by a mechanism which involves the initial formation of a radical pair.

Apparently, substitution of di(*tert*-butoxycarbonyl)nitromethyl group (rather than the nitro group) in triazine **32** is due to both the high electrophilicity of the triazine ring and the shielding of the nitro group with bulky *tert*-butoxycarbonyl substituents.

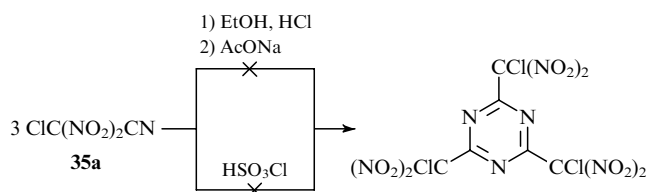
To the best of our knowledge, no methods for the synthesis of nitromethyl-1,3,5-triazines based on destructive nitration or cyclisation of the corresponding nitroacetonitriles have been reported so far.

2. Dinitromethyl derivatives

The known methods for the synthesis of dinitromethyltriazine derivatives are based on cyclotrimerisation of dinitrochloroacetonitrile (**35a**) under conditions of acidic and basic catalyses⁴³ and cyclotrimerisation of fluorodinitroacetonitrile⁴⁷ (**35b**) in methanol at 60 °C and 0.8 GPa. It is assumed⁴⁷ that the target 2,4,6-tris(dinitrofluoromethyl)-1,3,5-triazine (**36**) is formed but is converted into the corresponding mono- and dialkoxy derivatives **37** and **38** under the reaction conditions. These compounds could not be isolated in a pure state and their existence was judged from the respective transformation products, mass and NMR spectra. According to mass spectrometry data, the yields of the target triazines **37** and **38** were 45% and 19%, respectively, along with non-identified products.



The attempts at trimerisation of dinitrochloroacetonitrile (**35a**) in basic and acidic media were unsuccessful.⁴³ Two approaches were used, *viz.*, preparation of the corresponding imidate hydrochloride and *in situ* treatment with anhydrous sodium acetate at 0 °C and trimerisation of the nitrile with chlorosulfonic acid. Both methods gave negative results: a vigorous reaction with heating and evolution of nitrogen oxides occurred when the reaction product of the nitrile with ethanol was treated with sodium acetate; no trimerisation occurred in the presence of chlorosulfonic acid.

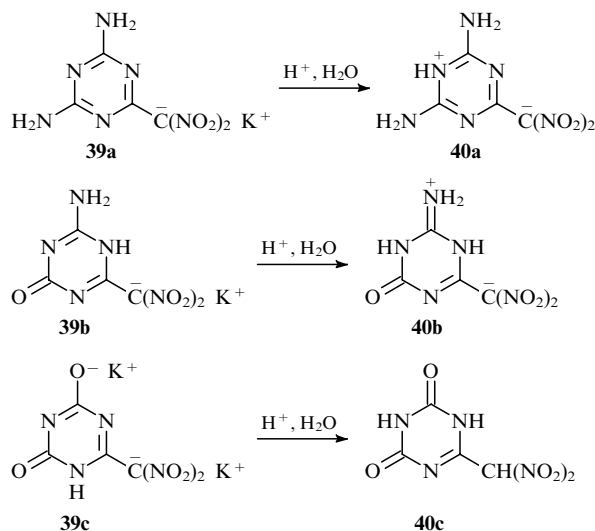


The known method for the synthesis of dinitromethyl derivatives from oximes of aromatic and heteroaromatic carbonyl compounds^{48–51} was not applied to triazine derivatives, although the synthesis of 1,3,5-triazine-2,4,6-tricarboxaldehyde trioxime had been reported.⁵² The authors of the review are unaware of the attempts to use dinitromethane salts for the synthesis of dinitromethyltriazine derivatives, although this method is applied in the case of halogenobenzenes activated by nitro groups.⁵³ 1,3,5-Triazines containing a dinitromethyl group together with amino and hydroxyl(oxo) groups have been described, but their synthesis has not been detailed.^{54, 55} Acidification of potassium salts of 2,4-diamino-6-dinitromethyl-1,3,5-triazine (**39a**),

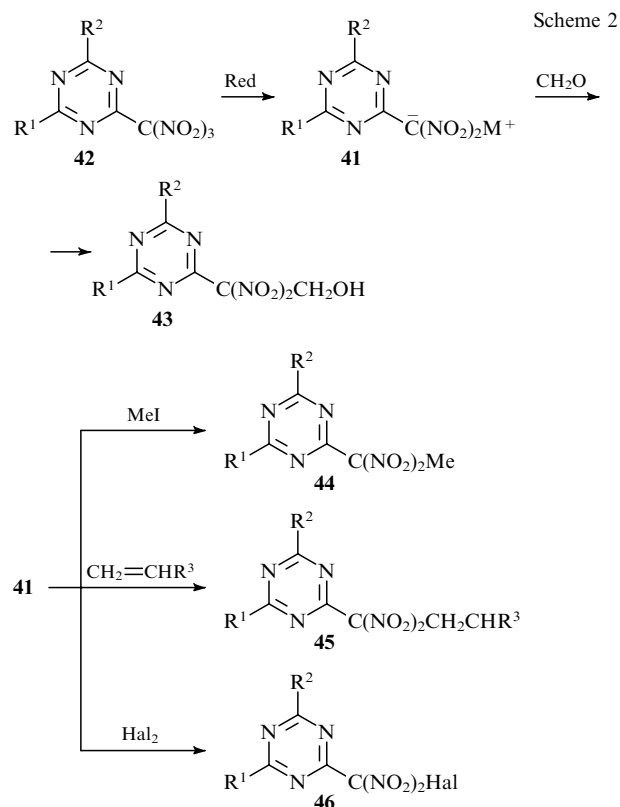
Table 1. Physicochemical and explosive characteristics of compounds **40a–c**.^{54, 55}

Parameter	40a	40b	40c
Single crystal density ρ_m / kg m ⁻³	1880	1910	2020
Initial temperature of intense decomposition T_d / °C	265	253	170
Enthalpy of formation ΔH_f° / kJ mol ⁻¹	-86.9	-291.3	-446.4
Ultimate stress σ_{lim} / MPa	91.2	86.3	94.2
Critical explosive stress p_{cr} / MPa	1500	1400	1500
Critical layer thickness Δ_{cr} / mm	2.2	1.6	2.5
Detonation rate D / m s ⁻¹ (at experimental charge density ρ / kg m ⁻³)	7350 (1.73)	7200 (1.76)	7320 (1.83)
Detonation rate determined by extrapolation of ρ to ρ_m , D_{max} / m s ⁻¹	7760	7680	8000

2-amino-6-dinitromethyl-4-oxodihydro-1,3,5-triazine (**39b**) and the dipotassium salt of 2-hydroxy-6-dinitromethyl-4-oxodihydro-1,3,5-triazine (**39c**) afforded dinitromethyl-substituted triazines **40a–c** in the zwitter-ionic (**40a,b**) or dioxotetrahydro-triazine form (**40c**).^{54, 55} The compounds synthesised possess high energy and high density and represent low-sensitivity explosives (Table 1).

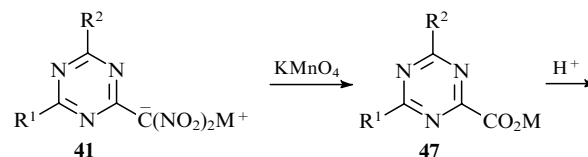


Salts of dinitromethyl-1,3,5-triazine derivatives (**41**) prepared by reduction of the corresponding C-trinitromethyltriazines **42** with conventional reducing agents were used in the synthesis of functionalised dinitromethyl-1,3,5-triazines.⁵⁶ It was shown that under conditions of acid catalysis formaldehyde enters into the Henry reaction with the salts **41** to give (2-hydroxy-1,1-dinitroethyl)-1,3,5-triazine derivatives **43** (Scheme 2). The same authors performed the alkylation of the salts **41** with methyl iodide in aprotic solvents to the corresponding dinitroethyl derivatives **44** (yields 70%–90%). Salts of C-dinitromethyl-1,3,5-triazine derivatives **41** enter into the Michael reaction with various derivatives of acrylic acid, particularly with methyl acrylate and acrylonitrile, to give 4-(2-R¹-4-R²-1,3,5-triazin-6-yl)-4,4-dinitrobutyric acid derivatives **45**. The halogenation of the salts **41** proceeds differently depending on the halogen used. Chloro- and bromodinitromethyl-1,3,5-triazine derivatives **46** are formed in good yields (80%–95%) in reactions with chlorine and bromine; fluorination gives a complex mixture of products.

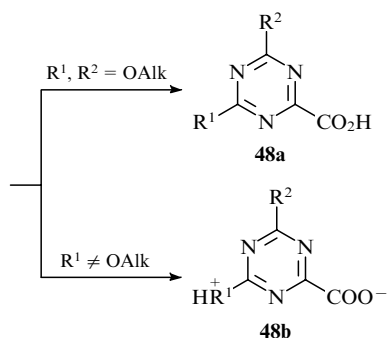


Red is a reducing agent; M = Na, K, NH₄ etc.; R¹, R² = OAlk, OAr, NH₂, NHAik, NAlk₂, N₃ etc.; R³ = CO₂H, CO₂Me, CN, COMe; Hal = Cl, Br.

The oxidation of the salts **41** with potassium permanganate in an aqueous medium yields the carboxylic acid salts **47**; depending on the substituents in the triazine ring, their acidification gives either the carboxylic acids **48a** (R¹ and R² are the alkoxy groups), or the zwitter-ionic compounds **48b** (if at least one of the substituents represents an amino group). This can be attributed to the differences in the basicities of dialkoxy- and alkoxyamino-triazines. The interest in the synthesis of dinitromethyl-1,3,5-triazines is due to the fact that these compounds manifest diverse biological activities including the cytotoxic (antitumour) activity.^{57, 58} It was shown that the level of the cytotoxic effects of the most active synthetic compounds is commensurate with that of clinically important 1,3,5-triazines;⁵⁷ the highest activity ($GI_{50} = 10\text{--}80\text{ }\mu\text{mol litre}^{-1}$) is manifested by some representatives of C-(2-hydroxy-1,1-dinitroethyl)-1,3,5-triazines (**43**: R¹ = R² = OMe; R¹ = C(NO₂)₂CH₂OH, R² = NMe₂).[‡]

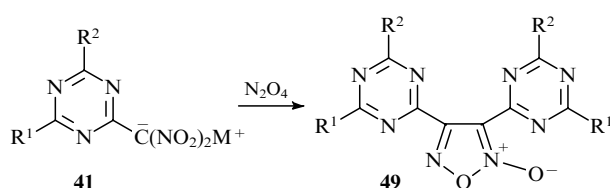


[‡] GI_{50} is the concentration of the tested substance which causes 50% inhibition of growth of tumour cell cultures under standard conditions *in vitro* (this methodology was developed at the National Cancer Institute).



M = Na, K, NH₄ etc.; R¹ = NH₂, NAlk, NAlk₂, OAlk;
R² = OAlk, R¹.

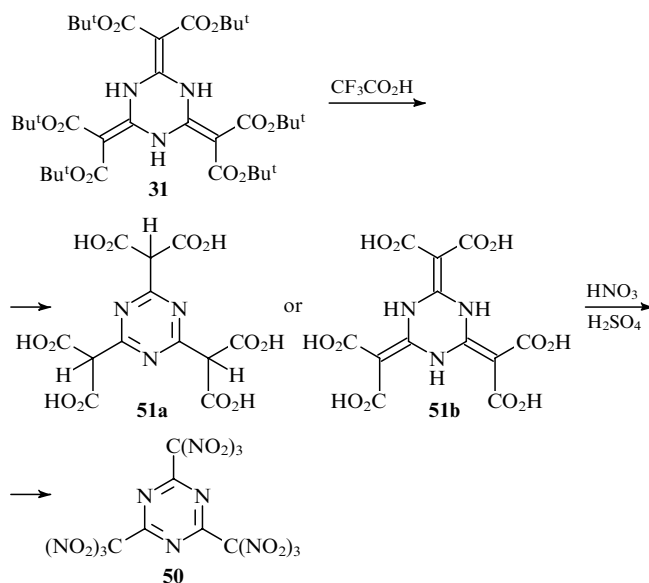
Reactions of the salts of the dinitromethyl-1,3,5-triazine derivatives **41** with nitrogen dioxide in organic solvents afford furoxanes **49**.⁵⁶



M = Na, K, NH₄ etc.; R¹ = R² = OMe, NMe₂.

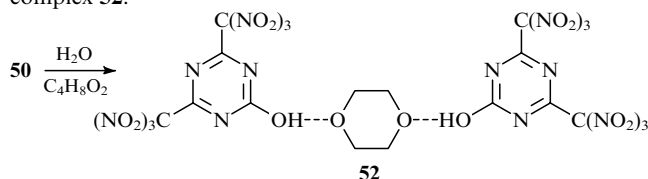
3. Trinitromethyl derivatives

Trinitromethyl-1,3,5-triazine derivatives are synthesised by methods developed by Khmel'nitskii for aromatic and heteroaromatic compounds containing trinitromethyl groups.^{48–51, 59} 2,4,6-Tris-(trinitromethyl)-1,3,5-triazine (**50**) presents the greatest interest among other 1,3,5-triazines both in the academic and practical aspects; however, numerous attempts at its synthesis did not give any positive results until recently.⁶⁰ This compound could be obtained only after the synthesis of 2,4,6-tris(dicarboxymethyl)-1,3,5-triazine (**51a**),⁶⁰ which presumably exists in the ylidene form **51b**. Its destructive nitration with a mixture of sulfuric and nitric acids results in tris(trinitromethyl)triazine **50**.



2,4,6-Tris(trinitromethyl)-1,3,5-triazine (**50**) is a colourless crystalline substance, which is stable infinitely at room temperature (in the absence of water vapour). Its pycnometric density is equal to 1.91 g cm⁻³, m.p. = 91–92 °C (with decomposition), ΔH_f = 93 kcal kg⁻¹, impact sensitivity is 90% (2 kg/20 cm),

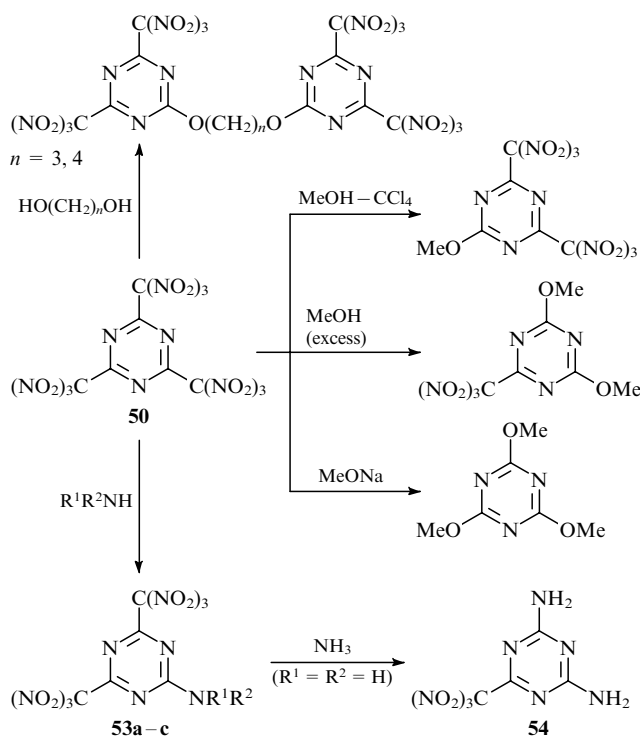
α = 1.5. The hydrolytic stability of this compound is rather low: after dissolution in aqueous dioxane, the hydroxy group is substituted for one trinitromethyl group to give a stable dioxane complex **52**.



The following characteristics of the complex **52** have been determined: decomposition temperature, 150–152 °C, impact sensitivity, 90% (2 kg/20 cm), ρ_m = 1.764 g cm⁻³ (X-ray diffraction data).⁶⁰

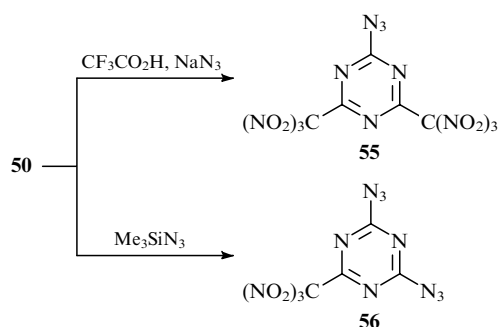
Reaction of compound **50** with nucleophiles can occur with the substitution of one, two or three trinitromethyl groups (Scheme 3).^{61,62} Thus reaction with ammonia or amines gives the monoamino derivatives **53a–c**; treatment of triazine **50** with an excess of ammonia gives the diamino derivative **54**.

Scheme 3



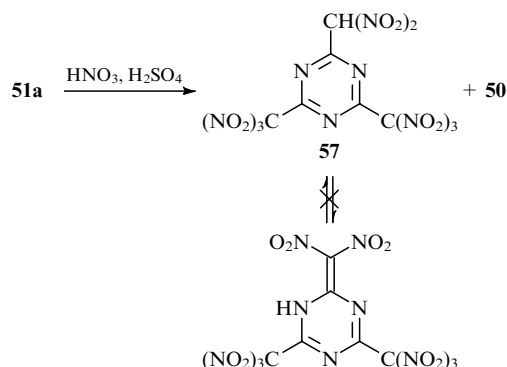
53: R¹ = R² = H (**a**), Me (**b**); R¹ = H, R² = Ph (**c**).

The use of various azide ion sources has enabled the synthesis of mono- and diazido derivatives **55** and **56**, respectively.⁶³



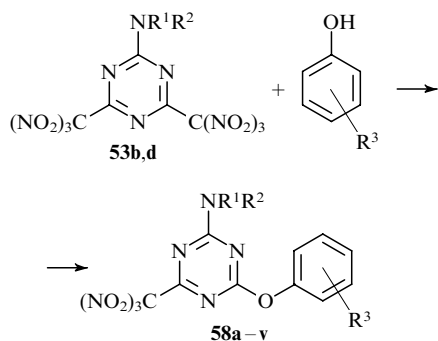
Under certain conditions,⁴³ nitration of the hexaoic acid **51a** yields, along with 2,4,6-tris(trinitromethyl)-1,3,5-triazine (**50**), the

dinitromethyl derivative, 2-dinitromethyl-4,6-bis(trinitromethyl)-1,3,5-triazine **57**, which exists in the dinitromethyl form.



Compound **57** is thermally and hydrolytically unstable. Attempts have been undertaken to reduce 2,4,6-tris(trinitromethyl)-1,3,5-triazine and to perform selective nitration of 2,4,6-tris(nitromethyl)-1,3,5-triazine;⁴³ however, no reducing agent could be found that did not cause nucleophilic substitution of the trinitromethyl group.

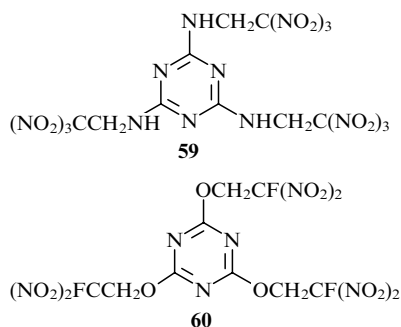
It was found⁶⁴ that substitution of phenols for the C(NO₂)₃ group in the bis(trinitromethyl)-1,3,5-triazine derivatives **53b,d** in the presence of a base occurs in a selective manner and results in 4-aryloxy-2-dimethyl(diethyl)amino-6-trinitromethyl-1,3,5-triazines **58a–v**.



53: R¹ = R² = Me (**b**), Et (**d**);

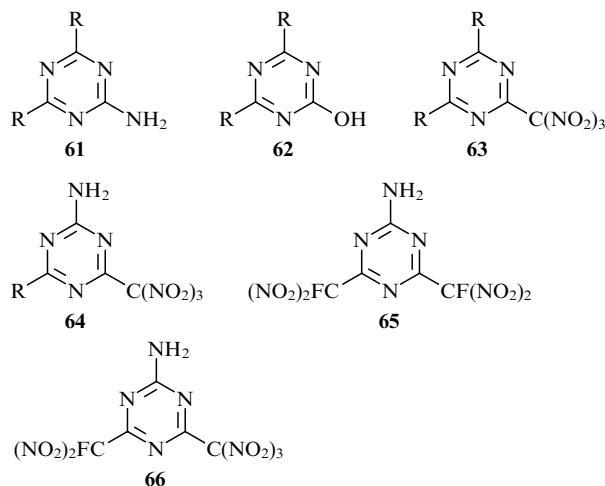
58: R¹ = R² = Me: R³ = *o*-Me (**a**), *m*-Me (**b**), *p*-Me (**c**), *o*-NO₂ (**d**), *m*-NO₂ (**e**), *p*-NO₂ (**f**), *o*-Cl (**g**), *m*-Cl (**h**), *p*-Cl (**i**), *o*-OMe (**j**), *m*-OMe (**k**), *p*-OMe (**l**), *o*-CO₂Me (**m**), *m*-CO₂Me (**n**), *p*-CO₂Me (**o**); R¹ = R² = Et: R³ = *o*-Me (**p**), *p*-OMe (**q**), *m*-CO₂Me (**r**), *p*-NO₂ (**s**), *o*-Cl (**t**), 2,4-(NO₂)₂ (**u**), H (**v**).

The substituted 1,3,5-triazines **59** and **60** containing trinitromethyl and fluorodinitromethyl groups linked to the triazine ring through the aminomethyl or oxymethyl bridge have been described.^{65–67}



Compound **59** has the following characteristics:⁶⁵ detonation rate, 7700 m s^{−1} at ρ = 1.54 g cm^{−3}, impact sensitivity, 50% (2 kg/20 cm). For compound **60**, m.p. = 76–77 °C, ρ_m = 1.795 g cm^{−3};⁶⁶ however, its synthesis has not been

detailed. 1,3,5-Triazines containing both trinitro(fluorodinitro)-methyl and 2,2,2-trinitro(2-fluoro-2,2-dinitro)-ethoxy groups are reported;⁶⁸ some physicochemical and thermodynamic characteristics of these compounds are given, but the methods for their synthesis are omitted.⁶⁸ These include 6-amino-2,4-bis(2-fluoro-2,2-dinitro-ethoxy)-1,3,5-triazine (**61**), 6-hydroxy-2,4-bis(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**62**), tri-2,4-bis(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**63**), 6-amino-4-trinitromethyl-2-(2-fluoro-2,2-dinitroethoxy)-1,3,5-triazine (**64**), [4,6-bis(fluorodinitromethyl)-1,3,5-triazin-2-yl]amine (**65**) and [6-trinitromethyl-4-(fluoro-dinitromethyl)-1,3,5-triazin-2-yl]amine (**66**).



R = OCH₂CF(NO₂)₂.

Compound	M.p. /°C	ρ _m /g cm ^{−3}	Compound	M.p. /°C	ρ _m /g cm ^{−3}
61	91–92 (with decomposition)	1.78	64	94–95	1.84
62	144–145	1.89	65	109–111	1.86
63	113–114	1.82	66	73–75	1.83

* * *

Some nitro-substituted 1,3,5-triazines considered in this review (e.g., nitramino-1,3,5-triazines, trinitromethyl-1,3,5-triazines) belong to the class of high-energy compounds and present potential as explosives or components of explosive mixtures. Many of them are promising chemical reagents for the synthesis of novel representatives of 1,3,5-triazines, such as trinitromethyl-1,3,5-triazines and nitromethyl-1,3,5-triazines. All nitro-substituted triazines can be used as NO donors;⁶⁹ some dinitromethyl-substituted 1,3,5-triazines were found to manifest high cytotoxic activity.^{57, 58} An interesting feature of trinitromethyl-1,3,5-triazines is the ease of substitution of various nucleophiles for the trinitromethyl group. Since the major part of these compounds has been obtained relatively recently, in-depth investigation of 1,3,5-triazine nitro derivatives is a topical matter.

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Combustion and explosion processes in physical chemistry and technology of inorganic materials[†]

A G Merzhanov

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Abstract. This review is the first attempt to generalise, in a descriptive-conceptual form, material-synthesising and material-affecting combustion and explosion processes and relevant physicochemical, technological and materials science problems with special emphasis on their practical (technological and industrial) applications. The bibliography includes 127 references.

I. Introduction

Combustion and explosion are physicochemical processes where transformations of substances are accompanied by intense release of energy and exchange of heat and mass with the environment. These processes, which have been known since ancient times, have made a significant contribution to the technological progress and ensured high level of development of modern civilisation. Combustion and explosion processes can be implemented in miscellaneous media, *viz.*, gaseous, condensed and multiphase (homogeneous, heterogeneous, organic, inorganic, *etc.*) and are therefore widely spread in nature and technology.

Combustion and explosion processes have both common and distinctive features. Common to both processes are high energy and nonlinearity, while distinctive features include the nature of their effects, self-propagation mechanisms, characteristic time scales and approaches to their theoretical description (Table 1).

It is noteworthy that common features prevail over distinctions. It is not therefore surprising that studies in the field of combustion and explosion are being developed in the framework of a single problem as can be judged from the establishment of the Integrated Scientific Council on Combustion and Explosion at the Presidium of the Russian Academy of Sciences, the journal 'Combustion, Explosion and Shock Waves', joint symposia on combustion and explosion, *etc.*

Combustion and explosion processes are described in terms of a specially developed scientific methodology based on the analysis

of feedforwards and feedbacks of exothermic reactions and transport processes. This methodology was used for the description of numerous specific phenomena and effects typical of these processes. It is the existence of a particular scientific methodology that allowed consideration of combustion and explosion as an independent area of knowledge.

The place of the combustion and explosion science in the family of related scientific disciplines some of which are concerned with the studies of chemical reactions, while others deal with transport processes, is shown in Fig. 1.

As regards the uniqueness of the scientific methodology and the range of their practical applications, combustion and explosion processes are unrivalled. Some areas of practical applications of these processes are shown in Fig. 2.

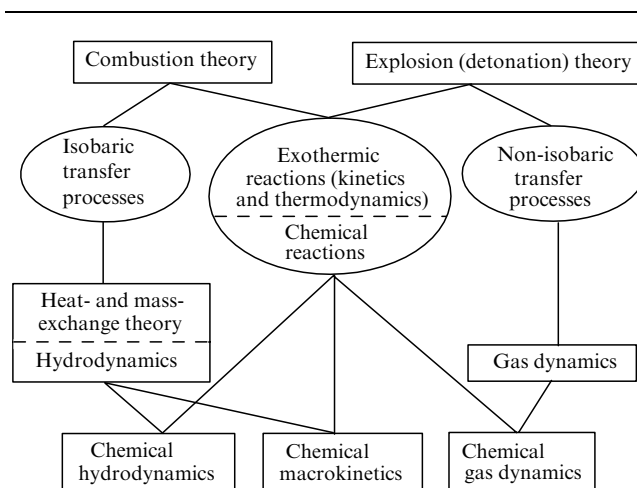


Figure 1. The position of combustion and explosion science in the family of related scientific disciplines.

A G Merzhanov Institute of Structural Macrokinetics and Materials Science, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. Fax (7-095) 962 80 40. Tel. (7-095) 962 80 00. E-mail: merzh@ism.ac.ru

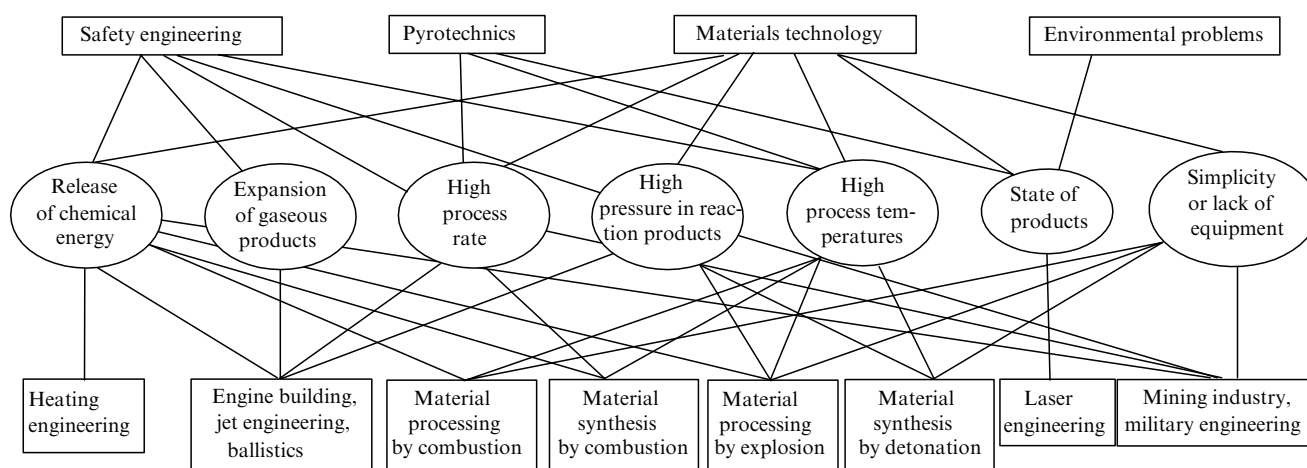
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Table 1. Some common and distinctive features of combustion and explosion processes.

Process	Nature of effect	Mechanism of self-propagation	Characteristic time scale	Areas of knowledge used for theoretical description of the process
Combustion	heat	heat transmission, diffusion	milliseconds and more	chemical kinetics + theory of heat and mass exchange
Explosion	gas-dynamic	shock compression	microseconds	chemical thermodynamics + gas dynamics

**Figure 2.** Practical applications of combustion and explosion processes.

A tremendous contribution to the chemistry of combustion and explosion has been made by Soviet (Russian) scientific schools.

— The school of N N Semenov laid the foundations of the modern theory of combustion and explosion. Its brilliant representatives Ya B Zeldovich, D A Frank-Kamenetsky, A F Belyaev, *etc.*, have won international recognition for their studies in the field of combustion and explosion.^{1–6}

— The schools of M A Lavrent'ev and M A Sadovsky developed the gas-dynamic principles of the explosion theory and substantiated the practical aspects of detonation effects (*e.g.*, surface shots, material processing by explosion, *etc.*) on various substances.

— The schools of B P Zhukov and V S Shpak worked out problems of combustion of solid propellants.

Solid flame combustion (SFC) and self-propagating high-temperature synthesis (SHS) have been developed especially intensively. Studies in these areas were initiated and developed for a long time only in the USSR; however, researches and developments in the field of SHS are currently under way in 47 countries as can be judged from the ever increasing number of publications (totalling ~ 10 000 at a rate of about 2 articles per day). The largest research centres dealing with in-depth studies of SHS are situated in Russia [Institute of Structural Macrokinetics and Materials Science of the Russian Academy of Sciences (ISMAN), SHS Research-and-Educational Centre of the Moscow Institute of Steel and Alloys and ISMAN, Department of Structural Macrokinetics of the Tomsk Research Centre of the Siberian Branch of the Russian Academy of Sciences, Samara State Technological University, Altai State Technological University], USA (University of Notre Dame, Northwestern University, University of California at Davis, Colorado School of Mines), Japan (Ryukoku University, Osaka University, Tokyo Institute of Technology), China (Wuhan University, Beijing University of Science and Technology, Harbin Institute of Technology), France (Montpellier University) and Israel (Israeli Institute of Technology). A significant contribution to SHS has been made by

specialised international symposia and the 'International Journal of Self-Propagating High-Temperature Synthesis'.

This review considers only those combustion and explosion processes which are aimed at the development of materials with predetermined properties, namely, the synthesis of novel materials or imparting novel properties to the existing materials by virtue of their processing. The former approach entails material-synthesising combustion and detonation processes, while the latter is confined to material processing.

In considering miscellaneous material-synthesising processes, special attention will be given to combustion and explosion products as subjects for the synthesis and mechanisms of transformation of the starting elements in combustion and detonation waves (chemical reactions, phase transitions, structure formation of final products, *etc.*) and theoretical aspects of combustion and explosion. The main emphasis in the analysis of material processing will be laid on processing of materials by combustion and explosion, effects of high temperatures and high pressures on materials and interactions of processed materials with the green mixture.

II. Material-synthesising technological combustion and explosion processes

Material-synthesising processes include:

- classical technologies, *e.g.*, blast-furnace processes, out-of-furnace metallurgy, incomplete combustion of hydrocarbons, *etc.*;
- self-propagating high-temperature synthesis (primary and advanced SHS);
- processes carried out in shock and detonation waves.

1. Classical processes. Out-of-furnace metallurgy

Some examples of classical processes aimed at the preparation of novel materials by combustion and explosion are given in Table 2. Although these technologies are out of date and are being

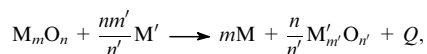
Table 2. Classical processes of industrial combustion.

Process	Combustion regime	Raw materials	Final product
Blast furnace process	filtration	coke, ore, additives, air	cast iron
Out-of-furnace metallothermy	liquid flame	ground ore or metal oxides	ferroalloys and reinforcers or reduced metals
Combustion of rich hydro-carbon-air mixtures	condensation	gaseous or liquid hydrocarbons, air	industrial carbon (soot)

developed at a very slow pace, they still find application as industrially useful processes.

Out-of-furnace metallothermy,⁷ *i.e.*, a redox process carried out in powder mixtures of metal oxides and reducing metals in a combustion mode, is one of the most well-developed and well-studied classical processes. It was first implemented by N N Beketov and, later, by V M Goldschmidt as early as the 19th century; however, the first theoretical combustion research into metallothermic compositions (thermites) were carried out by A F Belyaev and L D Komkova as late as 1950.⁸ The fundamental of out-of-furnace metallothermy has been detailed in the well-known book.⁷

The chemical scheme of an out-of-furnace metallothermic process can be presented as follows:



where M_mO_n is the oxide of the metal to be reduced, M' is the reducing metal and Q is the heat of combustion. If the heat of combustion is high, the combustion proceeds in a wave mode. Al (aluminothermy), Mg (magnesiothermy), Ca (calciothermy) and Si (silicothermy) are generally used as reducing metals. Out-of-furnace metallothermy is used for joining metals and alloys. The most significant achievements have been attained in the production of ferroalloy ingots, hardeners and rare metals.

Special attention in the development of out-of-furnace metallothermic processes should be given to aggregate states of the final and by-products. A chart of the aggregate states of two combustion products [a reduced metal (P_1) and a reducing metal oxide (P_2)], which is based on thermodynamic calculations, is shown in Fig. 3.³ The two coordinates, $T_{ad}/T_m(P_1)$ and $T_{ad}/T_m(P_2)$, reflect the correlation between the combustion and melting temperatures of the reduced metal and the reducing metal oxide. Here, T_{ad} is the adiabatic combustion temperature of the metallothermic mixture; $T_m(P_1)$ and $T_m(P_2)$ are the melting temperatures of the reduced metal and the reducing metal oxide, respectively.

There are four adiabatic combustion zones differing in the aggregate states of a metal to be reduced and a reducing metal, *viz.*, zone I, solid metal and solid oxide; zone II, solid metal and liquid oxide; zone III, liquid metal and liquid oxide and zone IV, liquid metal and solid oxide. As can be seen from Fig. 3, the theoretical points are localised in all the four zones.

Of particular interest is zone III where a heterogeneous molten mass consisting of liquid metal oxide and drops of a liquid metal is formed. The drops sediment in the gravitational field of the Earth to produce an ingot. Such a phase separation allows easy isolation of the final product.

The combustion temperatures of the aforementioned systems depend on the pressure of an external gas, which suppresses

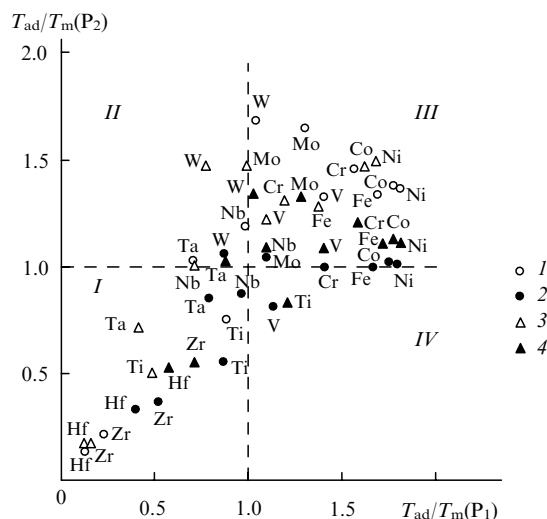


Figure 3. Aggregate states of combustion products prepared by out-of-furnace metallothermy. The pressure of the ambient gas is 0.1 MPa. Reducing metal: (1) aluminium, (2) magnesium, (3) silicon, (4) calcium. For description of zones I–IV see text.

gasification in the combustion. The dependences of the combustion temperatures on the gas pressure for some metallothermic systems are shown in Fig. 4.

Contamination of final products with reducing metals is the main disadvantage of out-of-furnace metallothermy.

Reduction of impurity content in the out-of-furnace ingots is a difficult task. Studies aimed at governing the chemical composition of Nb ingots prepared by aluminothermic reduction of Nb_2O_5 in the presence of Mg have been undertaken at ISMAN. In these studies green mixtures with the variable compositions and densities and variations of external gas pressures and of gravitational effects were used as the most modern methods for controlling the composition. The purest specimen of niobium obtained by this method contained 1.6 mass % Al, 0.04 mass % Mg and 0.74 mass % O. These results corroborate the conclusion by Yelyutin⁹ that out-of-furnace metallothermy and refinement can be used for the preparation of pure metals.

Recently, Freidin *et al.*¹⁰ have developed a method for the synthesis and refinement of molten products in a single technological step. To this end, a refining additive was mixed with a small

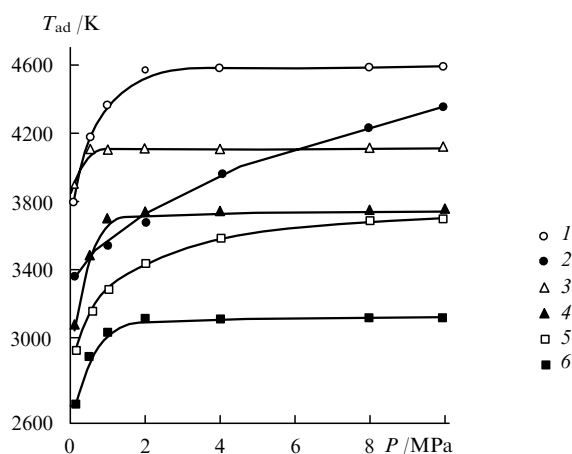


Figure 4. Dependence of combustion temperatures of various metallothermic compositions on ambient gas pressure (P). (1) $MoO_3 + 2 Al$, (2) $CrO_3 + 2 Al$, (3) $WO_3 + 2 Al$, (4) $V_2O_5 + 5 Ca$, (5) $2 WO_3 + 3 Si$, (6) $Ta_2O_5 + 5 Mg$.

‡ Calculations performed by I S Gordoplov, A G Merzhanov and V I Yukhvid (ISMN).

portion of the green mixture and placed under the bulk of the green mixture which gradually converted into a melt. The melt passed through the layer with the refining additive thus undergoing purification and crystallised. The ingots thus prepared contained lesser amounts of impurities. This approach proved to be especially efficient in the aluminothermic synthesis of phosphide copper¹¹ and high-purity iron (total content of impurities did not exceed 0.01%). The feasibility of this approach in the synthesis of a broad range of metallothermic products presents interest. The most recent achievements in this area have been documented.^{12, 13}

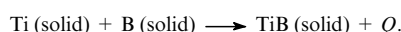
2. Solid-flame combustion and self-propagating high-temperature synthesis

Solid-flame combustion (SFC) is a self-sustained chemical wave process which yields fully or predominantly solid products (materials). The following types of SFC are known:

- gasless (solid-phase, liquid-phase, multiphase) combustion;
- infiltration combustion (with spontaneous or forced infiltration);
- condensation combustion (*e.g.*, of gases and condensed systems).

The phenomenon of SFC was discovered by Merzhanov *et al.*¹⁴ and registered in the USSR Register of State Inventions and Discoveries under No. 287 in 1967. It was found that slow self-inhibited solid-phase reactions may be concentrated in definite zones following local initiation and proceed thereafter at fast rates commensurate with the propagation rate of the combustion wave. This unique phenomenon and the products formed immediately evoked keen interest from investigators. This discovery was preceded by studies on 'ignition' of metallothermic mixtures (Beketov and Goldschmidt, around 1900) and combustion of thermites (Belyaev and Komkova, 1950)⁸ and copper acetylenide (Borovinskaya and Merzhanov, 1966)⁸ and by development of a gasless combustion model (Maksimov, Merzhanov and Shkiro, 1965).¹⁵ However, none of SFC processes could be implemented without a thorough knowledge of modern combustion theory.

Titanium monoboride was the first compound prepared by SFC.



The snapshots illustrating the formation of TiB from solid elements are shown in Fig. 5 which has become widely popular. These frames depict the main stages of the combustion process, *i.e.*, initiation (ignition), propagation of the combustion front and cooling of the solid product. Depending on the operational

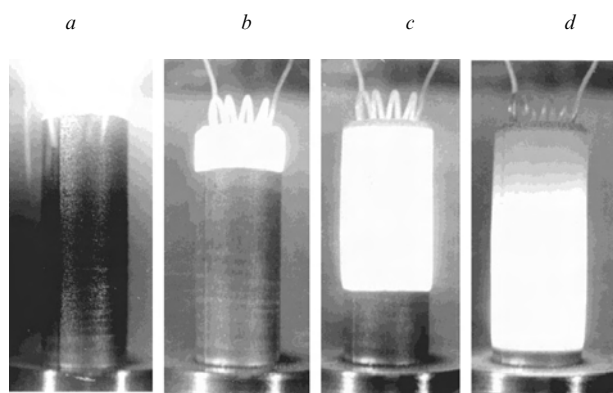


Figure 5. Frames of an SHS process; (a) initiation ($t = 0$), (b, c) propagation of the combustion front [$t = 0.1$ s (b) and 2.7 s (c)], (d) cooling ($t = 4$ s).

conditions, the solid formed may represent a substance, a material or an end product.

The synthesis of compounds by SFC has got the name of self-propagating high-temperature synthesis (SHS). SHS is used for obtaining chemical compounds with predetermined compositions, structures and properties.

SHS is usually subdivided into primary and advanced SHS. This classification reflects the rapid progress in this area, which has changed the very concept of this synthesis.

Under primary SHS is understood the combustion of 'solid + solid' and 'solid + gas' systems and the formation of high-melting (refractory) materials (carbides, borides, nitrides, silicides, *etc.*) by direct synthesis, *i.e.*, based on the exclusive use of chemical elements as the starting reactants. Advanced SHS includes all possible combustion modes and yields valuable solid products and materials.

The fundamental tasks of primary SHS are as follows:

- studies of regularities and mechanisms of combustion;
- mathematical simulation of combustion;
- establishment of a relationship between the product composition and operational conditions (combustion);
- optimisation of operational conditions for the preparation of single-phase compounds.

3. Primary SHS

Although the build-up period of primary SHS was relatively short (1967–1972), it was marked for fundamental discoveries.^{16–21}

First, the nature of solid-flame combustion was elucidated. Until that time, it was unclear how slow solid-phase reactions leading to solid products could occur in fast regimes, such as combustion. To rationalise this phenomenon, one had to abandon the equilibrium flame propagation theory proposed by Ya B Zeldovich and D A Frank-Kamenetsky.²² According to this theory, the width of the reaction zone in the combustion wave is much narrower than that of the preheating zone and can often be neglected.[¶]

However, in the solid-flame processes the reaction zone is significantly wider than that of the preheating zone due to strong self-inhibition of the combustion reaction[†] (the non-equilibrium theory). Moreover, the reaction zone may even involve the afterburning subzone, which does not influence wave velocity. The concept of broad reaction zones¹⁹ has subsequently become very popular. In terms of the non-equilibrium flame propagation theory, the SFC wave has a multizone structure and comprises three main zones, *viz.*, the preheating (preheating) zone ($T_0 - T_f$), the zone where the major heat is evolved, which determines the combustion rate ($T_f - T_*$), and the afterburning zone ($T_* - T_f$). Here, T_0 is the initial temperature, T_f is the temperature of the combustion front separating the preheating zone and the reaction zone (the inflection point on the temperature curve) and T_* is the temperature determining the combustion rate (Fig. 6). These fundamental concepts underlie the novel, non-equilibrium flame propagation theory.²³

According to this theory, the wave velocity U in broad zones is determined by the temperature T_* ($T_f < T_* < T_{ad}$) which reflects the incompleteness of conversion of the substance ($\eta_* < 1$)

$$U^2 = A \frac{T_*^2}{\eta_*} \exp\left(-\frac{E_a}{RT_*}\right),$$

where A is the value determined by the reaction rate and heat transfer constants, η_* is the degree of conversion at temperature T_* and E_a is the activation energy.

¶ This concept has been used in nearly all theoretical studies on flame propagation.

† The term 'self-inhibition' implies that the rate of combustion decreases drastically as the substances are burnt out. In the case of classical processes of flame propagation in gases, this effect is small.

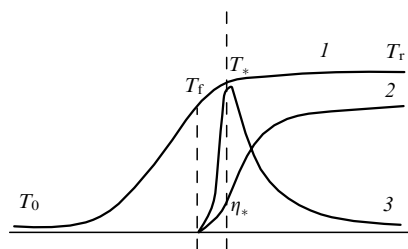


Figure 6. A schematic diagram of the structure of a solid-flame combustion wave (1), depth of conversion (2) and heat release rate in combustion (3).

Yet another important result is related to the elucidation of the infiltration combustion mechanism of ‘solid — one-component gas’ systems. Here it is necessary to distinguish between the gas inside and outside pores of a sample (internal and external reactants). At relatively low pressures, the propagation of the combustion wave is provided by infiltration of the external gas through the pores of the solid sample. Studies of combustion of zirconium in nitrogen¹⁷ have established two limiting modes: the layer-by-layer mode (Fig. 7a) and the surface (Fig. 7b) mode. The interconversion of these two processes has been studied (Fig. 7c). It was shown that the combustion mode is unambiguously described by the criterion π equal to the ratio of the characteristic times of infiltration (t_f) and the reaction occurring in the wave (t_r):

$$\pi = \frac{t_f}{t_r} \sim \frac{Ud}{P_0},$$

where d is the diameter of the sample and P_0 is the pressure of the ambient gas.

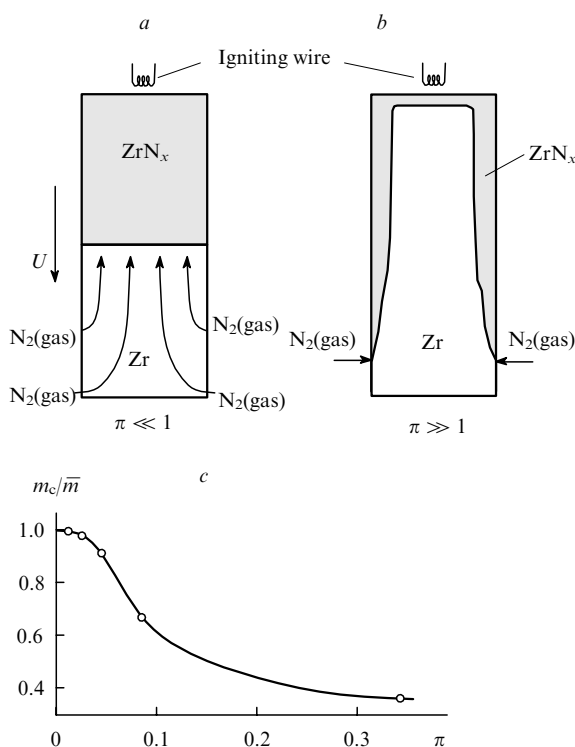


Figure 7. Layer-by-layer (a) and surface combustion (b) in ‘porous solid — gas’ systems and some regularities of their interconversions (c); m_c , nitrogen content in the centre of the sample, $\bar{m}$, average nitrogen content in the sample.

The infiltration (surface) combustion mode meets the criterion $\pi \gg 1$. In this case, the reaction is fast and the gas has no time to penetrate inside the sample; therefore, the combustion occurs only in the surface layers. The kinetic (layer-by-layer) combustion mode meets the criterion $\pi \ll 1$.

The development of infiltration concepts has provided a clue to uniform combustion of hybrid systems. The very first results in this area have stimulated numerous experimental and theoretical studies which culminated in the development of a general theory of infiltration combustion.²⁴

Yet another important event is the discovery of combustion spin waves.¹⁸ Under certain conditions, flame propagation occurs in an unstable mode, as a result of which the combustion centre begins to move along the sample by a spiral path rather than as a flat layer. A non-steady-state two-dimensional flame propagation model has been developed in order to elucidate the nature of this phenomenon.^{25,26} The frames (a) and computer simulation (b) of spin combustion are shown in Fig. 8. As can be seen (Fig. 8a), the combustion centre appears from the rear of the sample, moves in the lateral direction and disappears. The computer version was obtained after solution of the simplest two-dimensional non-steady-state problem of a transition to the post-ignition flame propagation mode:

$$\begin{cases} c\rho \frac{\partial T}{\partial t} = \lambda \left(\frac{\partial^2 T}{\partial x^2} + \frac{1}{x^2} \frac{\partial^2 T}{\partial \varphi^2} \right) \rho Q \frac{\partial \eta}{\partial t} - \alpha_t (T - T_0) \\ \frac{\partial \eta}{\partial t} = k_0 (1 - \eta) \exp \left(-\frac{E_a}{RT} \right) \end{cases}$$

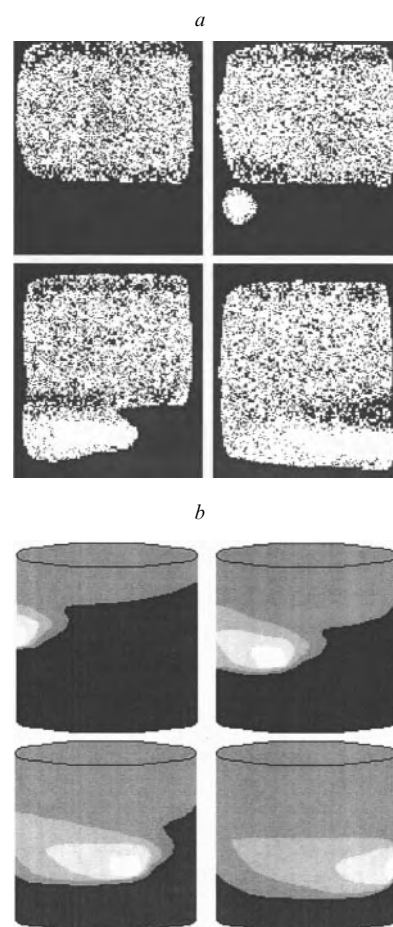


Figure 8. Snapshots of spin combustion of hafnium in a nitrogen — argon mixture (a) and visualisation of solutions of equations describing the spin waves (b).

Table 3. Examples of compounds prepared by primary SHS.

Compound	Metal content (mass %)		Non-metal content (mass %)		Lattice type	Unit cell parameters /Å	Micro-hardness /kg mm ⁻²
	total	free	total	free			
Titanium carbide	80.0	< 10 ⁻³	19.8	9 × 10 ⁻²	cubic NaCl	<i>a</i> = 4.323	2900
Zirconium carbide	88.2	< 10 ⁻³	11.4	< 10 ⁻²	"	<i>a</i> = 4.686	3040
Niobium nitride	86.9	< 10 ⁻³	13.0	—	"	<i>a</i> = 4.385	1670
Titanium nitride	77.6	< 10 ⁻³	21.4	—	"	<i>a</i> = 4.240	1800
Tantalum nitride	91.8	—	7.5	—	"	<i>a</i> = 4.323	3200
Boron nitride	43.8 ^a	0.2 ^a	55.7	—	hexagonal	<i>a</i> = 3.331, <i>c</i> = 3.518	—
Titanium diboride	68.6	—	31.0	10 ⁻¹	"	<i>a</i> = 2.619, <i>c</i> = 3.230	3500
Hafnium diboride	89.0	—	10.7	< 10 ⁻²	"	<i>a</i> = 3.134, <i>c</i> = 3.467	2890

^a Boron content is indicated.

with the following initial and boundary conditions:

$$\begin{aligned}
 &t = 0, x > 0: T = T_0, \eta = 0, \\
 &t > 0, x = 0: \begin{cases} T = T_{\text{ign}}, \text{ at } t \leq t_{\text{ign}} \\ \frac{\partial T}{\partial x} = 0, \text{ at } t > t_{\text{ign}} \end{cases} \\
 &t > 0, x = x_0: \frac{\partial T}{\partial x} = 0.
 \end{aligned}$$

Here, *c*, *ρ* and *λ* are the heat capacity, density and heat conductivity of the sample, respectively; *x* and *φ* are the integral and angular coordinates; *Q*, *E_a* and *k₀* are the thermal effect, activation energy and a preexponential factor, respectively; *α_t* is the heat exchange coefficient and *T_{ign}* and *t_{ign}* are the ignition temperature and the delay time, respectively.

An analysis of the calculated dependences *T(x, t)* and *η(x, t)* and the instantaneous linear combustion rate *dx/dt* at the point $(\partial\eta/\partial t)_{\text{max}}$ has shown that, depending on the parameters, the post-ignition process occurs in either a steady-state combustion mode or a spin, self-oscillating or chaotic (non-steady-state) mode. It should be noted that all the three unstable combustion modes, *viz.*, self-oscillating, spin and chaotic, can be realised in the same system for different parameters of the green mixture and under different operational conditions.

The discovery of spin waves gave impetus to the appearance of a huge number of publications and the spin wave has become a very popular subject of investigation in nonlinear dynamics.

However, the main result in the first stage of SHS development was associated with the synthesis of novel materials. A simple methodological scheme has been developed which included:

- elucidation of parameters determining the chemical and phase compositions of combustion products;
- analysis of their relationships;
- optimisation of conditions for the synthesis of homogeneous products.

Some examples of compounds obtained by SHS in the early stages of development of the method¹⁶ are given in Table 3.

As can be seen, SHS enables the synthesis of chemical compounds of very high quality. This circumstance has played a crucial role in the development of the SHS method as a whole.

Self-propagating high-temperature synthesis is a multiparametric process which is controlled by many mechanisms. This means that its optimisation presents a problem, but once optimum conditions have been established, one can obtain products exceeding in quality the products prepared with the use of low-parametric processes, *e.g.*, furnace synthesis.

Hence, primary SHS is a bright chapter in the history of solid-flame combustion.

4. Advanced SHS

A significant advance in the field of SHS has been made in the past 35 years after the discovery of the phenomenon of solid flame. These achievements include:

- considerable expansion of the raw material base for SHS, *i.e.*, the range of compounds applicable for SHS;
- further development of combustion chemistry, structural macrokinetics, nonlinear dynamics, three-dimensional simulation;
- elucidation of effects of physical fields on SHS;
- development of technologies and facilities (equipment) for SHS;
- calculation of technological and economic efficiencies of SHS;
- synthesis of various valuable SHS products;
- pilot-plant and large-scale production of SHS products;
- commercialisation and marketing;
- a search for novel SHS processes.

Here we outline only some general trends in the development of SHS and refer all those who are interested in this branch of chemistry to some recent reviews^{27–46} and papers.^{47–51}

The infrastructure of advanced SHS is shown in Fig. 9. It comprises three main areas where SHS studies are under way. However, these investigations differ in their intensities. Thus the fundamental principles of SHS are rather well-developed, while industrialisation and commercialisation aspects of SHS are the least explored. This is not surprising, since SHS has been following the route from science to technology.

5. Transformations in shock and detonation waves

Studies of chemical and physicochemical transformations of substances in shock and detonation waves under the action of waves with inherent high pressures, high temperatures and shear deformations are important areas of research which have considerable technological significance.

Two types of processes initiated by shock and detonation waves are shown in Fig. 10. In the former case, the necessary conditions for the transformation of a substance are generated by external factors; in the latter case, they are created by self-propagating detonation processes.

Both types of processes are used for the preparation of superstrong materials (*e.g.*, cutting diamonds and wurtzite-like BN).^{52–54} Studies of transformations of substances in shock and detonation waves have posed the question about their localisation: in the wave proper (over microseconds) or after passage of the wave front (*e.g.*, at residual temperatures 300–500 °C). Studies of transformations of various systems, *e.g.*, Al + Fe₂O₃, Sn + S, Sn + Te, Al + S, Zr + 2S, *etc.*, in shock waves carried out by S S Batsanov⁵⁵ have shown that in these systems the synthesis occurs directly in the shock wave and is over within 10⁻⁷–10⁻⁶ s.

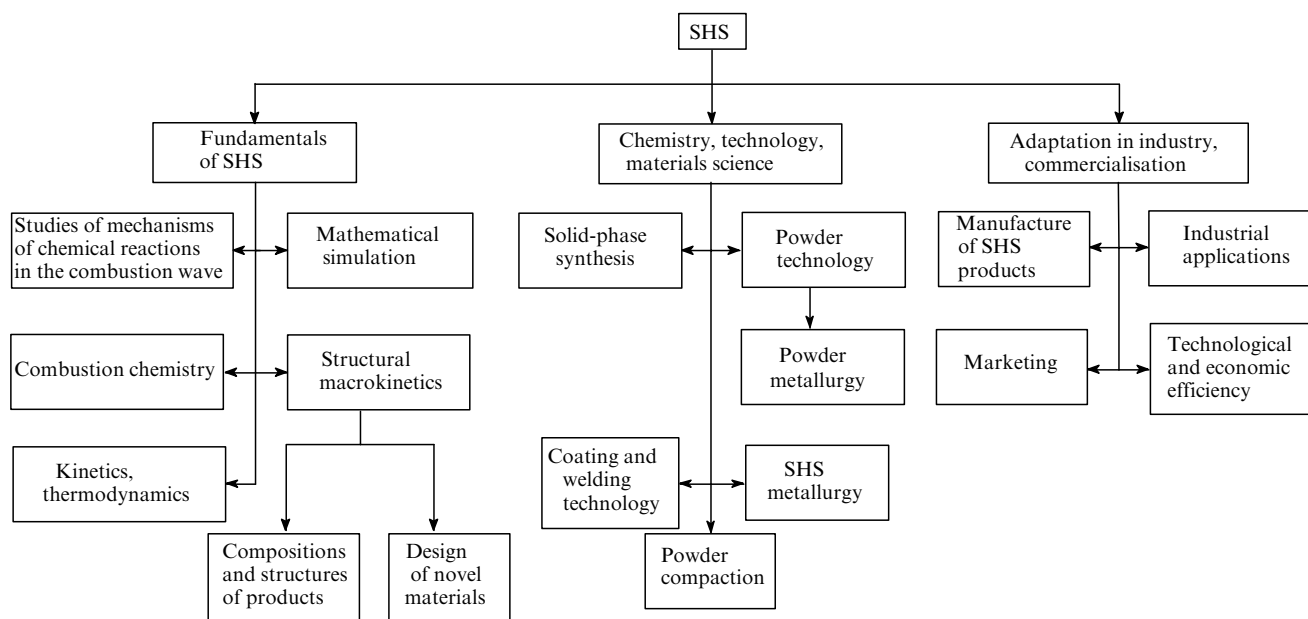


Figure 9. The infrastructure of SHS.

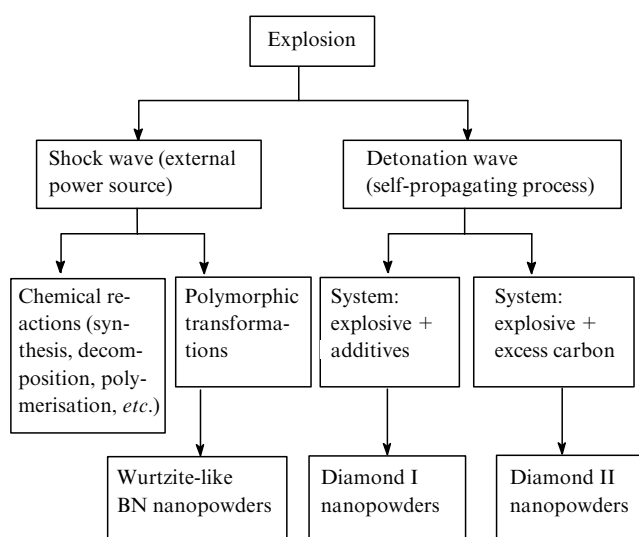


Figure 10. Chemical synthesis and physicochemical conversions in shock and detonation waves.

Numerous papers devoted to transformations of substances in shock waves have been published. For specialists in detonation techniques, their practical implementation presents no problem. The simplest approach consists in mixing of a tested substance or a sample with an 'explosive', formation of a blasting charge and initiation of explosion in a blasting chamber. An analysis of solid particles gathered after detonation gives some information about the explosion-induced transformations.⁵⁶

Transformation of substances in the detonation wave is a new trend in the chemistry of combustion and explosion. In this case, we deal with shock-driven SHS where self-propagation of the wave is initiated by shock compression rather than heat transmission. Obviously, such processes can be realised only if transformation of substances is accompanied by an increase in the volume, *e.g.*, due to concomitant evolution of gas. This can be achieved by adding gas-evolving inert additives to the green mixture. This technological approach is used for the preparation of a broad range of SHS products.

Apparently, SHS was first discovered by I P Borovinskaya²¹ at the dawn of SHS studies, more exactly, in experiments with combustion of a boron powder in liquid nitrogen in a sealed vessel. If nitrogen was taken in excess, SHS was accompanied by explosion. Interestingly, all the vessels split in two in the same place. This finding led the author to conclude that combustion passes into explosion. Later, special experiments aimed at initiating detonation confirmed the possibility of detonation in such systems. Unfortunately, at that and subsequent times these works did not receive proper attention.

Some new data on SHS in shock and detonation waves have been described.^{57, 58}

6. On thermal explosion

The interest in thermal explosion as a technological process for the synthesis of novel inorganic materials has increased considerably in recent years.^{59, 60} Whereas the combustion wave is initiated in some particular locus artificially, in thermal explosion the external source warms up the whole mass of the green mixture and ignition occurs spontaneously as a result of self-acceleration of the reaction. Where and how such ignition occurs and how transformation of substances proceeds under conditions of thermal explosion are these questions critical for conducting SHS syntheses.

Critical conditions and induction period are the most important characteristics of thermal explosion. Critical conditions are those in which the reaction passes from a slow (non-isothermic) mode to a detonation mode; the induction period is the explosion delay time. In other words, investigators are interested in whether and when the explosion takes place. Such a statement of the problem is aimed at the solution of safety problems.

The use of thermal explosion for the preparation of materials has posed some new questions: how does explosion develop in the post-induction period? what are the transformation modes? how does explosion affect thermal and concentration quasi-homogeneities? And so on.

The first explicit answers to these questions were given in a theoretical paper devoted to SHS.⁶¹ We studied thermal explosion in both induction and post-induction periods up to complete conversion of the reactants. It was concluded that the process depends essentially on the ratio of internal heat transfer and external heat emission, the so-called Bio criterion (*Bi*)

$$Bi = \frac{\alpha r}{\lambda},$$

where α is the heat emission coefficient from the surface of a sample, r is the characteristic size of the sample and λ is the thermal conductivity of the green mixture.

At nearly all values of Bi (with the exception of the ideal case where $Bi = 0$), the temperature and concentration fields in the sample are nonuniform. Ignition takes place at a point where the temperature in the induction period is the highest and is accompanied by rapid elevation of temperature. The reaction spreads further from the spontaneous ignition site in the form of a combustion wave causing layer-by-layer transformation of the reacting charge into the reaction product.

There are two modes of combustion wave propagation. One of them is characterised by higher values of Bi and consists in the transmission of heat from high-temperature products to initial reactants by a classical flame propagation mechanism. In the other mode, the process is controlled by the temperature gradient generated in the induction period. In the latter case, the wave propagation is apparent being unrelated to the heat transfer mechanism and is initiated by sequential (layer-by-layer) adiabatic self-ignition of the green mixture. The second mode is realised at very low Bi values ($Bi \ll 1$).

Theoretical studies^{62–64} are devoted to a detailed analysis of the nature and mechanisms of thermal explosion in the post-induction period. The results of these studies correlate with the aforementioned concepts which have considerable methodological significance. In current literature, thermal explosion was often opposed to SHS under the *a priori* assumption that thermal explosion represents three-dimensional combustion of the green mixture. It was found, however, that at $Bi \neq 0$ thermal explosion comprises a stage corresponding to the self-propagating process involving up to 80% of the reacting green mixture. After publication of the work,⁴⁸ two SHS modes came to be argued: artificial initiation of SHS and spontaneous (although local) initiation.

Until recently, there have been no experiments aimed at the application of thermal explosion to material-forming processes. The ideas developed in theoretical studies have long remained unclaimed which can be attributed to the difficulties in the implementation of SHS because of significant fluctuations in temperature, temperature gradients and characteristic time scales in a single technological process. Notwithstanding, recently such publications did appear (for a review see Ref. 60). It was shown that the synthesis of materials by thermal explosion is more applicable to those reactions that are not sufficiently exothermic where local ignition fails to induce further propagation of the combustion wave due to heat losses.

It was shown^{65,66} that thermal explosion in specially designed moulds and SHS compaction of the reaction product gives useful (from the standpoint of materials science) results.

Unfortunately, all the works aimed at the synthesis of materials by thermal explosion are carried out with no relation to macrokinetic concepts and studies which leads to a significant impoverishment of experimental data.

III. Material-affecting combustion and detonation processes

Processing of materials by combustion includes all kinds of flame coating: gas-thermal spraying (gas flames), aluminothermic welding ('liquid' flames), induction welding (microwave-induced thermal explosion) and condensation coating (chain flames). This category also includes remelting of reject or waste intermetallic articles and welding of components by electrothermal explosion.

In combustion and explosion processes, processable material is loaded into the reaction chamber together with the green mixture. The position of the green mixture relative to the processable material can be different: (1) the processable material

is inside the green mixture; (2) the processable material and the green mixture are spatially apart but are in contact with one another and (3) the processable material and the green mixture are spatially apart and do not contact.

1. Material-affecting combustion

Combustion-induced material-affecting is carried out at high temperatures generated upon burning of the charge.

Aluminothermic welding, *i.e.*, coating of moulded hard alloys onto flat steel surfaces, is the most popular procedure.²⁷ The principle of this method is very simple and consists of the following. A layer of an aluminothermic green mixture able to form a 'hard' alloy is applied onto a steel plate (Fig. 11 *a*). After combustion of the mixture, a heterogeneous melt consisting of the 'hard' alloy and liquid alumina is formed on the surface of the plate. Under the action of gravitational forces, the melt stratifies in such a way that the lower layer adjacent to the steel base consists of the hard alloy and the upper layer consists of alumina. The latter performs an accessory function by protecting the hard alloy from oxidation by atmospheric oxygen. Thermal and chemical interactions of the 'hard' alloy with the steel plate result in a broad gradient intermediate layer (Fig. 11 *b*). After crystallisation of all layers, the oxide layer peels off leaving a steel part coated with the hard alloy.

The distribution of concentrations of chemical elements and microhardness as a function of the distance from the alloy (the molten layer) to the base are shown in Figs 12 and 13. The

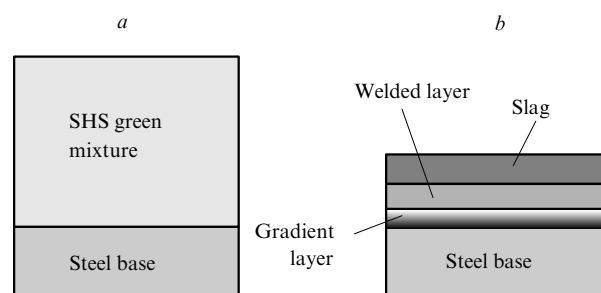


Figure 11. Application of a moulded coating onto a steel base (SHS welding); (a) prior to processing by combustion, (b) after processing.

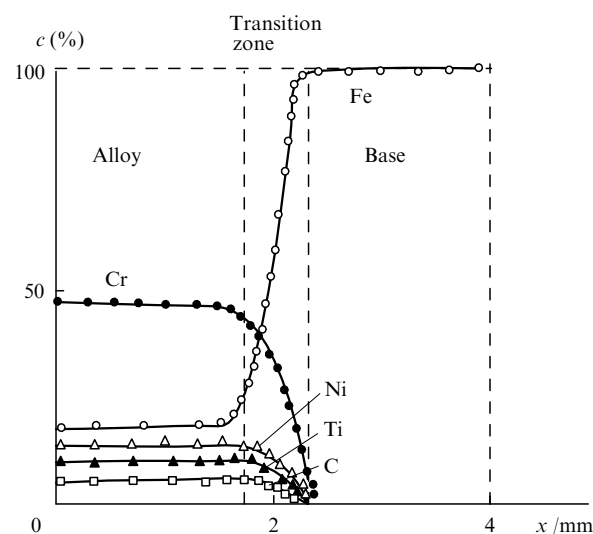


Figure 12. Distribution of chemical elements in a layer welded onto a steel plate (x is the layer height). Composition of the green mixture: $\text{TiO}_2 + \text{CrO}_3 + \text{NiO} + \text{Al}$.

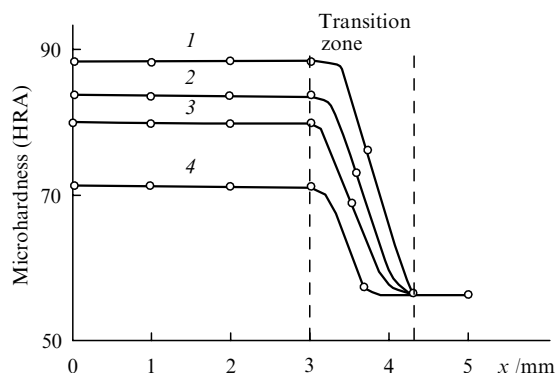


Figure 13. Distribution of microhardness according to Rockwell, the hardness scale A (HRA) in a welded layer.
The starting mixture: (1) Cr–Ti–C–B–Ni, (2) Cr–Ti–C–Ni, (3) Cr–C–Ni, (4) Cr–C–Fe.

presence of a distinct, broad (from 0.5 to 1.5 mm) intermediate zone is an obvious advantage of SHS welding, since it eliminates adhesion owing to the high degree of binding between the coating and the base.

Aluminothermic welding allows application of relatively 'thick' (> 0.5 mm) layers. Thinner layers are coated by induction SHS welding. This process is technologically similar to that described above, except that the charge layer is smaller and the process is implemented in a high-frequency electromagnetic field.⁶⁷ Numerous green mixture compositions aimed at the solution of miscellaneous practical tasks have been developed.

Electrothermal welding is yet another example of a material-affecting SHS.^{68–70} In this process, the conducting green mixture (welding compound) composed of chemical elements is loaded into a gap between the parts to be welded which also play the role of electrodes. When electric current is passed through the electrodes, the green mixture is heated to self-ignition. The parameters are chosen so that the thermal-explosion product is formed in the melt. This interacts with the submolten layers of the parts to be welded and forms a fairly strong welding joint after crystallisation. The strength of the welding joint can be increased, if the melt is extruded from the gap prior to crystallisation with a simultaneous decrease in its thickness.

This approach was used for welding refractory parts of Nb, Ta, W, Mo and C to one another and between themselves. One of the most recent developments is welding of a hard alloy BK8 to the 40X steel.⁷⁰ A micrograph of a thin section of the welding joint is shown in Fig. 14. The Zr + Ni green mixture was used as the welding material.

The Zr + Ni green mixture ensures high strength of the welding joint: the break occurs in the hard alloy but not in the joint. Such a high breaking strength cannot be provided by conventional brass plating.

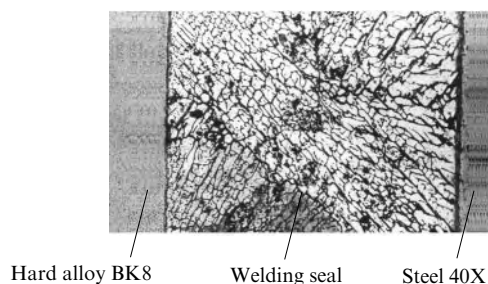


Figure 14. SHS welding. A micrograph of a longitudinal section of the solid alloy BK8 and the steel 40X.

Characteristics of the welding joints produced by SHS and traditional fusion are given in the table below.

Welding material	Flexural strength /MPa	Fracture surface
Ti + Ni	400–600 (welding)	welding joint
Zr + Ni	600–800 (welding)	hard alloy
Brass plating	200 (soldering)	welding joint

SHS welding is used for thermal bonding of refractory materials where conventional electric welding is of little effect.

2. Material-affecting explosion

A crucial role in material-affecting explosion is played by detonation energy which produces high pressure. Under the impact of high pressure, the processable material undergoes plastic deformation. Simultaneous action of pressure and temperature on the processable material induces physicochemical transformations.

All detonation effects on processable materials are subdivided into mechanical and structural. The former includes crushing, dispersion (brittle fracture), pressing, calibration, punching and cutting (plastic destruction); the latter includes reinforcement of metals (workhardening), compaction of metal powders (controlled structure formation) and welding (bonding) of metals.

Explosion-induced welding is the most popular and technologically efficient procedure. A welding scheme of two plates is shown in Fig. 15. After welding, the flat surfaces of both plates acquire a wave-like shape. Pictures of typical welding joints are shown in Fig. 16. Interestingly, the cross-sections of welding joints of homogeneous metals manifest a purely sinusoidal shape (Fig. 16a), whereas the S-shape of the welding joints of heteroge-

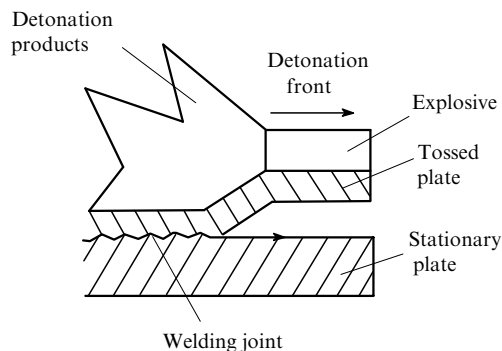


Figure 15. A schematic representation of detonation-driven welding.

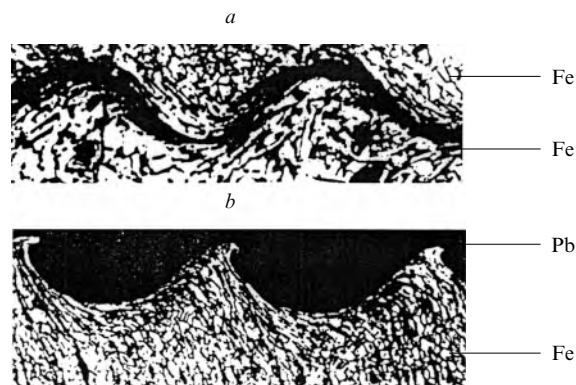


Figure 16. The sinuous structure of a welding joint obtained by detonation welding of the same (a) and different (b) metals.

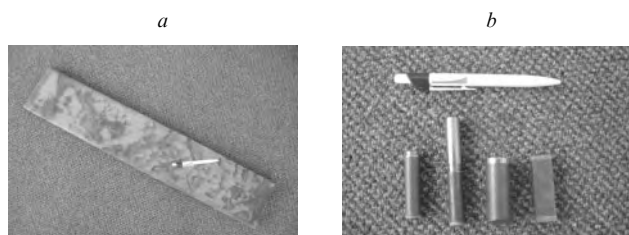


Figure 17. Some items prepared by detonation-driven welding: (a) thermobimetal, (b) trimetallic electrodes for a spectrograph.



Figure 18. Detonation cutting: cumulative charges (a) and slit items (b).

neous (or, more exactly, heterodense) metals is distorted due to the appearance of higher harmonics, which change the wave profile. This phenomenon was described in detail by Gordoplov.⁷¹ Wave formation is a useful process, since it increases the strength of the welding joint.

Pictures of some items prepared by explosion-induced welding are shown in Fig. 17.[‡] The most common practical task relates to the production of bimetallic rolled stock from billets obtained by explosion-induced welding.

Cutting of metals by explosion is also a highly efficient process. It is opposite to welding and is based on the use of cumulative jet streams generated by cumulative green mixtures. Significant progress in this field has been attained by a research team headed by V V Kalashnikov at the Samara State Technological University.⁷² Photographs of cumulative charges and items processed by this technology are shown in Fig. 18. Detonation is also used for cutting metals with thicknesses of 1 cm and more.

IV. Combustion and explosion in physical chemistry of inorganic materials

The physicochemical aspects of combustion and explosion science are sufficiently well-studied as can be evidenced from numerous publications (particularly, those devoted to combustion)[§] which have made a significant contribution to the development of high-temperature physical chemistry.

However, the boundaries of combustion and explosion as an independent trend of research in physical chemistry have not been adequately outlined. It remains to note that the science of combustion and explosion studies chemical and physicochemical transformations which occur spontaneously (after initiation) under non-isobaric and/or non-isothermal conditions, in a non-steady-state mode, have low characteristic times and yield (exclusively or predominantly) solid products.

The latter circumstance is of particular importance, since this review is devoted to materials.

[‡] These pictures were made by Yu A Gordoplov in 1978, they were presented in a Report of the United Institute of Chemical Physics of the Academy of Sciences of the USSR.

[§] A more prominent role in the explosion theory is ascribed to gas-dynamic factors.

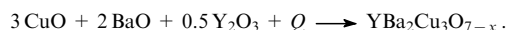
Let us consider briefly some recent trends in physical chemistry of inorganic materials related to combustion and explosion processes.

1. On the chemistry of combustion and explosion

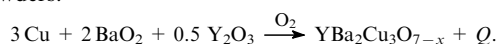
Study of the chemical mechanisms is one of the main areas of research in combustion and explosion science, which is sometimes referred to as the chemistry of combustion and explosion. Its main goals are as follows:

- determination of intermediate and final stages in combustion and detonation waves;
- development of methods for the isolation of intermediate products;
- characterisation of final products and its relationship to operational regimes.

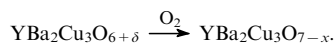
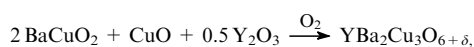
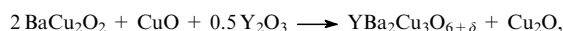
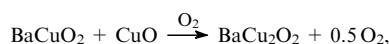
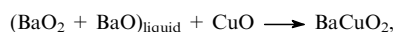
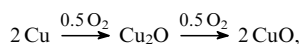
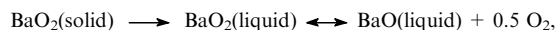
Let us consider the formation of yttrium–barium cuprate possessing superconducting properties in a combustion wave as an example. This synthesis is a very ‘capricious’ process, since the final compound is thermally unstable, easily loses oxygen and, as a consequence, its superconducting properties. Traditionally, it is prepared by furnace synthesis using the reaction:



It was recommended⁷³ to perform this synthesis from a mixture containing copper, barium peroxide and yttrium oxide powders.



Although combustion of this mixture is easily initiated, the preparation of a high-quality product demands optimisation of conditions of synthesis. To meet this goal, the mechanism of this reaction in the combustion wave was studied. The formation and consumption of intermediate products and the formation of the final product were studied using different techniques. The reaction mechanism is as follows:⁷⁴



The final stage represents a phase transition from a non-superconducting tetragonal phase to the superconducting orthorhombic phase with an insignificant overoxidation of the cuprate formed. The knowledge of this mechanism has made it possible to develop a technology for synthesising of a high-quality product with remarkable superconducting properties.⁷⁴ Some characteristics of $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$ powders synthesised in the combustion wave (grade SHS samples) and by furnace synthesis (other samples) are given in Table 4 (see Ref. 75). A comparative study of these powders was carried out by the US company ‘Super Conco’. As can be seen from the Table, the SHS-J2 powder prepared by SHS is by far the best.

2. Kinetics of chemical reactions at high temperatures

Whereas the knowledge of chemical mechanisms of reactions occurring in a combustion wave helps control the quality of final products, kinetic studies are necessary for elucidation of mechanisms of self-propagation of the combustion wave. In the latter case, the main interest is focused on the kinetics of heat evolution.

Table 4. Comparative characteristics of powders of the high-temperature superconductor $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$ prepared by the furnace method and SHS.

Sample	Content of oxygen ^a (a.u.)	Transition temperature /K	Y_{123} orthorhombic phase content (%)	Main impurities	Average particle size / μm
SC5-S	6.92	93.5	98	CuO	40.0
SC-P	6.87	93.5	99	CuO	8.2
SC5-6.5	6.88	90.5	97	BaCuO_2	6.8
SC5-7	6.85	92.5	99	CuO	5.7
CPS A-1203	6.85	92.0	99	BaCuO_2	3.0
SSC 03-0065	6.89	92.0	99	—	6.5
SHS-J1	6.90	92.0	97	CuO	9.0
SHS-J2	6.92	93.5	99	—	8.0

^aOxygen content was determined by iodometry.

It should be noted that the kinetic aspects of explosion science are not sufficiently developed (here, thermodynamic and gas-dynamic interests 'dominate'). In contrast, in combustion science these aspects constitute an independent and well-developed area of research. Direct kinetic studies are hardly possible due to high reaction rates and high temperatures; therefore, kinetic information is derived from the very combustion experiments using indirect methods. Determination of effective activation energy, E_{eff} (see Refs 76 and 77) using the formula:

$$U^2 = AT_{\text{ad}}^2 \exp\left(-\frac{E_{\text{eff}}}{RT_{\text{ad}}}\right)$$

is an example of such an approach.

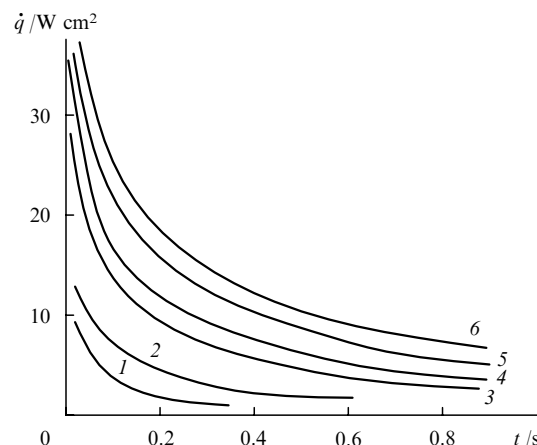
A method for processing temperature profiles in the combustion wave aimed at determination of the heat evolution rate $\dot{q}$ (dq/dt) as a function of the temperature T and the amount of evolved heat q , has been developed.⁷⁸ It is reduced to the solution of the kinetic equation:

$$\dot{\eta} = f(T, \eta), \quad \eta = \frac{q}{Q},$$

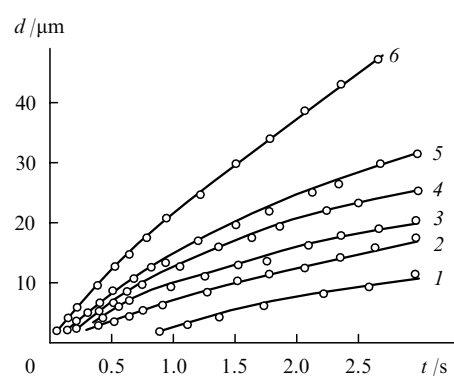
where $\dot{\eta}$ is the reaction rate. Correct determination of the initial stages of transformations of various substances by this method is difficult: it provides reliable kinetic information only at more advanced stages of the conversion. Nevertheless, direct kinetic studies of chemical reactions in the temperature range close to that of the combustion wave were carried out for one class of reactions, *viz.*, high-temperature reactions of metals with gases. The method in question represents electrothermography for kinetic studies.^{79, 80}

The principle of the method is simple and well-known. A system of two reactants, *viz.*, a thin filament made of the tested metal and a gas, is considered. The metal filament is heated by electric current and thus plays the role of a reactant and a high temperature source. The advantage of this method^{79, 80} is that it employs an optical or electrical monitoring system and heat evolution compensation for maintaining the constant temperature of the filament by attenuation of the electrical power. This procedure allows recording time dependences of heat evolution rates at different constant temperatures. The process can easily be stopped by switching off the current (the cooling is complete within fractions of a second); the kinetics of growth of diffused layers is deduced from metallographic analysis of filament sections. The electrographic method was used to study the kinetics of reaction of some transition metals (Groups IV and V of the Periodic Table) with nitrogen, oxygen, hydrogen, silane and some hydrocarbons.

The dependences of heat evolution rates on the growth time and the width of the tantalum nitride film (product) for the

**Figure 19.** Kinetics of heat evolution in the high-temperature nitrogenation of tantalum.

$T/^{\circ}\text{C}$: (1) 2210, (2) 2300, (3) 2610, (4) 2700, (5) 2850, (6) 2970.

**Figure 20.** Kinetics of product layer growth (d) during high-temperature nitrogenation of tantalum.

$T/^{\circ}\text{C}$: (1) 2420, (2) 2570, (3) 2650, (4) 2750, (5) 2840, (6) 2930.

reaction of tantalum with nitrogen are shown in Figs 19 and 20.^{81, 82} An analysis of experimental results revealed that this process is described by a kinetic equation:

$$\dot{q} = 8.6 \times 10^{-2} \exp\left(-\frac{40\,800}{R}\right) q^{-1} \text{ (kcal}^2 \text{ cm}^{-4} \text{ s}^{-1}\text{)},$$

which reflects the parabolic oxidation law. Note that these results were obtained in a high-temperature range [2210–2970 $^{\circ}\text{C}$ (!)].

Interesting studies of reactions of metals with complex gases (hydrocarbons, silane, *etc.*) have been carried out by Kharatyan *et al.*^{83–85} In these multistep processes, decomposition of the gas on the surface of the filament and the formation of a solid film (carbon, silicon) were followed by the interaction of the latter with the metal by a diffusion mechanism.

3. Thermochemistry and thermodynamic calculations

An important line of investigations includes quantitation of the amount of heat evolved during reactions of chemical elements in a combustion mode. These data enable easy determination of the heats of formation of various compounds with allowance for incomplete burning and impurities. The heats of formation of some high-melting materials prepared by SHS (carbides, silicides, borides) have been determined.⁸⁶ Direct measurement of heats of formation in a combustion mode gives more accurate results than the conventional method based on combustion of tested substances and the starting reactants in oxygen or fluorine. In the classical method, the values of the heats of formation represent a small difference of large numbers, which is a potential source of errors.

For carbides and silicides, which are readily burnt in oxygen or fluorine, the scatter in the values of heats of formation obtained by different authors is small. The values of the heats of formation obtained by direct measurement of the amount of the heat evolved in SHS are in good agreement with the literature data.

Borides are more stable compounds and their combustion is often incomplete, hence the scatter in the values of heats of formation cited in the literature. For these compounds, the direct measurements are more important in principle. The heats of formation of titanium-, zirconium-, hafnium- and other metal borides obtained by both methods are listed in Table 5.

Table 5. Heats of formation of metal borides.

Reaction	Heat of formation /kcal mol ⁻¹	
	SHS	classical method ^a
Ti + B → TiB	40.0 ± 0.8	38
Ti + 2B → TiB ₂	71.5 ± 1.4	63.6; 66.8; 70.07; 77.4
Zr + 2B → ZrB ₂	66.7 ± 1.3	63.1; 72.0; 73.0; 77.0
Hf + 2B → HfB ₂	62.6 ± 1.2	74.2; 80.0
Nb + 2B → NbB ₂	52.7 ± 1.0	41.9; 49.7
Ta + B → TaB	38.6 ± 0.8	—
Ta + 2B → TaB ₂	47.5 ± 1.0	46.3; 50.0; 52.0
Mo + B → MoB	26.9 ± 0.5	16.7

^a Published data.

An important role in thermodynamic studies is ascribed to calculations of adiabatic temperatures and equilibrium compositions of combustion and detonation products. However, in the case of detonation processes such calculations are complicated due to the lack of reliable information about equations of state at high pressures and temperatures. As regards combustion and especially SHS, these processes are sufficiently well documented. There are two approaches to thermodynamic calculations.

In the first (approximate) approach, combustion temperature is determined under the assumption that the compositions of the products are known.⁴⁴ The calculations are made according to the equation:

$$\int_{T_0}^{T_{ad}} c(T) dT = (Q - \sum_{i=0}^n L_{ph}^i) - \mu_{ph} L_{ph},$$

where c is the thermal capacity of the product, Q is the heat of formation at T_0 , L_{ph}^i are the heats of phase transitions at $T_{ph}^i < T_{ad}$, n is the number of phase transitions at $T_0 < T_{ph} < T_{ad}$, L_{ph} and μ_{ph} are the heats of phase transitions and the content of the high-temperature phase in the combustion product at $T_{ph} = T_{ad}$, respectively. At $T_{ph} > T_{ad}$ $\mu_{ph} = 0$, at $T_{ph} < T_{ad}$ $\mu_{ph} = 1$.

This method was used⁸⁷ for the calculation of T_{ad} for many self-propagating high-temperature reactions which yield a single product. The data obtained shed more light on the combustion mechanisms of many specific systems.

In the general case, the calculations are performed using a complete procedure which allows simultaneous determination of T_{ad} and equilibrium compositions of reaction products at T_{ad} . Originally, this approach was used in combustion studies of propellants, but after some modifications it was extended to material-synthesising combustion processes.

The first calculation of this kind was performed for direct synthesis of iron from iron oxide by reduction with methane.⁸⁸ A three-dimensional diagram of the combustion products is shown in Fig. 21 (the hatched area corresponds to the formation of reduced iron as a single condensed product).

Numerous thermodynamic calculations have now been performed. A special ISMAN-TERMO programme and a database

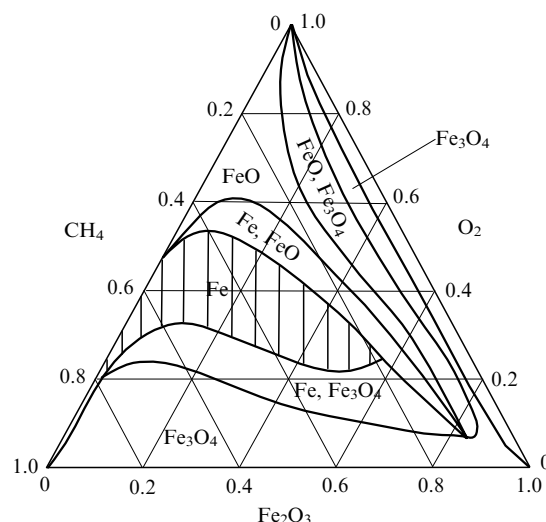


Figure 21. A triple diagram of combustion products in the $\text{Fe}_2\text{O}_3 + \text{CH}_4 + \text{O}_2$ system.

of adiabatic combustion temperatures of binary and ternary systems have been developed by the researchers of ISMAN.

4. Physicochemical effects in the mechanisms of combustion and detonation

Material-synthesising combustion and explosion are associated with evolution and transfer of heat (combustion) or a release of energy and shock-driven compression (detonation). As a rule, these processes are accompanied by various (mostly, physicochemical) effects and involve phase transitions. Their analysis falls also under the scope of physical chemistry of inorganic materials.

Let us consider several examples. Combustion of powder mixtures of low-melting metals (Ti, Zr) with more refractory non-metals (C, B) is accompanied by a very important effect termed 'capillary spreading'.⁸⁹ The mechanism of this effect is as follows. Prior to reaction with a non-metal in the precombustion zone, the metal reactant melts and spreads over the surface of refractory non-metal particles. Since the sizes of carbon and boron particles are usually 2–3 orders of magnitude smaller than those of the metal particles, the above-mentioned process results in spontaneous homogenisation of the green mixture, which increases the reaction rate and, correspondingly, the combustion rate. The experimental values of the combustion rates of the Ti + C systems are 10–15 cm s⁻¹. Such high rates for processes occurring in the condensed phase can be attributed exclusively to a significant increase in the reactivity of the green mixture.

Phase transitions (e.g., melting) have a significant effect on the structure of the combustion wave. The temperature profile of the combustion wave is distorted due to phase transitions, these induce the appearance of isothermal plateaus on the temperature curve and a shift of the combustion zone, which determines the wave velocity, from the high- to the low-temperature zone (see, e.g., Ref. 23).

Let us consider another example of a detonation process associated with physicochemical transformations in shock waves. After investigators of detonation have learnt to preserve the integrity of samples exposed to the shock wave, their attention came to be focused on the nature of changes caused by detonation. First of all, they posed themselves the question: where do phase transitions take place: in the shock wave proper (for an order of microseconds) or after passage of the wave at high residual temperatures? An answer to this question came after successful attempts to record the shock adiabat (the compression curve). The distortions in the smooth curve (shock adiabat) testified to physicochemical transformations in the shock wave. The shock

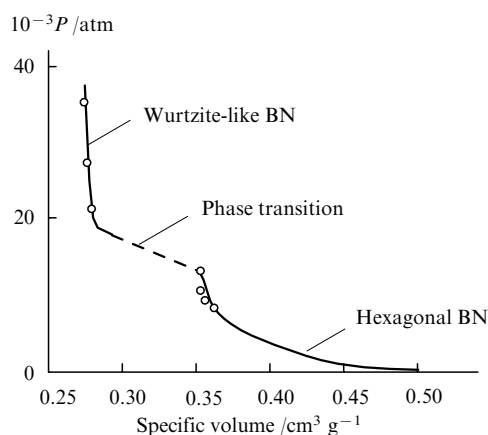


Figure 22. A shock adiabat of boron nitride.

adiabat for boron nitride shown in Fig. 22⁹⁰ provides an illustrative example of a phase transition from the hexagonal phase of BN to the wurtzite-like phase at increasing pressures.

At present, shock adiabats have been established for a broad range of compounds and are used for elucidation of shock compression mechanisms.

V. On the theory and mathematical simulation

Theoretical studies into material-synthesising combustion and detonation processes were largely concentrated on solid-flame combustion and made use of classical approaches developed in the flame propagation theory by Ya B Zeldovich for gases and further extended with account of formation of solid products (see, *e.g.*, Refs 6 and 35 and references cited therein). High thermal capacities, possible phase transitions of solid products and solid reactants and the lack of diffusion-driven transfer of products are the main factors responsible for the immense complexity of flame propagation modes.

Let us consider some key aspects.

As a rule, the information on the structure and velocity of the combustion wave is obtained through the solution of the simplest steady-state flame propagation equations:

$$\lambda \frac{d^2 T}{dx^2} - c\rho U \frac{dT}{dx} + Q\rho\varphi(T, \eta) = 0$$

(heat conduction equation),

$$U \frac{d\eta}{dx} = \varphi(T, \eta)$$

(kinetics equation)

where x is the linear coordinate of the combustion wave and $\varphi(T, \eta)$ is the kinetic function for the boundary conditions:

$$x = -\infty, T = T_0, \eta = 0$$

and

$$x = +\infty, \frac{dT}{dx} = \frac{d\eta}{dx} = 0.$$

The linear transfer of the reaction product was neglected in the solution of these equations; material-synthesising processes (*i.e.*, solid-phase reactions yielding solid products) were described by

the 'non-classical' kinetic functions $\varphi(\eta)$.[†] The following kinetic functions were employed in the very first theoretical studies:^{6, 19}

$$\varphi(\eta) = \exp(-m\eta)\eta^{-n},$$

where m and n are the constants.

More advanced theoretical studies took into account various features of evolution and transmission of heat in different systems, such as melting and formation of molten layers, transfer of mass and heat by infiltration after impregnation of initial porous green mixtures with the melt, multistep character of reactions, *etc.*^{91–93}

Description of flame propagation processes in hybrid 'porous body–gas' systems is a more complicated task. At relatively low gas pressures, solid reactants do not contact with one another and the transformation of the solid demands the delivery of a gaseous reactant to the combustion zone. Usually, this situation is analysed for one-component gases which are fully consumed upon reaction. This assumption suggests that their transport proceeds in a purely infiltration mode (if another gas is present, allowance is made for diffusion).

Numerous studies on filtration combustion modes have been carried out. One-dimensional filtration was found to occur in cylindrical samples with gas-impermeable lateral surfaces and open edges. The results of one-dimensional combustion studies have been generalised.⁹⁴ A theoretical analysis of more complex filtration regimes, *e.g.*, combustion with lateral filtration leading to limiting surface and layer-by-layer modes and high-pressure combustion, has been carried out.^{95, 96}

Of substantial interest are material-synthesising combustion implemented in non-steady-state modes (in unstable regions, in particular). Studies by Ya B Zeldovich have shown that the enthalpies of condensed systems in combustion waves exceed those of the starting reactants (at initial temperatures) or final products (at combustion temperatures) which are equal. The excess of enthalpy is the reason for the instability of the wave propagation. In the case of gas-releasing systems, such as explosives, instability leads to extinction of the process. Owing to their high thermal capacity, the condensed products prevent extinction and wave propagation continues, however, in a complex or abnormal mode. The existence of one-, two- and three-dimensional non-steady-state modes reflects the complex nature of spatiotemporal instability.

In the case of one-dimensional instability, the smooth (nearly flat) combustion front characteristic of steady-state modes is preserved, and only time instability is observed. In this case, we deal with the so-called self-oscillations where the instantaneous value of the combustion front velocity fluctuates around a certain mean value (the so-called harmonic or relaxation oscillations, Fig. 23). Figure 23 shows curves for the time changes in the instantaneous front velocity in dimensionless coordinates for different limiting stability loss values (α_{st}).

A novel mode of combustion has been established in model studies of two-dimensional instability of a hollow cylinder with account of temperature distribution and degree of conversion along the height and circumference of the cylinder with no allowance for the radial direction.¹⁸ Here we deal with the aforementioned spin wave where the reaction is concentrated in a centre moving along the sample by a spiral path. After a certain period of time, the velocity of the centre becomes constant indicating spatial instability, but temporal stability remains. Such regimes are usually described within the framework of a thin cylindrical shell model with allowance for longitudinal and tangential (angular) heat exchange components.

[†] The classical kinetic functions for the reactions of the n th-order appears as $\varphi(\eta) = (1 - \eta)^n$.

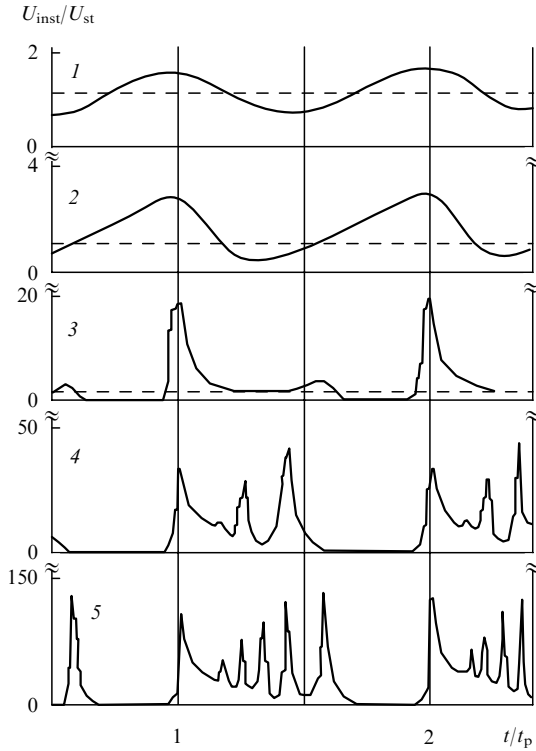


Figure 23. Self-oscillations of the front velocity as a manifestation of one-dimensional instability (U_{inst} and U_{st} are instantaneous and steady-state combustion velocities, respectively). The structure of pulses at different deviations from the stability limit $\alpha_{\text{st}} = 0.99$ (1), 0.94 (2), 0.82 (3), 0.64 (4), 0.50 (5).

Three-dimensional waves are generated in solid cylindrical samples under the action of a radial heat-exchange component. Such waves propagate in diverse modes which depend upon:

$$\alpha_{\text{st}} = \left(9.1 \frac{c\rho T_{\text{ad}}}{Q} - 2.5 \right) \frac{RT_{\text{ad}}}{E}$$

and

$$r = r_0 \left[\frac{Q}{c} \frac{E}{RT_{\text{ad}}^2} \frac{kT_{\text{ad}}}{a} \right]^{1/2}.$$

The former parameter corresponds to the stability loss limit (the smaller α_{st} the greater the instability), while the latter represents a dimensionless radius of a cylinder, *i.e.*, the ratio of the cylinder radius to the characteristic width of the narrow reaction zone. The smaller α_{st} and the larger r the more complex the instability pattern. Some novel three-dimensional non-steady-state combustion modes, *viz.*, spin waves with self-oscillations of the centre velocities, intermittent spin waves with temperature fluctuations, multipoint periodic waves with recurrent non-steady-state temperature and concentration fields and chaotic waves, have been described.^{97–101} Studies of heat losses to the environment have established several novel regimes of combustion wave propagation described by paraboloid-type functions.

Interestingly, all these previously unknown regimes are described by a classical system of equations which is physico-chemically the simplest, *viz.*, by the heat conduction equation in the cylindrical coordinates:

$$c\rho \frac{\partial T}{\partial t} = \lambda \left(\frac{\partial^2 T}{\partial r^2} + \frac{1}{r} \frac{\partial T}{\partial r} + \frac{1}{r^2} \frac{\partial^2 T}{\partial \varphi^2} + \frac{\partial^2 T}{\partial h^2} \right) + \rho Q \frac{\partial \eta}{\partial t}$$

and the kinetics equation:

$$\frac{\partial \eta}{\partial t} = \begin{cases} k_0(1 - \eta) \exp\left(-\frac{E}{RT}\right) & \text{for } \eta < 1, \\ 0 & \text{for } \eta \geq 1, \end{cases}$$

where r , φ and h are the spatial coordinates (r is the radial, φ is the angular and h is the longitudinal axes of the cylinder) supplemented by the following boundary conditions:

$$t = 0: T = T_0, \eta = 0;$$

$$t > 0: r = r_0, \quad \frac{\partial T}{\partial r} = -\alpha_t(T - T_0);$$

$$h = 0: \frac{\partial T}{\partial h} = 0;$$

$$h = h_0: \begin{cases} T = T_{\text{ign}} & \text{for } t \leq t_{\text{ign}}, \\ \frac{\partial T}{\partial h} = 0 & \text{for } t > t_{\text{ign}}, \end{cases}$$

where T_0 is the ambient temperature and the initial temperature of the sample; T_{ign} is the ignition temperature; α_t is the heat-transfer coefficient from the surface to the environment; r_0 and h_0 are the radius and the height of the cylinder, respectively, and t_{ign} is the duration of the initiating pulse.

The structure of a combustion front for a chaotic regime is shown in Fig. 24.

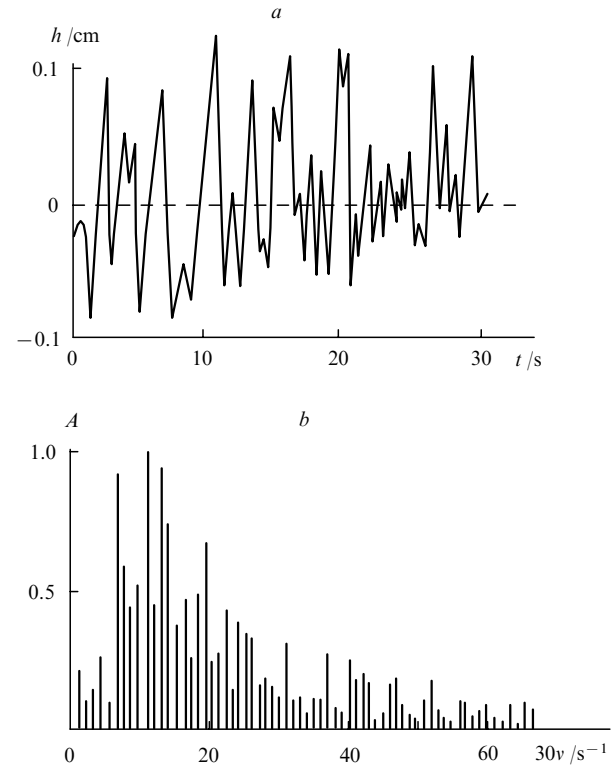


Figure 24. An example of a chaotic combustion regime in the $\text{Cr}_2\text{O}_3 + \text{Al} + \text{Al}_2\text{O}_3$ system (h , lead of screw thread; A , amplitude); (a) vibrations of the front coordinate relative to the average value, (b) amplitude–frequency spectrum.

All of the foregoing discussions related to processes occurring in mixed systems (powder mixtures). A more complex, but less explored instability pattern is observed in hybrid ‘porous sample – gas’ systems.

Unstable self-excited waves generated in various material-synthesising processes have become an attractive subject of

investigations in nonlinear dynamics. Investigators are contemplating the problem of making these processes more practicable.

VI. Materials science of combustion and explosion products

This important trend of research has a number of specific features, since the conditions of material-synthesising combustion and explosion differ dramatically from those used in ordinary processes, which cannot but reflect on the structures and properties of the final products.

Studies in the field of materials science develop along four main lines (chemical, physical, technical and theoretical).

The chemical materials science studies mechanisms of chemical and structural transformations in the combustion wave, dynamics of formation of the final structures of reaction products and their individual components (phase, crystalline, granular, porous, *etc.*), chemical properties of the reaction products (chemical analysis) and their relationship with conditions and parameters of the corresponding processes. Physical properties of materials and physical material processing fall under the scope of physical materials science. Technological materials science is concerned with the study of operational characteristics and applications of combustion and explosion products in different branches of science and technology. Theoretical materials science deals with structural and macrokinetic simulation and analysis of physical (equilibrium or non-equilibrium) states of reaction products in relation to thermal regimes.

The problem of equilibrium and non-equilibrium character of combustion and explosion products is very interesting and widely debatable. Peremptory and often erroneous judgements exist that the products formed are of non-equilibrium character, since the underlying processes are non-equilibrium. The incorrectness of this statement is due to the ambiguity of its solution, which depends on the criterion S :

$$S = \frac{t_{st}}{t_{tr}}$$

where t_{st} is the characteristic time of structure formation and t_{tr} is the characteristic product cooling time. If $S \ll 1$, the cooling period is long and the product undergoes self-annealing under long-term action of high temperatures, which leads to the formation of an equilibrium product. Synthesis in SHS reactors where the cooling time is 1–1.5 h and structural relaxation is complete is an example of a process for the preparation of equilibrium products.

At $S \gg 1$, the cooling time is short and self-quenching[†] takes place. In this case, non-equilibrium products are formed instead of equilibrium ones.

The structure of the product in the remaining broad intermediate variability domain of parameter S may be very complex.[‡] For example, the equilibrium can be reached for one parameter, *e.g.*, chemical composition of the products, but cannot be reached for other parameters, *e.g.*, crystal phase structure.

Let us consider an interesting example. In 1970, I P Borovinskaya came to obtain an unexpected result in an attempt to synthesise boron nitride by combusting boron in nitrogen under high pressures (~ 300 MPa).²¹ In one of these experiments, the tube broke and rapid release of pressure resulted in hardening of the burnt product. The sample of boron nitride thus obtained appeared to be amorphous. These studies have demonstrated the possibility of obtaining both non-equilibrium and amorphous products by hardening.

[†] Quenching is a rapid (10^3 – 10^4 deg s⁻¹) cooling of a sample and is usually implemented in two modes: in liquid nitrogen and in massive brass blocks for wedge-shaped samples.

[‡] The term 'structure' is very broad and polysemantic. It entails chemical structure, phase state, grain size (in the case of granular structures), *etc.*

Rogachev *et al.*^{102, 103} have described an original procedure for hardening of combustion products using a large copper block with a wedge-shaped cavity filled with a green mixture. Combustion was initiated at the wide base of the wedge and gradually spread deeper into the narrow channel. Increasing heat losses caused the flame to fade at some distance from the wedge base. Layer-by-layer analysis of combustion products made it possible to draw the dependences of chemical and phase compositions, grain size and other reaction parameters as a function of the combustion coordinate, *i.e.*, the distance from the combustion front. These dependences provide indirect (with some errors connected with the hardening time) information about the processes occurring in the combustion zone.

The picture of a combustion process carried out in a wedge-shaped cavity and the micrographs of the granular structures of the samples formed at different distances x from the wedge base are shown in Fig. 25. Figure 26 illustrates the dependence of the mean grain size on the combustion coordinate for TiC, TiB₂, *etc.* Based on the results obtained, it was concluded that after termination of chemical reactions occurring in the combustion wave the system undergoes intense recrystallisation as a result of which the size of the grains increases. The particles formed in the combustion zone have submicron and micron sizes which may increase by orders of magnitude in the course of recrystallisation. This hardening method provides a key to control over the granular structure and, correspondingly, the properties of the materials synthesised.

Studies of dynamics of phase transitions (polymorphous transformations) in the combustion wave are yet another impor-

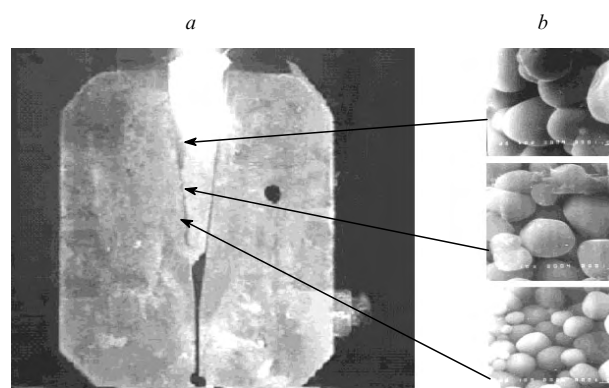


Figure 25. Combustion in a wedge-shaped gap: a picture (a) and micrographs of product structures taken at different distances from the combustion front (b).

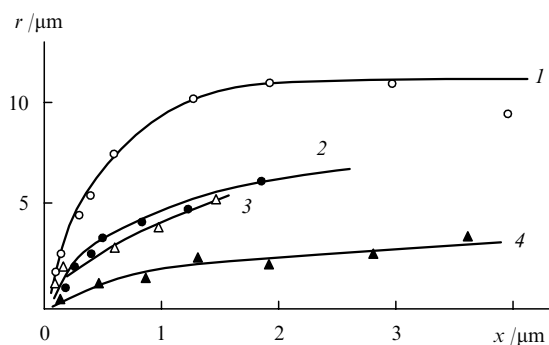


Figure 26. Distribution of grain sizes (r) of combustion products behind the combustion wave front (x is the distance behind the front) for processes of formation of TiC (1), TiB₂ (2), Ti₅Si₃ (3) and TiC + 20%Ni (4).

tant line of research. This required the development of novel techniques for the control over dynamics of phase transitions in all stages: from starting reactants to final products. In addition to hardening, these methods include dynamic X-ray phase analysis based on synchrotron radiation, standard analyses using X-ray tubes and other techniques. The principle of X-ray phase analysis is very simple. The X-ray beam is directed at a definite point on the lateral surface of the sample which is usually flat. When the combustion wave reaches this point, X-ray photographs are taken at definite intervals of time. X-Ray patterns allow the analysis of dynamics of phase transitions and, particularly, of the dynamics of formation of the final products.

Practical implementation of this technique requires the use of X-ray beams of high intensity and rapid shooting of X-ray patterns. The use of synchrotron radiation is the most appropriate to this end. The pioneering studies in this area were carried out on a synchrotron of the Institute for Nuclear Research of the Siberian Branch of the Russian Academy of Sciences by a research team headed by V V Boldyrev.¹⁰⁴ An Ni + Al system used in this study was subsequently employed in other model studies.^{105, 106} A schematic representation of this experiment is shown in Fig. 27; the first dynamic phase formation curves are depicted in Fig. 28.

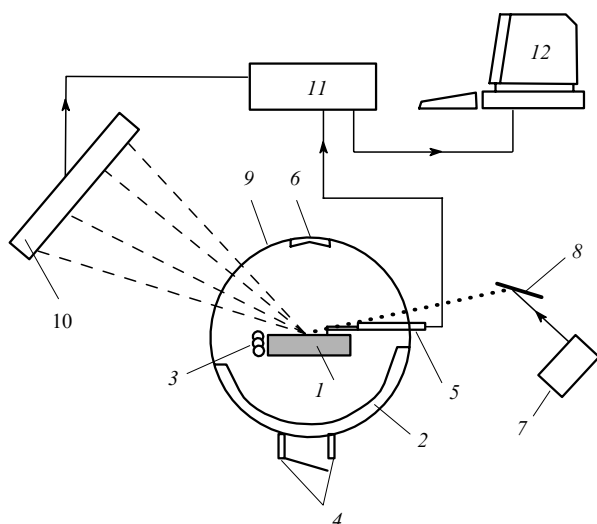


Figure 27. Dynamic X-ray analysis of SHS; (1) sample, (2) reaction chamber, (3) igniting wire, (4) gas inlet and outlet (He), (5) thermocouple, (6) quartz window, (7) X-ray tube, (8) monochromator, (9) beryllium window, (10) linear detector, (11) interface unit, (12) computer.

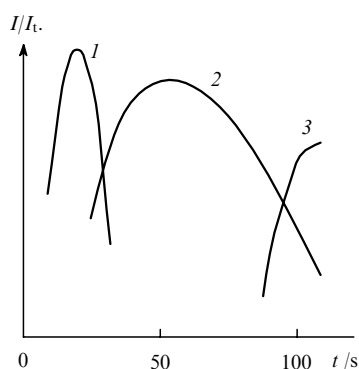


Figure 28. First dynamic curves of phase formation obtained in combustion in the Ni + Al system (I is the intensity of radiation); (1 and 2) intermediate phases, (3) final product.

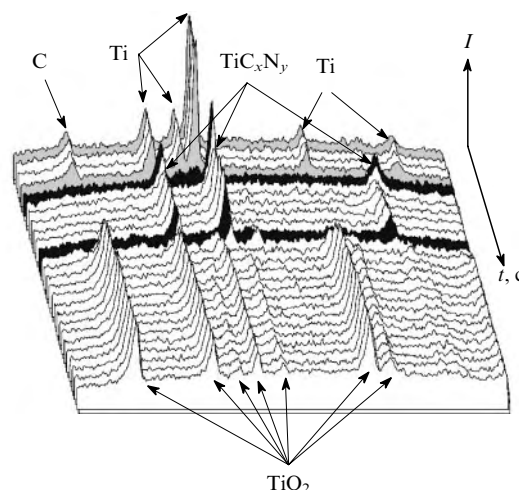
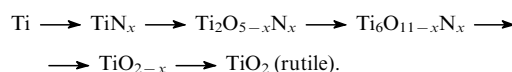


Figure 29. A series of dynamic patterns obtained in the combustion of the Ti-C system in air.¹⁰⁹

A simpler design of a laboratory-scale X-ray diffraction analysis on an ordinary diffractometer supplied with a special detector was developed in further studies.^{107, 108} A set of dynamic X-ray patterns obtained by this method is shown in Fig. 29 (see Ref. 109). Their processing made it possible to draw the concentration profiles of the combustion wave (patterns).

Interesting patterns were obtained in the studies of combustion of a titanium powder in air (Fig. 30).¹¹⁰ These diagrams clearly demonstrate that the metal reacts with nitrogen rather than with oxygen to afford an intermediate nitride which undergoes subsequent oxidation to yield titanium oxide (TiO_2) as the final product.



A method for processing patterns was proposed, which provides information about the mechanism of phase formation in the combustion wave.³⁰ The dynamic phase transformation curves are treated in the y - ξ coordinates, where y is the completeness of phase formation and ξ is the dimensionless spatial coordinate:

$$\xi = \frac{U^2 t}{a},$$

where a is the thermoconductivity of the substance.

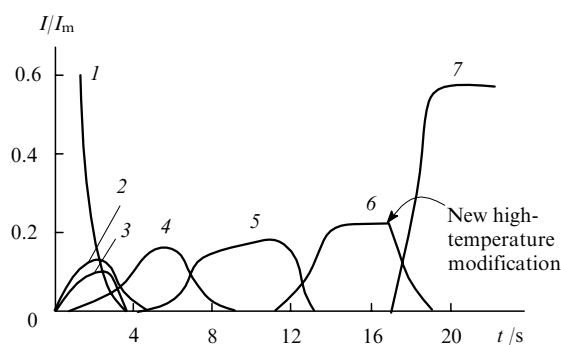


Figure 30. X-Ray phase diagrams obtained in the combustion of a titanium powder in air; (1) α -Ti + solid solution, (2) β -Ti, (3) TiN_x , (4) $\text{Ti}_3\text{O}_{5-x}\text{N}_x$, (5) $\text{Ti}_6\text{O}_{11-x}\text{N}_x$, (6) TiO_{2-x} , (7) TiO_2 (rutile).

If $0 < \xi < 1$, the structure formation follows the Khaikin–Aldushin–Merzhanov equilibrium mechanism where chemical reactions and structure formation occur simultaneously. At $\xi \gg 1$, the process follows the Borovinskaya non-equilibrium mechanism, *i.e.*, the final product is formed at a sufficiently large distance from the combustion front due to decomposition of unstable intermediate products formed in the combustion wave.^{6, 19, 27} An example of this process is given in Fig. 31.

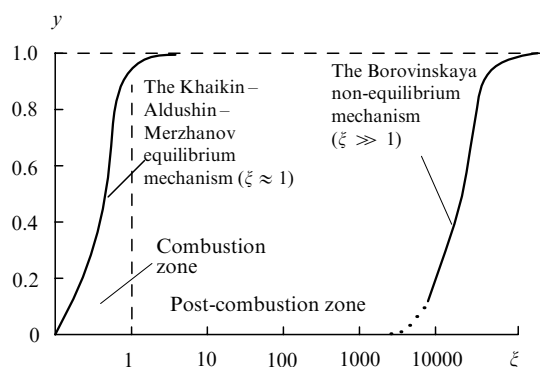


Figure 31. On the mechanism of structure formation in combustion processes.

To some extent, synchrotron and diffractometric methods are complementary. The former is more suitable for the study of fast burning systems, while the latter is more applicable to slowly

burning systems. However, none of these methods allows identification of the initial stages of phase transitions. Therefore, increasing measurement sensitivity is a currently central methodological task.

A recently published paper¹¹¹ describes the use of the synchrotron method for obtaining information about processes occurring in the detonation wave.

Numerous papers are devoted to a comparison of miscellaneous characteristics of combustion and detonation products to those prepared by conventional methods. This is important from both the scientific and practical point of view, especially for SHS products, because here, like in no other field, their competitiveness with respect to products prepared by conventional methods had to be argued. Some characteristics of AlN powders prepared by SHS and sintered materials therefrom in comparison with particulate materials prepared by furnace synthesis are given in Table 6. Aluminium nitride is a very popular ceramic material which is widely employed in electronics for preparation of microchip boards where quality requirements are especially high. As can be seen from Table 6, the quality of the SHS product exceeds that of the furnace-made analogues in the content of fixed nitrogen and admixed oxygen, but the content of admixed iron in the former is higher. Sintered SHS materials prepared from AlN are also distinguished for high quality.

The next example is related to the synthesis of diamonds. In Table 7, specifications of diamonds prepared by two detonation methods are compared to those synthesised under static conditions at high pressures and temperatures. Diamonds prepared by the three methods differ in grain size (from nanosizes to millimetres) and hence in application fields. All artificial diamonds complement each other rather than compete.

Table 6. Comparative analysis of AlN powders obtained by SHS and by furnace synthesis.

Method	Sample brand ^a	Manufacturer (country)	Impurities (mass %)			Specific surface $S/\text{m}^2 \text{ g}^{-1}$	Mean diameter (d_{50})/ μm	Characteristics of sintered powders		
			N ^b	O	Fe			λ /W K ⁻¹ m ⁻¹	strength /MPa	electric strength /kW m ⁻¹
SHS	SHS-T	ISMAN (RF)	31.5–32.5	1.2–1.5	0.1–0.2	—	—	—	—	—
	SHS-C	ISMAN (RF)	33.5–33.8	0.5–0.8	0.06–0.1	0.6–0.8	<15	—	—	—
	SHS-G	ISMAN (RF)	33.3–33.5	0.7–1.0	0.06–0.1	2.5–3.5	1.0–1.4	160–190	370–390	>20
Furnace	—	RPC 'Reaktiv-Elektron' (RF)	31.0–32.6	0.4–2.9	0.3	—	—	—	—	9.6
	AlNeL [®]	ART (USA)	33.0	1.0	<0.01 (see ^c)	2.0–5.0	—	200	—	10
	CER-ALLOY	Ceradyne (Great Britain)	—	—	—	—	—	120–170	207–280	—
	Grade F	Tokuyama Soda (Japan)	33.6	0.9	0.001	3.2–3.5	1.5	170 ± 10	350	>20

^a Designations: SHS-T, technical grade; SHS-C, pure, conglomerates; SHS-G, pure, ground; ^b stoichiometric content is 34.19 mass %; ^c ppm.

Table 7. Specification of artificial diamonds.

Method for synthesis	Mechanism of formation	Size of crystal grains	Areas of application	Authors
Statical at high pressures and temperatures	phase transition of graphite into diamond in the presence of catalysts	< 5 mm	jewelry, boring/stone-working instrument, polishing tools	V N Bakul', L F Vereshchagin
Detonation-I	phase transition of graphite into diamond in a mixture of an explosive with graphite	0.01–5.00 μm	composite materials with metal/elastomer templates	O N Breusov, A N Dremine <i>et al.</i>
Detonation-II	formation of diamond from carbon present in the explosive	2–4 nm	superfinish polishing, motor oil additives	G V Sakovich, V M Titov <i>et al.</i>

The two detonation methods differ in principle. In one of them, carbon particles are incorporated into the explosive green mixture and diamonds are formed in the detonation wave. In another approach, explosives containing excess carbon (with respect to oxygen balance) are used without additives. Excess carbon atoms are condensed in the detonation wave into small (nanodimensional) particles. Such diamonds virtually represent condensed products of an explosion-induced chemical reaction. This is an example of detonation-driven SHS (see above).

A comparison of various characteristics of products prepared by different methods allows correct choice of a synthetic procedure depending on the practical task.

VII. Material-synthesising and material-affecting combustion and explosion processes in technology and industry

Combustion and explosion processes present substantial practical interest.

Numerous unique technologies based on combustion and explosion processes have been developed; the number of SHS processes alone, which include six technological types, exceeds 30.²⁷

The advantages of combustion and explosion technologies are well known. They include considerable saving of electric energy, simplicity, high productivity, structural and functional diversity of final products, possibility of attaining high quality and optimum parameters, *etc.* Their main disadvantage (especially with regard to material-synthesising processes) is non-versatility. Combustion and explosion can be implemented exclusively in high-energy self-transforming systems. To other drawbacks of these technologies one can add high inflammability and explosibility of high-energy systems used therein. However, in spite of these 'drawbacks' these processes have occupied a prominent place in up-to-date technology.

By virtue of their specific features, combustion and detonation processes are related to the category of alternative (as opposed to conventional) techniques for synthesising inorganic materials. Combustion and explosion can be used in virtually all currently known technological processes. Some examples of conventional technologies and alternative combustion and explosion processes used for synthesising inorganic materials are given in the table below.

Conventional technologies	Combustion and detonation analogues of conventional processes
Furnace and plasma-chemical synthesis of powders	SHS
Synthesis of superhard materials under static conditions	shock wave and detonation synthesis
Sintering, hot-pressing	SHS sintering, STIM technology (STIM stands for synthetic hard instrumental materials)
Plastic metal working	explosive compaction, STIM technology
Flame spraying	powder spraying
CVD processes, diffusional saturation	gas-transport SHS technology
Metallothermic melting of materials, alloys, compounds	SHS metallothermy
Electric arc welding	SHS welding
Electric welding	explosion-induced welding, SHS welding

In choosing a particular technological process, special attention should be given to its efficiency and expected characteristics of final materials. Unfortunately, it does not always work.

There is a large body of evidence on practical applications of materials prepared or processed with the use of combustion and

explosion technologies. Without going into details, we shall confine ourselves to providing a cumulative list of materials (which is far from being complete) and branches of industry where they are employed.

Branch of industry	Materials
Mechanical engineering	abrasives, hard alloys and articles thereof, welded parts including bimetallic rolled stock, superhard materials (diamonds, wurtzite-like BN)
Metallurgy	cast iron; ferro- and foundry alloys including nitrogenated alloys; refractory materials including oxygen-free (nitride) materials; particulate materials for powder metallurgy; moulded high-melting articles including pipes with internal wear-resistant coatings; heat-resistant alloys
Chemical industry	technical-grade carbon; boron and its compounds; pigments; luminophores; fumigants; catalysts; filters for gases and liquids
Electrical and electronic engineering	ceramic (including ferrite) powders; thermal insulators; microcircuit boards; high-temperature heaters; solid conductive lubricants; green mixtures for growing oxide single crystals; powders of high-temperature superconductors
Medicine	storage media and implants

Combustion and explosion products are used successfully in building materials, aircraft industry, *etc.*

Of special importance are industrial applications of combustion and explosion technologies. This includes large-scale production of cast iron and ferroalloys, which have long been known to metallurgy and chemical industry, and some novel SHS technologies carried out in proving grounds and blasting chambers.

Numerous works aimed at assimilation of SHS technologies and organisation of production lines at pilot plants and experimental-industrial enterprises have been carried out at ISMAN together with the Interbranch Research-and-Production Complex (IRPC) 'Termosintez'. Other developments included large-scale production of technical-grade boron (Dal'negorsk), MoSi₂ (Kirovakan), TiC, BN and AlN (Baku), β -Si₃N₄ (Makeevka), ferrites (Razdan), LiNbO₃ (Dzerzhinsk), refractory materials ('Furnone') (Alma-Ata), cutting blades (Nizhny Novgorod), high-temperature ceramic insulators (Samara), nitrogenated ferroalloys (Chusovaya, Izhevsk), titanium alloys (TiC, TiC-Cr₃C₂, TiH₂) (Transcarpathia) and other SHS products (Chernogolovka). Altogether, over 2000 tons of miscellaneous products were manufactured in the last year of existence of the USSR (and, actually, of the IRPC 'Termosintez'). The most recent SHS developments were realised at the fully automated plant 'SHS Ceramicas' (Spain) utilising the ISMAN technology. The production of pipes with internal antiwear coating for transportation of abrasive media (*e.g.*, cement, carbon, minerals, *etc.*) has been set up in China. This production successfully combines the fundamental concepts of the effect of an artificial gravity field on combustion developed by researchers at ISMAN¹¹² with the rich experience of Japanese specialists in the production of large-diameter pipes.^{113, 114} This technology has been introduced at ten Chinese plants with the annual output of 10 000 tons.

Pioneering works aimed at industrial implementation of explosion technologies were undertaken by researchers at the Lavrentyev Institute of Hydrodynamics. Their longstanding efforts have culminated in the establishment of an Engineering-and-Design Institute for Hydraulic Pulse Technology. Its main products include bimetallic (steel-copper, steel-titanium, steel-AO20) preforms. Production of diamond nanopowders in a blasting chamber has been started at the Federal Research-and-

Production Centre 'Altai'. This blasting chamber allows explosion of charges weighing up to 6 kg with frequency of 30 blasts per hour; its productivity is 2.5 tons of refined diamonds per year, which is more than satisfactory for detonation synthesis.

The detonation line installed at the Penza State University and designed for batch production of segnetoelectric materials and articles by explosion-induced compaction of metal powders followed by sintering is also operating with high efficiency. The operational characteristics of these materials have been improved through the formation of fine-grain high-strength structures with well-developed contact surfaces.

The construction of stable explosion chambers has made it possible to enlarge industrial implementation of explosion technologies.

Despite the 'uncommonness' of combustion and explosion technologies, they hold great promise.

VIII. Conclusion

Studies of material-synthesising and material-affecting combustion and explosion are under way. Theorists are working out structural and macrokinetic combustion models which would provide a description not only of characteristics of the combustion wave but also of the structures of final products. Similar problems are being explored in explosion studies aimed at the construction of structural and gas-dynamic detonation models. The first theoretical works in this area were devoted to the solution of three-dimensional combustion problems. Three-dimensional simulation presents interest in principle, since it permits one to follow transformations of substances in the bulk of a burning or detonating body, which cannot be attained by conventional methods.

Many important problems remain to be solved by methodologists. These include studies of structural dynamics of combustion and explosion processes by methods similar to dynamic X-ray diffractometry. Another important task is adequate monitoring of changes in porous structures and microstructures (*e.g.*, grain size) of substances in combustion and detonation waves.

Experimentalists are actively engaged in the study of processes occurring in chemically and physicochemically complex systems. The problem of separation of the primary from the secondary in the totality of processes has been a challenge to investigators at all times.

Some new trends, *viz.*, gas-phase and gas-disperse SHS,^{115, 116} mechanochemical SHS,^{117–121} thermal explosion SHS and high-field-assisted SHS, have emerged relatively recently.^{122–124} Practical implementation of gasless detonation processes is an important task.¹²⁵

Production engineers are concerned with the development of continuous combustion and explosion processes. Some progress has been made in the field of high-energy technologies. However, continuous material-synthesising processes based on combustion and explosion, *e.g.*, production of powders, melts, compacted long-sized items, *etc.*, are still very rare.

This problem is closely connected with utilisation of combustion energy and its transformation into electric energy by conventional methods. Thus, development of energotechnological processes is of interest.¹²⁶ This is topical for continuous processes. Implementation of thermoconjugated modes where one (strongly exothermic) reaction initiates another (weakly exothermic) reaction is especially important for periodic processes.

The use of 'chemical furnaces' is becoming a popular trend in modern research practice.

The major challenge facing designers is in the construction of quasi-adiabatic SHS reactors with large cooling times (of the order of weeks) allowing the synthesis of SHS products in the form of small (of the order of millimetres) crystals. Works on the construction of an SHS attritor for mixing reactants, SHS conducting and grinding the product in one technological step are currently under way. Many practical tasks are related to the

design of special moulds for SHS compaction and tubes for loading and conservation of substances under shock waves, *etc.*

Yet another important trend is a search for novel applications of material-synthesising and material-affecting combustion and explosion technologies.

Recently, the Scientific Council for Combustion and Explosion at the Presidium of the Russian Academy of Sciences has worked out the concept on the development of combustion and explosion processes as a branch of scientific and technological progress. All those who are interested in this problem are referred to the recently published book¹²⁷ which contains sections devoted to materials and technology.

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^h — *Mendeleev Chem. J. (Engl. Transl.)*

ⁱ — *Crystallogr. Rep. (Engl. Transl.)*

Intercalation compounds based on vanadium(V) oxide xerogel

G S Zakharova, V L Volkov

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Abstract. Data published during the last 15 years on the intercalation of metal and *n*-alkylammonium ions, organic molecules and organometallic complexes in vanadium(V) oxide xerogel are generalised and described systematically. The possible mechanisms of intercalation processes are considered. The possibility of using hybrid materials in electrochemical and optical devices and as precursors for the preparation of anhydrous and nanotubular forms of oxide compounds is discussed. The bibliography includes 159 references.

I. Introduction

In intercalation compounds (insertion compounds), ions or guest molecules are located in the crystallographic vacant sites of such host substances as, for instance, simple or complex oxides, sulfides, *etc.* Basically, these are layered compounds with sandwich-like structure or one-dimensional channel-like substances (tubulenes). Layered compounds possess higher intercalation capacities as compared with tubulenes. Currently, researchers are paying special attention to the intercalation compounds based on vanadium(V) oxide xerogel,¹ which manifests properties of both the original vanadium–oxygen matrix and the intercalated substances. A characteristic feature of these compounds is a quasi-one-dimensional structure and a turbostratic disorder of their layers. Both cations and organic molecules can easily be intercalated into this structure.

This property distinguishes the xerogel under consideration from crystalline V_2O_5 , the three-dimensional lattice of which can be intercalated only by metal ions.² The high intercalation capacity of xerogel is explained by its nature (this is polyvanadium acid, *viz.*, $H_2V_{12}O_{31} \cdot nH_2O$) and is ensured by the negative charge of the vanadium–oxygen layers, which is distributed along the V_2O_5 fibres.³ Intercalation may occur owing to dipole absorption, ion-exchange or redox processes. In all cases, this results in a change in the interlayer distance, which corresponds to the

insertion of one or several layers of an intercalant and does not change the structure of the xerogel itself. Solid solutions in which vanadium is replaced by hexa-, penta- or tetravalent ions can be obtained based on vanadium(V) oxide xerogel. These solid solutions have larger homogeneity regions than anhydrous complex oxides. Such solid solutions can easily be obtained in the form of films, superfine powders and nanocomposites using energy-saving environmentally friendly technologies. That is why they are promising for designing materials for various electrochemical and optical devices,⁴ they can be used in the synthesis of catalysts and as precursors for anhydrous and nanotubular forms of oxide compounds.

Intercalation compounds are usually obtained by a sol–gel method in aqueous, organic or aqueous–organic media. For the large-scale synthesis of $V_2O_5 \cdot nH_2O$ xerogel, a vanadium(V) oxide melt is poured into water, the sol $V_2O_5 \cdot \delta \cdot nH_2O$ obtained is transformed with time into the gel which is dehydrated. By choosing the conditions for dehydration, it is possible to obtain xerogels with different specific surface areas.⁵ An efficient method for the synthesis of intercalation compounds with the general composition $M_xV_{2-y}T_yO_{5+\delta} \cdot H_2O$ (*M* is a mono-, di- or trivalent cation, *T* = Mo, W, Cr, Ti) consists of dissolution of the corresponding oxides, hydrides or metals in hydrogen peroxide followed by decomposition of the peroxide compounds.¹

By passing solutions of alkali metal metavanadates through a cation-exchange resin, a yellow solution of decavanadium acid $H_6V_{10}O_{28}$ is obtained, which becomes dark-red with time and transforms into the stable V_2O_5 gel.⁵ Polymerisation is accompanied by partial ($\sim 1\%$) reduction of V^{5+} to V^{4+} . Intercalation compounds containing cations M^{z+} and different amounts of tetravalent vanadium in particular, can be obtained by hydrolysis of organovanadium compounds⁶ and alkali-metal vanadates.⁷ Intercalation compounds based on vanadium(V) oxide xerogel can possess both mainly ionic or electronic and mixed conductivity.⁵ The ionic component is determined by the mobility of cations M^{z+} and depends on the relative humidity of air, while the electronic component depends on the content of tetravalent vanadium.

In the present review, special attention is given to the studies of the synthesis, structure and physicochemical properties of the intercalation compounds based on vanadium(V) oxide xerogel that have been carried out in recent years. In addition, a new class of these compounds, *viz.*, VO_x -nanotubulenes with intercalated organic substances, is considered.

G S Zakharova, V L Volkov Institute of Solid State Chemistry, Urals Branch of the Russian Academy of Sciences, ul. Pervomayskaya 91, 620219 Ekaterinburg, Russian Federation. Fax (7-343) 274 44 95. Tel. (7-343) 249 30 09. E-mail: volkov@ihim.uran.ru (V L Volkov)

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II. Structure of intercalation compounds

Studies of the structure of intercalation compounds have been carried out on film samples of $V_2O_5 \cdot nH_2O$ xerogel, which is considered to be an insertion product of water molecules in vanadium(V) oxide.⁸ The xerogel has a layered structure, which is deduced from the diffractograms of the $V_2O_5 \cdot nH_2O$ film (Fig. 1). The vanadium–oxygen layers are formed by tangled fibres and connected by water molecules. The interlayer distance (d) depends on the water content and equals 11.57 Å for the composition $V_2O_5 \cdot 1.6H_2O$ (phase I). On heating to 50 °C, this parameter changes only slightly ($d = 11.30 \pm 0.05$ Å). At ~ 100 °C, phase I gradually disappears and phase II ($V_2O_5 \cdot 0.5H_2O$) is formed. The formation of the latter is completed at 250 °C. The diffractograms of phase II also suggest a layered structure, but the interlayer distance equals 8.75 Å in this case. At temperatures above 350 °C, chemically bound water is removed and crystallisation of vanadium(V) oxide occurs. It was found by electronography that the fibres are flat ribbons 1000 Å in length and 100 Å in width (Fig. 2). In the plane of the ribbon, their structure is analogous to that of orthorhombic V_2O_5 and is characterised by the following parameters: $a = 27.0$ and $b = 3.6$ Å. According to the IR spectroscopic analysis, the short-range ordering in $V_2O_5 \cdot nH_2O$ xerogel is similar to that in crystalline oxide. The main absorption bands of IR irradiation for the vanadium(V) oxide xerogel, viz., 1605, 1015, 910, 760 and 530 cm^{-1} , correspond to the following vibrations: $\delta(H-O-H)$, $\nu(V=O)$, $\delta(V-O \cdots H)$, $\delta(V-O-V)$ and $\delta(V-O)$.² Orthorhombic units constituting the ribbons do not lie in the common plane, but rather form a relief structure with an ‘amplitude’ of 2.8 Å. It

was established by neutron and X-ray diffraction that the distance between the basal planes in $V_2O_5 \cdot nH_2O$ changes from 8.8 Å ($n = 0.1-0.5$) to 40 Å ($n = 18.5$ or higher) as the water content (n) increases. For $n \geq 5-6$, the parameter d_{001} increases in a stepwise manner by 3 Å, which corresponds approximately to the thickness of the interstitial water layer. Usual water freezes at the temperatures below 273 K by several degrees to form hexagonal ice crystals. In the xerogel, an interlayer distance of ~ 15 Å, caused by the presence of ordered bilayers of non-freezing water in the range $110 < T < 230$ K, was found by neutron diffraction technique. As the temperature increases to 270 K, the d_{001} value increases to 19 Å and the ordered state of the water layers is violated. The ordering of water in the hydrated layered systems is characteristic of not only $V_2O_5 \cdot nH_2O$ gel but also, for instance, clays.

The structure of the double vanadium–oxygen layer up to now has been controversial. According to one opinion (see, e.g., Ref. 9), it consists of two $VO_{1.5}$ planes, with a distance of 2.8 Å between the planes (Fig. 3). Such a structure is similar to that of the δ -phase of oxide vanadium bronzes of the $M_xV_2O_5$ type ($M = K, NH_4$).² According to another opinion,¹⁰ the V_2O_5 layers are 4.368 Å apart from one another and consist of one $VO_{1.5}$ plane. The axial-distorted tetragonal V_2O_5 pyramid in the $V_2O_5 \cdot nH_2O$ xerogel includes one short vanadyl bond with a length of 1.55–1.58 Å and a nearly planar system formed by four $V-O$ bonds with a length of ~ 1.90 Å.¹¹

Elucidation of the structure of the $V_2O_5 \cdot nH_2O$ xerogel requires the study of the state of its hydrogen–oxygen groups.¹² Two H_3O^+ groups per 6 $V_2O_5 \cdot 1.6H_2O$ molecules have been found. This correlates well with the data on ion exchange, which suggest that polyvanadates of the type $M_2V_{12}O_{31} \cdot nH_2O$ are formed under equilibrium conditions. The number of three-spin systems decreases linearly as the amount of M^+ ions in $V_2O_5 \cdot nH_2O$ increases, thus indicating the exchange of cations of the corresponding metals for these systems. The specimens contain relatively isolated protons as OH groups. Their content in $V_2O_5 \cdot 1.6H_2O$ correlates with the content of tetravalent vana-

The number of pulses

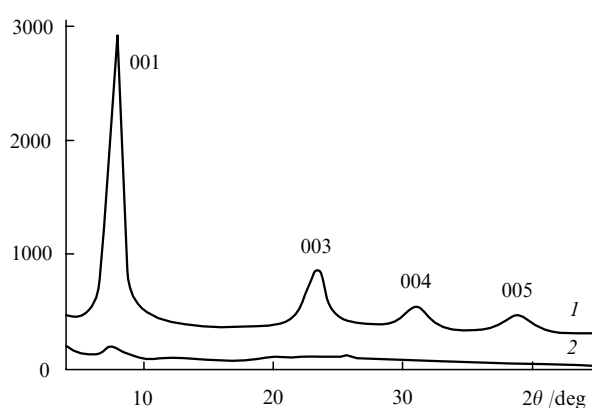


Figure 1. Diffractograms of the $V_2O_5 \cdot nH_2O$ xerogel film (1) and powder (2).

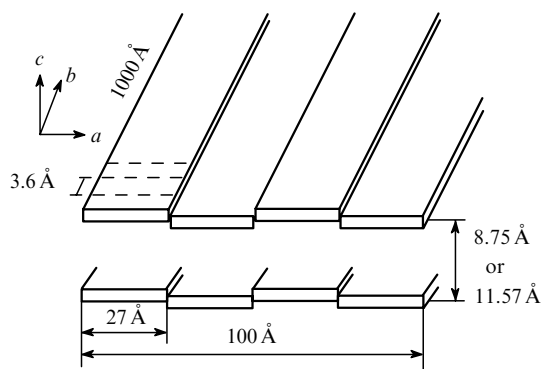


Figure 2. Schematic representation of the layered structure of the $V_2O_5 \cdot nH_2O$ xerogel.⁵

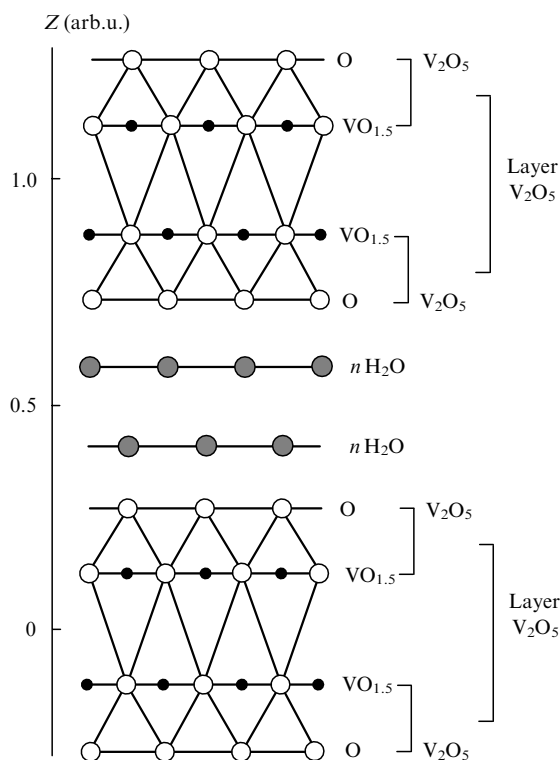


Figure 3. Structural model of the $V_2O_5 \cdot 1.7H_2O$ xerogel.⁹

dium. Comparison of the results obtained in ^1H NMR studies of polyvanadium acids with different compositions allows one to conclude that isolated protons are present in two non-equivalent states and that most of the protons are bound to tetravalent vanadium. Approximately one-half of the OH groups, appeared upon partial dehydration of three-spin systems with reduction of the water content in the xerogel from 1.6 to 1.4 moles, belongs to bridging groups $\text{V}^{5+}-\text{OH}$, which are exchange-active in contrast to the $\text{V}^{4+}-\text{OH}$ groups.

Based on the ^1H NMR data, the structure of the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel can be represented as a result of the interaction of water molecules with coordinatively unsaturated vanadium atoms of the orthorhombic oxide. This process is accompanied by cleavage of $\text{V}-\text{O}-\text{V}$ bonds followed by formation of two bridging OH groups. These bind water molecules to give highly mobile three-spin systems. According to the suggested model (Fig. 4), three types of protons can be distinguished in polyvanadium acid $\text{H}_2\text{V}_{12}\text{O}_{31} \cdot n\text{H}_2\text{O}$ ($\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$): the protons of water molecules coordinated with $\text{V}=\text{O}$ groups belong to the first type (this is a zeolite-type water, which is absorbed reversibly and forms a network of hydrogen bonds); the protons involved in the three-spin systems (H_3O^+) belong to the second type; the protons of bridging hydroxo-groups (OH^-) chemically bound to vanadium atoms, which can be removed as the xerogel structure is destroyed, belong to the third type.

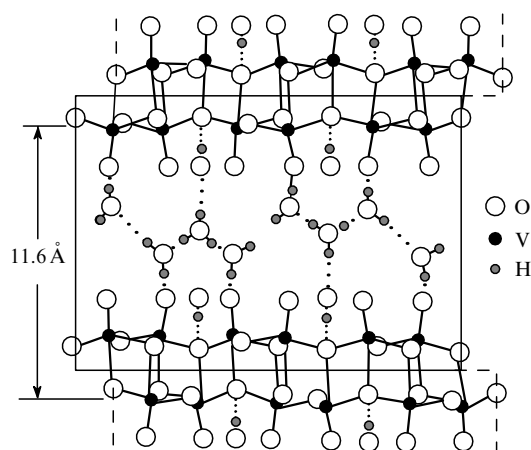


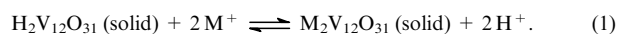
Figure 4. Structural model of the $\text{H}_2\text{V}_{12}\text{O}_{31} \cdot n\text{H}_2\text{O}$ xerogel.

Usually, $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel contains tetravalent vanadium ions which may be present in the vanadium–oxygen layers or in the hydrated $\text{VO}(\text{H}_2\text{O})^{2+}$ ions between the layers.¹³ The presence of V^{4+} ions can easily be detected by ESR¹⁴ and chemical analysis. Their content in the samples depends on the nature of the reducing agent used in the synthesis of the gel and can reach 20 mass %.^{5,15} The study of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ by X-ray photoelectron spectroscopy has revealed¹⁶ that the positions of the V2p-band correspond to binding energies of 517.5 and 516.5 eV for penta- and tetravalent vanadium, respectively. The O1s binding energies are equal to 530.1 for $\text{O}-\text{V}$, 531.6 for the OH groups and ~ 533.2 eV for water molecules.

It should be mentioned that the structural characteristics of vanadium(V) oxide xerogel are similar to those of anhydrous intercalated phases of the $\text{H}_x\text{V}_2\text{O}_5$ and $\text{M}_x\text{V}_2\text{O}_5$ types (see Ref. 2). For instance, $\text{H}_x\text{V}_2\text{O}_5$ ($x \leq 0.5$) has a structure of V_2O_5 with unit cell parameters $a = 11.51$, $b = 3.56$, $c = 4.37$ Å; the IR spectrum of the former compound is analogous to that of V_2O_5 with the exception of the band at 928 cm^{-1} , which is attributed to the OH bond. This band is also present in the spectrum of polyvanadium acid. The unit cell of the β -phase of $\text{M}_x\text{V}_2\text{O}_5$ (the composition of which corresponds to the formula $\text{M}_x\text{V}_{12}\text{O}_{30}$) can adopt four intercalated monovalent ions.

III. Intercalation of cations

Vanadium(V) oxide xerogel exhibits ion-exchange properties.^{12,17} The presence of exchangeable protons in the xerogel can be detected by adding an excess of any alkali metal salt to an aqueous suspension of $\text{H}_2\text{V}_{12}\text{O}_{31} \cdot n\text{H}_2\text{O}$. The following reaction occurs:



The liberating protons are titrated with alkali and the ratio $\text{M}:\text{V}$ is calculated taking into account the amount of the original xerogel. For the monovalent cations, the mean value of this ratio equals 0.17 ± 0.01 , which is in good agreement with the formula of polyvanadium acid. Hydrated polyvanadates with different degrees of replacement of the protons by alkali or alkaline-earth metal ions can be obtained by the ion-exchange method. IR and ^{51}V NMR spectra of such samples are similar to the corresponding spectra of the original polyvanadium acid, thus indicating the unique chemical nature of these compounds. The mean $\log K_{\text{H,M}}$ values at 295 K ($K_{\text{H,M}}$ is the coefficient of the exchange of protons in polyvanadium acid by alkali metal cations or NH_4^+), which depend linearly on the radii of hydrated cations, are given in Table 1. Taking into consideration the ion-exchange coefficients, the cations can be arranged in the following series according to their ability to replace the protons: $\text{La}^{3+} > \text{K}^+ \gg \text{Ba}^{2+} > \text{NH}_4^+ > \text{Ca}^{2+} > \text{Na}^+ \gg \text{Al}^{3+} > \text{Sr}^{2+} > \text{Mg}^{2+} \gg \text{Ni}^{2+} \gg \text{Zn}^{2+} \gg \text{Mn}^{2+} > \text{Cd}^{2+} > \text{H}^+ > \text{Li}^+$ (see Ref. 18).

Table 1. Ion exchange coefficients of the protons of polyvanadium acid for metal cations or NH_4^+ ($T = 295\text{ K}$).¹⁸

Cation	$\log K_{\text{H,M}}$	Cation	$\log K_{\text{H,M}}$	Cation	$\log K_{\text{H,M}}$
Li^+	0.40 ± 0.05	Ca^{2+}	1.21 ± 0.03	Mn^{2+}	0.28 ± 0.02
Na^+	0.54 ± 0.04	Sr^{2+}	1.03 ± 0.04	Co^{2+}	0.48 ± 0.04
K^+	1.07 ± 0.03	Ba^{2+}	2.10 ± 0.12	Ni^{2+}	0.44 ± 0.02
NH_4^+	0.99 ± 0.06	Zn^{2+}	0.43 ± 0.03	Al^{3+}	1.60 ± 0.02
Mg^{2+}	0.45 ± 0.11	Cd^{2+}	0.27 ± 0.02	La^{3+}	3.50 ± 0.30

It was estimated by the potentiometric titration method,¹⁹ that the exchange capacity of the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ specimens with respect to the cations of monovalent metals ($\text{M}^+:\text{V}_2\text{O}_5$) is close to 0.3. The rate of exchange $\text{H}^+:\text{M}^+$ is mainly limited by the diffusion of cations at the xerogel–electrolyte solution interface. The values of the diffusion coefficient (D) determined for the alkali metal ions and protons agree well with the data on the selectivity of ion exchange for polyvanadium acid:

Ion	Na^+	K^+	Cs^+	H^+
$10^8 D\text{ cm}^2\text{ s}^{-1}$	5.0 ± 0.4	4.8 ± 0.4	2.1 ± 0.2	1.6 ± 0.2

Upon intercalation of sodium, potassium and cesium monovalent cations into the interlayer space of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel, the interlayer distances become equal to 10.9, 11.0 and 11.1 Å, respectively.

It was found²⁰ that the x value in the formula of xerogel $\text{M}_x^{z+}(\text{V}_2\text{O}_5)^{(0.3-0.4)-} \cdot n\text{H}_2\text{O}$ is mainly determined by the exchange capacity and equals 0.33–0.36, 0.16 and 0.11 for mono-, di- and trivalent cations, respectively. Two types of cations were distinguished: the first type of cations are solvated with one water layer ($d = 10.9\text{--}11.3$ Å), while solvation of the second type of cations takes two water layers ($d = 13.4\text{--}14.2$ Å). For the first type of cations, the charge-to-radius ratio is $z/r < 1.67\text{ e Å}^{-1}$, all of them, except Ba^{2+} , are monovalent ions. For the second type of cations (di- and trivalent ions), $z/r > 1.67\text{ e Å}^{-1}$. Analogous correlation is observed for the parameter characterising the change in the enthalpy upon hydration of the ions: intercalation of the cations is accompanied by the formation of a monolayered hydration shell if $\Delta H > -1465\text{ kJ mol}^{-1}$, while a double hydration layer is formed if $\Delta H < -1465\text{ kJ mol}^{-1}$. The interrelation-

ship between the ionic radii of the intercalated cations and the degree of their hydration has been established. This depends on the number of water molecules associated with the ions during their movement through the solution and equals the amount of water which is determined at temperature below 160 °C. The cations M^{z+} can be arranged in the following order with respect to the degree of hydration: $Li^+ > Na^+ > K^+ > Rb^+ > Cs^+$ and $Mg^{2+} > Ca^{2+} > Sr^{2+} > Ba^{2+}$.

Interesting results were obtained²¹ in the studies on the topochemistry and kinetics of the intercalation of polycation $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}$ (Al_{13}) into $V_2O_5 \cdot nH_2O$ xerogel powders and films. Insertion of this polycation is accompanied by a gradual change in the interlayer distance up to a constant value of 17.5 Å. Obviously, the rate of intercalation is mainly influenced by such geometrical factors as the specific surface area of the xerogel and the length of the possible path of migration of intercalated cations. With the Al_{13} polycation, stable xerogels, based on vanadium(V) oxide, can be obtained by double ion exchange.²¹ In the first stage of the ion-exchange process, $V_2O_5 \cdot nH_2O$ xerogel is involved in the exchange with any mono-, di- or trivalent cation including VO^{2+} . In the second stage, the replacement of M^{z+} in the compounds obtained $M_x^{z+}V_2O_5 \cdot nH_2O$ via $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}$ occurs. Finally, stable layered materials $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}-V_2O_5$ are formed. If the cations characterised by the ratio $z/r < 1.67 \text{ e Å}^{-1}$ are used in the first step, the xerogel $Al_{13}-V_2O_5$ with $d \approx 15 \text{ Å}$ and a specific surface area $s_0 = 10-30 \text{ m}^2 \text{ g}^{-1}$ is obtained. If VO^{2+} or the ions characterised by $z/r > 1.67 \text{ e Å}^{-1}$ are involved in the ion-exchange process, compounds with $d \approx 18 \text{ Å}$ and a specific surface area $> 80 \text{ m}^2 \text{ g}^{-1}$ are formed. The second type of compounds can be considered as xerogels $Al_{13}-V_2O_5$ with pillared structure, because the specific volume of their micropores amounts to $\sim 0.3 \text{ ml g}^{-1}$, while the distance between the vanadium-oxygen layers is close to 9.4 Å, which corresponds to the diameter of the Al_{13} cation.

Xerogels with a similar pillared structure are formed in the ion-exchange process of polyvanadium acid with clusters $M_6Cl_{18}(OH)_n(H_2O)_m^{(4-n)+}$ ($M = Mo, Nb$).²² For this purpose, an aqueous suspension of $V_2O_5 \cdot nH_2O$ xerogel is mixed with 1.6 M ethanolic solution containing the cluster ion. The compound obtained has an interlayer distance of $\sim 14.3 \text{ Å}$, its specific surface area is $15 \text{ m}^2 \text{ g}^{-1}$.

$V_2O_5 \cdot 1.9H_2O$ obtained by hydrothermal treatment of the xerogel exhibits a high ion-exchange capacity, which is comparable with that of zeolites, and significant selectivity with respect to Cs^+ ion.²³ In the presence of highly concentrated aqueous solutions of salts MCl_z , where $M = Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Ba^{2+}$ and Sr^{2+} ($M^{z+}:Cs^+ = 250$), the xerogel absorbs cesium ions selectively. The selectivity with respect to the cesium cation changes in the following sequence: $Li^+ > Mg^{2+} > K^+ > Na^+ > Ca^{2+} > Sr^{2+} > Ba^{2+}$. The cesium distribution coefficient changes in the same sequence from 226 for Ba to 981 for Li^+ . This selectivity of the xerogel allows one to use it for the extraction of Cs^+ from radioactive solutions.

The ion-exchange properties of xerogel $V_2O_{4.86} \cdot 2.2H_2O$ obtained under hydrothermal conditions have been studied in detail.²⁴ This compound is characterised by a high content of V^{4+} ; the interlayer distance is 14.2 Å. The main exchangeable groups in $V_2O_{4.86} \cdot 2.2H_2O$ are VO^{2+} ions, and the formula of this oxide can therefore be written as $(VO)_{0.10}V_2O_5 \cdot 2.3H_2O$. Compounds $Na_{0.37}V_2O_5 \cdot 1.1H_2O$, $K_{0.32}V_2O_5 \cdot 0.9H_2O$, $Rb_{0.31}V_2O_5 \cdot 0.8H_2O$ and $Cs_{0.28}V_2O_5 \cdot 0.8H_2O$ in which the interlayer distances are close to 11 Å were isolated upon treatment of the initial xerogel with 0.2 M solutions of M_2SO_4 ($M = Na, K, Rb, Cs$). In the case of the exchange reaction involving Li^+ cations, only 20% of the VO^{2+} ions are replaced and compound $Li_{0.12}(VO)_{0.08}V_2O_5 \cdot 2.4H_2O$ is formed. The order of selectivity $Li < Na < K < Rb < Cs$ reported coincides with that for the xerogel obtained under usual conditions.¹⁸ Commonly, the insertion of vanadyl ions between the layers of $V_2O_5 \cdot nH_2O$ xerogel leads to

three phases of compound with the general formula $(VO)_{0.10}V_2O_5 \cdot nH_2O$: phase I ($n = 2.30$, $d = 14.21 \text{ Å}$) is formed at room temperature, phase I- α ($n = 1.12$, $d = 11.64 \text{ Å}$) is formed at 70 °C and phase I- β ($n = 0.45$, $d = 12.21 \text{ Å}$) is formed at 122 °C.²⁵ In these compounds, two V_2O_5 planes and an interstitial plane of VO^{2+} and water molecules can be distinguished; the twin V_2O_5 planes in the layer are situated at a distance of 2.7 Å from each other. Phase transitions are accompanied by transformation of the four interlayer planes present in phase I into two planes in the formation of phase I- α and then into one plane in the formation of phase I- β .

An ion-exchange method was used for the synthesis of precursors of new structures resembling the structures of α -phases of oxide vanadium bronzes.²⁶ Intercalation compounds $Ba_{0.16}V_2O_5 \cdot 1.52H_2O$ ($d = 11.2 \text{ Å}$), $Ni_{0.16}V_2O_5 \cdot 2.47H_2O$ ($d = 13.4 \text{ Å}$), $Fe_{0.11}V_2O_5 \cdot 2.35H_2O$ ($d = 14.1 \text{ Å}$), $Al_{0.11}V_2O_5 \cdot 2.78H_2O$ ($d = 14.2 \text{ Å}$) were obtained by the interaction of $V_2O_5 \cdot nH_2O$ xerogel with aqueous solutions of the corresponding salts. Further thermal treatment at the temperature of crystallisation of the compounds, viz., at 520 (Ba and Ni), 535 (Fe) and 600 °C (Al) leads to the formation of α -phases of $M_xV_2O_5$. The parameters of the unit cells of these compounds do not depend on the nature of the metal M and are equal to $a = 11.43$, $b = 3.55$ and $c = 4.35 \text{ Å}$.

$Al_{0.11}V_2O_{5.15}$ was obtained by an analogous method with thermal treatment at 520 °C for 2 h (see Ref. 27). The specimen contained 1%–2% V^{4+} and had the following unit cell parameters: $a = 11.51$, $b = 3.56$ and $c = 4.38 \text{ Å}$. Upon the interaction of $V_2O_5 \cdot nH_2O$ xerogel with aqueous Ag^+ solutions, β - $Ag_{0.35}V_2O_5$, α - $AgVO_3$ and a new compound, viz., δ - $AgVO_3$, which crystallises in the monoclinic syngony with the unit cell parameters $a = 32.96$, $b = 2.60$, $c = 3.62 \text{ Å}$ and $\beta = 91.88^\circ$, were obtained at different relative silver and vanadium concentrations in the reaction media (see Ref. 28).

Interactions of lanthanide trichlorides with polyvanadium acid in water result in the formation of xerogels of lanthanide polyvanadates.²⁹ After keeping the reaction mixtures for 24 h, the solid phase was filtered out, washed with water and acetone and dried in a vacuum. According to the results of elemental analysis, the following compounds were obtained: $Pr_{0.15}V_2O_5 \cdot 3.7H_2O$, $Nd_{0.11}V_2O_5 \cdot 3.5H_2O$, $Sm_{0.12}V_2O_5 \cdot 2.7H_2O$, $Eu_{0.12}V_2O_5 \cdot 2.1H_2O$, $Ho_{0.13}V_2O_5 \cdot 3.2H_2O$, $Er_{0.13}V_2O_5 \cdot 3.2H_2O$, which may be represented more correctly as the corresponding salts of polyvanadium acid $H_2V_{12}O_{31} \cdot nH_2O$ with incomplete substitution of the lanthanide cations for the protons. The X-ray diffraction studies on these compounds have shown that their structures are less ordered than the structure of $H_2V_{12}O_{31} \cdot nH_2O$. The 001 reflections appear as most intense ones for $Nd_{0.007}V_2O_5 \cdot 1.4H_2O$ ($d = 13.6 \text{ Å}$), $Nd_{0.11}V_2O_5 \cdot 1.7H_2O$ ($d = 14.5 \text{ Å}$) and for $Nd_{0.20}V_2O_5 \cdot 2.0H_2O$ ($d = 14.9 \text{ Å}$), the average size of the xerogel particles is 242 Å. The IR spectra of these substances are similar to each other, but the band at 1010 cm^{-1} corresponding to the vibration of the $V=O$ bond in the initial acid, is displaced to 1032 cm^{-1} for $Nd_{0.20}V_2O_5 \cdot 2.0H_2O$.

Compounds $M_{0.11}V_2O_5 \cdot nH_2O$ ($M = Cr^{3+}, Fe^{3+}$) were obtained by ion exchange for 20 min at room temperature.³⁰ $V_2O_5 \cdot 1.6H_2O$ ($d = 11.60 \text{ Å}$) and a 0.1 M solution of $M(NO_3)_3$ were used as the starting compounds. The interlayer space of the resulting compounds ($d = 14.10$ for $M = Fe^{3+}$, 14.40 Å for $M = Cr^{3+}$) contains two layers of water molecules. It appears to be more correct to call these compounds polyvanadates $M_xV_{12}O_{31} \cdot nH_2O$ as in the case of the intercalation of lanthanides.²⁹ Dehydration of $Cr_{0.11}V_2O_5 \cdot 2.34H_2O$ proceeds in a step-wise manner in the intervals 20–200 °C and 200–350 °C and is finished by the crystallisation of amorphous products of thermolysis at 410 °C accompanied by an exothermic effect. At 520 °C, mixed oxides $M_{0.11}V_2O_{5.16}$ are formed, which give only 001 peaks in the diffractograms of their film samples. Ion exchange is employed for the preparation of xerogels of the polyvanadates $M_2(V_{12}O_{31})_3 \cdot nH_2O$ ($M = Ln, Al, Ga, In$, n changes in the range

$27 \leq n \leq 40$ depending on the air humidity)¹¹ and xerogels of cerium(III) and cerium(IV) polyvanadates with the compositions $\text{Ce}_2(\text{V}_{12}\text{O}_{31})_3 \cdot n\text{H}_2\text{O}$ ($11.0 \leq n \leq 15.0$) and $[\text{Ce}(\text{OH})_2]_x\text{H}_{2-2x} \cdot \text{V}_{12}\text{O}_{31} \cdot n\text{H}_2\text{O}$ ($0.07 \leq x \leq 0.50$ and $11.0 \leq n \leq 27.0$).³¹

Metal ions present in the dispersion medium affect the properties of vanadium(V) oxide gel.³² In the presence of Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ , Mg^{2+} , Ca^{2+} , Ba^{2+} , Al^{3+} , Cr^{3+} and La^{3+} cations, the aggregative stabilities of the hydrosols depend on the amount of metal ions included in the layered structure. The influence of intercalated cations on the absorption of water by $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ has been studied.³³ Lithium cations affect weakly the water absorption. This is explained by their small charge and their ability to form highly hydrated compounds. Intercalated Na^+ , K^+ , Rb^+ , Cs^+ , Mg^{2+} , Ca^{2+} , Sr^{2+} , Ba^{2+} , Al^{3+} , Cr^{3+} and La^{3+} cations exert a dual effect on the water absorption. The hydrophilicities of the cations favour higher absorption of water vapour from air at low relative humidity. At the same time, the energy of the system increases upon intercalation of such cations due to the increase in the interlayer electrostatic charge, which lowers the ability of the layers to move apart.

Intercalation of the NH_3 molecules into $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel has been studied.³⁴ It was found that the first absorbed NH_3 molecules interact with water of the hydrate to form the NH_4^+ ions [according to our data, with the formation of the compound $(\text{NH}_4)_2\text{V}_{12}\text{O}_{31} \cdot n\text{H}_2\text{O}$]. Later on, NH_3 molecules or the NH_4^+ ions, which cannot be detected by IR spectroscopy, were identified on the surface of the xerogel. After the introduction of water vapour in the gas phase containing NH_3 , the topotactic formation of ammonium metavanadate takes place in the 001 plane of the xerogel. In this process, the NH_3 and H_2O molecules occupy the positions between the vanadium–oxygen layers, then dissolution of the hydrate structure occurs followed by crystallisation of NH_4VO_3 .

Intercalation of cations into vanadium oxide xerogel can be carried out with the use of the corresponding organometallic compounds.³⁵ The reaction of $\text{V}_2\text{O}_5 \cdot 0.4\text{H}_2\text{O}$ aerogel with dibutylmagnesium, trimethylaluminium and dimethylzinc in heptane at room temperature gave the corresponding composites, which contained 4 moles of Mg^{2+} , 3.33 moles of Al^{3+} and 2.5 moles of Zn^{2+} per mole of V_2O_5 .

A new type of mixed composites was synthesised based on vanadium(V) oxide xerogel and montmorillonite clay, namely, bentonite. The green-coloured product has the composition $\text{Al}_2\text{O}_3 \cdot 4(\text{SiO}_2)_2 \cdot x(\text{V}_2\text{O}_5) \cdot y\text{H}_2\text{O}$ ($x = 2.7\text{--}3.5$ and $y = 2.6\text{--}3.5$)³⁶ or bentonite $\cdot y\text{V}_2\text{O}_5 \cdot z\text{H}_2\text{O}$ ($y = 1.5\text{--}4.0$ and $z = 5\text{--}12$).³⁷ The composite is promising as a cathode material for chemical current sources: it possesses high conductivity inherent in the vanadium–oxygen xerogel layers and ion-exchange properties characteristic of the laminar clays. The compound has a layered type structure with $d = 12.8$ Å. This value is intermediate between the d values of 10.8 and 15.2 Å, which correspond to the initial substances, viz., $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel and bentonite. According to thermogravimetric analysis,³⁶ dehydration of the composite occurs in discrete steps. In the first step, 2.5 moles of weakly bound water are removed at a temperature below 120 °C. The second step, close to 180 °C, corresponds to the removal of 0.6 moles of stronger bound water. Full dehydration with removal of the remaining 0.4 moles of H_2O occurs at 400 °C. The formation of V–O–Si bonds in the mixed composite was confirmed by a comparative analysis of the IR spectra of the compounds. A new intense absorption band at 835 cm^{-1} appears and vibrations of the V=O and Si–O bonds in the region 1010–1045 cm^{-1} become weaker. Intercalation of the redox-active hexaammineruthenium complex in the interlayer space of the composite bentonite– $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel leads to an increase in its electrochemical response by at least 4 orders of magnitude. It thus follows that the films of the intercalated composite can be used as a material for the preparation of modified electrodes. Moreover, this composite is stable in aqueous solutions, and therefore no special polymeric coatings are needed.

A layered structure of vanadium(V) oxide xerogel is retained upon replacement of vanadium by tetra- and hexavalent ions. The chemistry, thermodynamics and properties of the intercalation compounds $\text{M}_x\text{V}_{2-y}\text{T}_y\text{O}_{5\pm\delta} \cdot n\text{H}_2\text{O}$ (M is proton, an alkali or alkaline-earth metal ion; T = Ti, Mo, W, Cr) have been documented.^{38–48} It was found that even small additives of the element T favour polymerisation of the sol to give stable gels. High intercalation capacity with respect to M^{z+} and thermal stability are characteristic of the intercalation compounds based on such complex vanadium oxides. Depending on the proportion of V to T, the compounds exhibit predominantly the properties of electronic or ionic conductors.

Vanadium-containing intercalation compounds include layered substances of the general formula $\text{VTO}_5 \cdot n\text{H}_2\text{O}$ ($\text{VTO}_4 \cdot n\text{H}_2\text{O}$) and intercalation compounds based on them, $\text{M}_x\text{VTO}_5 \cdot n\text{H}_2\text{O}$ (T = P, As, Nb, S, Mo).⁴⁹ The latter compounds are obtained by redox intercalation of the cations $\text{M} = \text{Li}^+$, Na^+ , K^+ , Rb^+ , Cs^+ , NH_4^+ , Mg^{2+} , Ba^{2+} , Mn^{2+} , Co^{2+} , Ni^{2+} , Fe^{3+} and Zn^{2+} in aqueous and non-aqueous media in the presence of a reducing agent.^{50–53} The reduction of vanadium is mediated by intercalation of a reducing agent followed by reduction of the isolated V^{5+} centres rather than by electron transport through a lattice of $\text{VTO}_5 \cdot 2\text{H}_2\text{O}$. Intercalation of inorganic cations into $\text{VPO}_5 \cdot 2\text{H}_2\text{O}$ disturbs the short-range order, as follows from both the broadening and the decrease in intensity of the diffraction maxima, and lowers the crystallinity of the initial vanadium(V) phosphate. $\text{VO}(\text{HPO}_4) \cdot 0.5\text{H}_2\text{O}$ also has a layered structure. Studies on the intercalation of Zn^{2+} , Ni^{2+} and Pd^{2+} into this compound have shown that the activities of intercalation compounds as catalysts of hydrogenation depend on the method of intercalation.^{54,55}

IV. Intercalation of organic compounds and complex ions

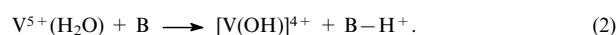
The study of the intercalation of a homologous series of compounds $\text{C}_n\text{H}_{2n+1}\text{N}(\text{CH}_3)_3\text{Br}$ ($n = 1\text{--}18$) and $\text{C}_n\text{H}_{2n+1}\text{NH}_2$ into $\text{V}_2\text{O}_5 \cdot 1.6\text{H}_2\text{O}$ xerogel has revealed⁵ the influence of steric factors on the structure of the complex formed. Depending on the length of the hydrocarbon chain, its orientation with respect to the vanadium–oxygen planes changes: the chain can be parallel ($n < 7$), inclined ($7 \leq n \leq 11$) or perpendicular ($n > 11$) to these planes. The interlayer distance changes correspondingly (Table 2). With the parallel arrangement of alkylammonium ions or alkylamines, the distance between vanadium–oxygen layers does not depend on the length of the alkyl chain and is equal to 12.9 and 12 Å for the compounds of the $\text{RN}(\text{CH}_3)_3\text{Br}$ and RNH_2 types, respectively. On average, the complex compound contains 0.3–0.4 moles of the intercalant per mole of V_2O_5 . These complexes are stable up to 160 °C, at higher temperatures amorphous vanadium(V) oxide is formed, which transforms into orthorhombic V_2O_5 at 400–450 °C. Intercalation of trimethylammonium ions occurs by a cation-exchange mechanism, while in the case of amines, the mechanism is more complex and includes transfer of the electrons between the matrix and the compounds being intercalated.

Table 2. Interlayer distances (Å) for complexes $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O} - \text{C}_n\text{H}_{2n+1}\text{N}(\text{CH}_3)_3\text{Br}$ (I) and $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O} - \text{C}_n\text{H}_{2n+1}\text{NH}_2$ (II).⁵

<i>n</i>	I	II
12	31.1	27.9
13	—	29.4
14	33.5	30.6
15	—	32.1
16	36.5	33.7
18	38.0	36.3

Amine-intercalated layered vanadium(V) oxides of the general formula $V_2O_5(H_2O)(C_nH_{2n+1}NH_2)_2$ ($n = 4, 6, 8$) have been synthesised.⁵⁶ The synthesis was carried out by vigorous stirring of a suspension of $V_2O_5 \cdot 0.6H_2O$ and an n -alkylamine (molar ratio 1:15) at room temperature for 48 h. The compositions of the compounds obtained may be expressed by the formulae $V_2O_5(H_2O)_{1.00}(C_4H_9NH_2)_{1.69}$, $V_2O_5(H_2O)_{1.09}(C_6H_{13}NH_2)_{1.82}$ and $V_2O_5(H_2O)_{1.26}(C_8H_{17}NH_2)_{1.80}$. The compounds possess laminar structures with interlayer distances of $d_{001} = 13.8, 16.4$ and 19.6 Å for butyl-, hexyl- and octylamine, respectively. The study of the ion-exchange properties of amine-intercalated compounds in aqueous 4 M solutions of CH_3COONa and CH_3COOK showed that alkylammonium ions form bilayers between the vanadium–oxygen layers. These ions are easily replaced by Na^+ or K^+ cations, which decreases the interlayer distance to 7.9 and 7.0 Å, respectively, independent of the length of a hydrocarbon substituent. A structural model for vanadium oxide intercalated with octylamine is shown in Fig. 5. On heating of this compound to 200 °C, its structure changes and d_{001} becomes equal to 22 Å. This d_{001} value as well as a layered structure are preserved up to 400 °C. Above 600 °C, a crystalline phase of V_2O_5 is formed.

IR, XPS and ESR studies of the interlayer absorption of ammonia, pyridine (py) and pyrazine into $V_2O_5 \cdot nH_2O$ xerogel have revealed the protonation of the nitrogen-containing bases (B) absorbed in the interlayer space.⁵⁷



Despite partial reduction of pentavalent vanadium upon absorption, the mechanism of intercalation consists mainly of protonation of the base by hydroxonium ions, which compensate the negative charge of the vanadium–oxygen layers (0.2 e per vanadium ion) and/or by water molecules with the formation of OH groups. Treatment of $V_2O_5 \cdot nH_2O$ xerogel with ammonia or pyridine resulted in the disappearance of the hyperfine structure from the ESR spectra. In the IR spectra of the compounds obtained, the absorption band at 975 cm^{-1} appears, which relates to $\nu(V^{4+}=O)$ vibrations. These vibrations contribute much less than the stretching vibrations $V^{5+}=O$ with the maximum absorption at 1020 cm^{-1} . Treatment of $V_2O_5 \cdot 1.5H_2O$ xerogel with ammonia and pyridine affords compounds with the compositions $V_2O_5(NH_4^+)(OH^-) \cdot 0.5H_2O$ and $V_2O_5[(pyH^+)(OH^-)]_{0.3} \cdot 0.6H_2O$ with interlayer distances 10.53 and 13.00 Å, respectively.

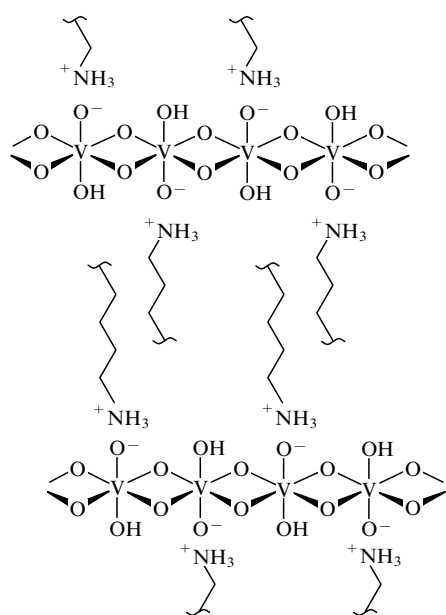


Figure 5. Structural model of the vanadium(V) oxide xerogel intercalated with octylamine.

The orientation of the pyH^+ ions is such that the C_2 axis of the heterocycle is perpendicular to the vanadium–oxygen layers.

Molecules of various solvents can easily replace water molecules in the $V_2O_5 \cdot 1.6H_2O$ xerogel;⁵ the interlayer distance changes in this case (Table 3). Mono- or divalent cations solvated by the molecules of organic solvents are also intercalated into the xerogel.⁵ The interlayer distance in the complexes obtained by intercalation of Li^+ , Na^+ , K^+ , Rb^+ , Cs^+ and Mn^{2+} into the xerogel is determined by the nature of the solvent and by the charge-to-effective radius ratio characterising the guest cation (Table 4).

Table 3. Maximum (d_1) and intermediate (d_2 – d_4) interlayer distances (Å) for composites $V_2O_5 \cdot nH_2O$ –organic solvent.⁵

Solvent	d_1	d_2	d_3	d_4
Sulfolane	22.7	17.6	—	13.9
Propylenecarbonate	22.2	21.6	17.5	13.0
Ethylenecarbonate	20.6	—	—	—
<i>N</i> -Methylacetamide	18.9	—	15.8	—
Dimethyl sulfoxide	17.6	—	16.5	—
Glycerol	16.6	—	—	—
Ethylene glycol	16.6	—	13.0	—
2-Aminoethanol	16.2	—	—	—
Formamide	14.4	—	—	—
Diethyl carbonate	14.2	—	—	—
<i>N</i> -Methylformamide	13.9	—	—	—
Tetrahydrofuran	13.8	—	—	—
Acetamide	12.7	—	—	—

Table 4. Interlayer distances ($d/\text{Å}$) for intercalation compounds $V_2O_5 \cdot nH_2O$ –organic solvent– M^{z+} (Ref. 5).

Solvent	d for intercalation compound with M^{z+}					
	Li^+	Na^+	K^+	Rb^+	Cs^+	Mn^{2+}
Dimethyl sulfoxide	18.4	18.7	14.1	11.0	11.0	18.3
<i>N,N</i> -Dimethylformamide	16.6	16.8	13.6	13.7	11.0	16.5
<i>N</i> -Methylacetamide	18.7	18.8	19.1	14.8	11.0	18.1
<i>N</i> -Methylformamide	16.1	16.6	16.4	14.6	11.0	16.2

Intercalation of molecules of n -alcohols into $V_2O_5 \cdot nH_2O$ has been considered⁵⁸ as the absorption of alkyl chains containing a different number of carbon atoms and having a polar OH group. It was found that methanol and ethanol molecules are oriented parallel to the vanadium–oxygen layers, while the molecules of alcohols with more than two carbon atoms have a perpendicular orientation. From the character of the alcohol absorption–desorption isotherms it was determined that ~ 0.5 moles of an alcohol are irreversibly intercalated into 1 mole of $V_2O_5 \cdot nH_2O$. These alcohols can be displaced by the action of water vapour followed by evacuation. The interlayer distances in the complexes do not depend on the vapour pressure of the alcohol in the case of alcohols with the number of carbon atoms $n = 2–4$, while in the case of $n > 4$, a noticeable increase in d is observed, which is not proportional to the size of the alcohol molecule. It is obvious that the mechanism of intercalation of n -alcohol molecules differs from that of alkylammonium cations and alkylamines.

The study of the thermal decomposition of complexes $V_2O_5 \cdot nH_2O$ – n -alcohol has revealed⁵⁹ that a layered structure of the matrix is retained up to 100 °C. Upon oxidation of the intercalated alcohol at $200–300$ °C, the vanadium–oxygen framework is destroyed. However, the decomposition products hamper crystallisation of vanadium oxide and the sample remains amorphous up to 550 °C according to X-ray diffraction analysis.

In the case of intercalation of such readily oxidisable organic molecules as aniline,^{60,61} pyrrole⁶² and thiophene,^{5,63} layered composite materials are obtained which contain a conducting polymerised layer in the interlayer space of the xerogel and combine a unique laminar microstructure of the matrix and the properties of a conducting polymer. The formation of these compounds is based on the redox reaction in which a monomer undergoes oxidation and polymerises, while vanadium(V) is partially reduced to a tetravalent state. The complex compound $(\text{C}_6\text{H}_4\text{NH})_{0.44} \cdot \text{V}_2\text{O}_5 \cdot 0.5 \text{H}_2\text{O}$ is a dark-blue colour and retains the layered structure of the xerogel with $d = 13.94 \text{ \AA}$. The conductivity of the compound obtained is higher than that of the original $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel by 4 orders of magnitude and amounts to $\sim 0.5 \Omega^{-1} \text{ cm}^{-1}$ at room temperature. Intercalation of 2,2'-bithiophene affords a black xerogel with the composition $(\text{C}_8\text{H}_4\text{S}_2)_{0.44} \cdot \text{V}_2\text{O}_5 \cdot 0.54 \text{H}_2\text{O}$ possessing metallic lustre, its conductivity amounts to $0.1 \Omega^{-1} \text{ cm}^{-1}$ at room temperature.

Layered intercalation compounds of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel with the cations $(\text{CH}_3)_4\text{N}^+$, $(\text{C}_2\text{H}_5)_4\text{N}^+$ and $\text{C}_6\text{H}_5\text{NH}_3^+$ are synthesised in aqueous solutions of tetramethylammonium, tetraethylammonium and anilinium salts, respectively.⁶⁴ The diffractograms of these compounds are characterised by the very narrow lines of the 00l reflections. The interlayer distances in the compounds synthesised are equal to 12.9, 13.1 and $13.9 \text{ \AA}$, respectively.

An aerogel composite vanadium(V) oxide–polypyrrole (PPyr) is obtained⁶⁵ as a co-polymerisation product of pyrrole and a vanadylalkoxide precursor. Hydrolysis of $\text{VO}(\text{OC}_3\text{H}_7)_3$ in a mixture pyrrole + water + acetone leads to the formation of a monolithic green–black gel, drying of which yields aerogel with a specific surface area of $150\text{--}257 \text{ m}^2 \text{ g}^{-1}$ and a density of $0.1\text{--}0.2 \text{ g cm}^{-3}$. Electroconductivity of this composite decreases with the increase in the content of pyrrole. When V_2O_5 and the colloidal polypyrrole are used as the starting compounds, the latter compound is intercalated into the ribbons of vanadium(V) oxide. This microcomposite gel (the specific surface area is $80\text{--}140 \text{ m}^2 \text{ g}^{-1}$) has an electroconductivity equivalent to that of V_2O_5 .

The microstructure and properties of the aerogel composite $\text{V}_2\text{O}_5\text{--PPyr}$ depend on the method of its synthesis.^{62,66} The composite prepared by dispersion of presynthesised polypyrrole particles into $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ (the matrix) has a nano-dimensional scaly nonhomogeneous structure. 'Post-gel' polymerisation, which includes sequential polymerisation of inorganic and organic phases, improves the microstructure of the hybrid material. The electroconductivity of the preformed specimens with the composition $(\text{PPyr})_{0.35}\text{V}_2\text{O}_5 \cdot 1.8 \text{H}_2\text{O}$ is equal to $(2\text{--}7) \times 10^{-3} \Omega^{-1} \text{ cm}^{-1}$. This value lies in the interval between the conductivities of aerogel $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ ($< 10^{-5} \Omega^{-1} \text{ cm}^{-1}$) and polypyrrole ($5.6 \times 10^{-2} \Omega^{-1} \text{ cm}^{-1}$). The results of a study of the hybrid material by cyclic voltammetry showed that its capacity with respect to reversibly intercalated lithium ion amounts to 1.4 moles of Li per mole of $(\text{PPyr})_{0.35}\text{V}_2\text{O}_5$. The specific discharge capacity of the cathode based on this material is twofold less than that of the cathode prepared from aerogel $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ and is equal to 95 mA h g^{-1} . 'Joint synthesis', consisting of simultaneous spontaneous polymerisation of the organic and inorganic precursors, leads to the formation of the hybrid composite $(\text{PPyr})_{0.8}\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ with nano-dimensional scaly homogeneous microstructure. The intercalation capacity of this material with respect to lithium equals 3.0 moles per mole. Redox intercalation of polypyrrole into the laminar hybrid material bentonite–vanadium(V) oxide xerogel affords a semiconducting ternary composite,⁶⁷ which combines the properties of layered V_2O_5 and the conducting polymer.

Redox-mediated intercalation of aniline and its salts into the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel can be accompanied by their polymerisation.^{61,68} At the molar ratio of anilinium iodide to $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ equal to 4, compound $(\text{C}_6\text{H}_5\text{NH}_3)_{0.4}\text{V}_2\text{O}_5 \cdot 0.4 \text{H}_2\text{O}$ was obtained, while in the case of oxidative polymerisation of aniline, the

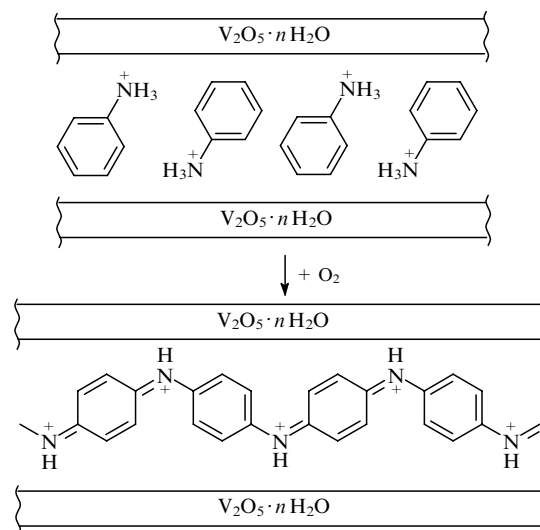


Figure 6. Schematic representation of the polymerisation of anilinium in the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel.⁶¹

complex $[(1/n)(\text{C}_6\text{H}_4\text{NH})_n]_{0.4} \cdot \text{V}_2\text{O}_5 \cdot 0.4 \text{H}_2\text{O}$ (Fig. 6) is formed.⁶¹ IR spectra of these substances differ noticeably in frequencies of the stretching vibrations of V–O bonds: the main bands appear at $1000, 750, 496 \text{ cm}^{-1}$ and at $990, 852, 530 \text{ cm}^{-1}$ for the former and the latter compound, respectively. Intercalative intralaminar growth of the polymer in the nanocomposites polyaniline (PAni)– $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ is promoted by molecular oxygen which is activated by vanadium ions. The process results easily in the formation of the monolayers of PAni with the interlayer distance of $5.6 \text{ \AA}$.⁶⁸ Both during and after polymerisation, oxygen plays the role of the electron acceptor.

The study of the hybrid system PAni– $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel with different molar ratios of the components has revealed the formation of two phases, viz., $(\text{C}_6\text{H}_4\text{N})_{0.6}\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ and $(\text{C}_6\text{H}_4\text{N})_{1.2}\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$.⁶⁹ The interlayer distance in the former phase is $14 \text{ \AA}$, which corresponds to the intercalation of one monolayer of PAni into the xerogel. In the latter phase, the interlayer distance is $\sim 20 \text{ \AA}$, which is consistent with intercalation of two monolayers of PAni. On ageing of the nanocomposites $(\text{PAni})_x\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ in air, partial reoxidation of reduced vanadium and further oxidative polymerisation of the oligomers of PAni inside the layers of the xerogel occurs, which leads to elongation of the polymeric chains. The latter conclusion is confirmed by the increase in molecular mass of PAni extracted from aged intercalation compounds as compared to freshly prepared ones. Thermal stability is higher for the aged samples of PAni than for the initial ones. All the samples of $(\text{PAni})_x \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ are paramagnetic. Magnetic susceptibility obeys the Curie–Weiss law; the van Fleck contribution does not depend on temperature. Electroconductivity of the freshly prepared hybrid material PAni– $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ depends on the degree of polymerisation of aniline inside the layers of xerogel and is always higher for the aged samples. At room temperature, the electroconductivity is equal to $10^{-6}\text{--}10^{-1} \Omega^{-1} \text{ cm}^{-1}$, while the thermoelectric power has a negative value which changes from -30 to $200 \mu\text{V deg}^{-1}$ depending on the degree of polymerisation.

An analogous composite compound was obtained upon interaction of the emeraldin base with the V_2O_5 sol.⁷⁰ The interlayer distance in the dark-violet composite $(\text{PAni})_{0.65} \cdot \text{V}_2\text{O}_5$ amounts to $13.8 \text{ \AA}$, its electroconductivity is $3 \times 10^{-5} \Omega^{-1} \text{ cm}^{-1}$; this compound is virtually insoluble in most organic solvents. ESR studies have revealed that the electron density is transferred from the lone electron pair on the nitrogen atom of the polymeric chain to V^{5+} .

Dark-green complexes with the compositions $(\text{PAni} \cdot \text{HClO}_4)_{0.52} \cdot \text{V}_2\text{O}_5$ and $(\text{PAni} \cdot \text{HBF}_4)_{0.55} \cdot \text{V}_2\text{O}_5$ containing doped polyaniline have been described.⁷⁰ Their interlayer distances (14.0 and 13.8 Å, respectively) are somewhat larger than for $(\text{PAni})_{0.65} \cdot \text{V}_2\text{O}_5$. It is apparently caused by additional intercalation of the anion-dopant into the layered structure. Due to the presence of doped polymer in the compounds $(\text{PAni} \cdot \text{HClO}_4)_{0.52} \cdot \text{V}_2\text{O}_5$ ($\sigma = 8 \times 10^{-4} \Omega^{-1} \text{ cm}^{-1}$) and $(\text{PAni} \cdot \text{HBF}_4)_{0.55} \cdot \text{V}_2\text{O}_5$ ($\sigma = 9 \times 10^{-4} \Omega^{-1} \text{ cm}^{-1}$), their electroconductivities are higher than those of the non-doped $(\text{PAni})_{0.65} \cdot \text{V}_2\text{O}_5$. The composites synthesised are redox-active in both aqueous acidic and organic aprotic electrolytes. For instance, virtually no destruction of $(\text{PAni})_{0.65} \cdot \text{V}_2\text{O}_5$ occurred upon multiple cycling in 1 M HCl solution in the potential range of 0.2–1.0 V.

A new hybrid material based on a binary polymeric component including poly(2,5-dimercapto-1,3,4-thiadiazole) (PDMcT) and PAni was synthesised.⁷¹ It was reported⁷² that intercalation of the 2,5-dimercapto-1,3,4-thiadiazole (DMcT) dimer leads to its polycondensation with formation of the composite (PDMcT)/ V_2O_5 . Dithiol DMcT is a promising charge-accumulating material. Due to a reversible redox reaction, it polymerises upon oxidation (charge) and depolymerises upon reduction (discharge). It is known that DMcT and PDMcT are not conductors, but their participation in electrochemical processes allows one to increase the efficiency of exploitation of the conducting polymer, *e.g.*, PAni. A hybrid material (PDMcT)/ V_2O_5 is obtained by mixing a methanolic solution of the monomer DMcT with $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ gel in the molar ratio 1 : 2. The reaction mixture is then kept under constant stirring at room temperature for 24 h. The resulting brown precipitate is filtered off, washed with methanol and dried at 50 °C in a vacuum.

Synthesis of a green-coloured composite (PDMcT + PAni)/ V_2O_5 is carried out according to the same scheme with addition of aniline to the reaction mixture in the ratio $\text{V}_2\text{O}_5 : \text{Ani} = 1 : 1$. X-Ray and IR studies on the hybrid material built of a binary polymeric component and $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel confirmed cointercalation of DMcT and Ani with the formation of polymers, *viz.*, PDMcT and PAni, in the V_2O_5 matrix. In the IR spectrum, the band at 1015 cm^{-1} , corresponding to the vibrations of the V = O bond, is displaced to the low-frequency region up to 1000 and 1005 cm^{-1} for PAni/ V_2O_5 and (PDMcT + PAni)/ V_2O_5 , respectively. The interlayer distance in the xerogel increases from 11.79 to 13.83 Å for all the polymer-intercalated specimens. Studies on the electronic structure showed insignificant distortions of octahedral symmetry of VO_6 , which are accompanied by partial reduction of the V^{5+} ions. The specific discharge capacity for the composites polymer/ V_2O_5 is lower than that for the original $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel (205 mA h g^{-1}) and amounts to 200 and 187 mA h g^{-1} for PDMcT/ V_2O_5 and (PDMcT + PAni)/ V_2O_5 , respectively. This effect can probably be associated with a decrease in the vanadium oxidation state. However, the discharge capacity increased by 10% for PDMcT/ V_2O_5 and by 17% for (PDMcT + PAni)/ V_2O_5 after treatment of the specimens in the flow of oxygen at 100 °C for 3 h. Possibly, the enhancement of the electrochemical characteristics occurs due to partial reoxidation of vanadium ions and formation of longer polymeric chains in the interlayer space of the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel. Intercalated PDMcT can be considered as an active additive to PAni, intensifying a reversible process of lithium intercalation–deintercalation.

Intercalation compounds of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel with complexes $\text{M}(\text{bipy})_3^{2+}$ (M = Ru, Ni and Co; bipy is bipyridine) are of interest as photochemical materials and can be used in photocatalysis for decomposition of water.⁷³ The formation of an intercalation compound with the complex is accompanied by an increase in the interlayer distance by ~ 8 Å, which corresponds to intercalation of a monolayer of $\text{M}(\text{bipy})_3^{2+}$ (Table. 5). The content of $\text{M}(\text{bipy})_3^{2+}$ in the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel is somewhat less than the theoretical value (0.2 moles per mole of V_2O_5) and amounts to 0.16, 0.14 and 0.11 moles for M = Ru, Ni and Co, respectively.

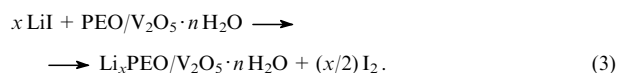
Table 5. Compositions and interlayer distances for intercalation compounds $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O} - \text{M}(\text{bipy})_3^{2+}$ (Ref. 73).

$\text{M}(\text{bipy})_3^{2+}$	M : V_2O_5	bipy : M	d_{001} / Å
$\text{Ru}(\text{bipy})_3^{2+}$	0.072	3.1	16.3
	0.12	3.1	17.1
	0.16	3.0	17.3
	0.16	3.2	17.1
$\text{Ni}(\text{bipy})_3^{2+}$	0.14	3.2	17.4
$\text{Co}(\text{bipy})_3^{2+}$	0.11	2.9	16.3

Thermal studies on this composite showed that a layered structure of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel is stabilised upon intercalation of cations.

Xerogel-based nanocomposites with the general formula $(\text{PEO})_x \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ were obtained by stirring aqueous solutions of poly(ethylene oxide) (PEO) with vanadium(V) oxide gel followed by slow evaporation of water.⁷⁴ The interlayer distance in the compounds obtained changes from 13.2 to 16.8 Å in the region $x = 0.5 - 1.0$, whereas, at $1 < x < 3$, it changes from 17.6 to 18.3 Å. It was established by means of X-ray diffraction that the composites contain a monolayer or a bilayer of PEO molecules when $x < 1$ and $x \geq 1$, respectively. The PEO chains are close to each other and fill completely the interlayer space of the xerogel by wavy mono- or bilayers.

Complex compounds of $(\text{PEO})_x \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ with alkali metal ions are actively studied with the aim of their use as solid electrolytes and as materials with electrochromic properties.⁷⁵ A red composite $(\text{PEO})_x \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ has an interlayer distance of 13.2 Å, the chains of PEO are situated linearly in the interlayer space. A single-phase specimen is obtained in the ratio $\text{PEO} : (\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}) < 0.8$. The composite is well moulded to a thin film which is more flexible than that of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$. The film of this specimen absorbs water reversibly, its content changes from 1.6 to 1.8 moles per mole of V_2O_5 . Besides, the film can be involved in redox intercalation according to the reaction



The composite is a dark-blue colour and the interlayer distance 13.0 Å; its electroconductivity is higher than that of the original xerogel.

The $\text{PEO}/\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ films are light-sensitive, they acquire a blue colour upon irradiation with a mercury lamp. These changes in colour are caused by the light-induced reaction in which PEO is oxidised by a pentavalent vanadium. The film of the original $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel is not light-sensitive. IR studies have shown that no structural changes occur on its irradiation. It has been revealed by ESR that the process is only accompanied by the increase in the concentration of V^{4+} centres. Measurements of the magnetic susceptibility have shown a noticeable increase in the magnetic moment which amounted to 0.8 μ_B per formula unit at 300 K. Upon irradiation of the intercalation compound, its conductivity increases by ~ 2 orders of magnitude, while the solubility decreases. A film with the composition $(\text{PEO})_{0.5} \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ exhibits semiconducting properties, its conductivity at room temperature equals $10^{-2} \Omega^{-1} \text{ cm}^{-1}$.

By intercalation of such water-soluble polymers as tetraakis(*N*-methyl-4-pyridyl)porphine,⁷⁶ poly(ethylene glycol),⁷⁷ poly(propylene glycol), poly(vinylpyrrolidone), methylcellulose⁷⁸ and poly(4-ethylphenol)⁷⁹ into the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel, ordered nanocomposite materials were obtained, their mechanical, optical and electrical properties can be controlled.

Intercalation of *N*-morpholinoisothiocyanate alone or together with copper ions into vanadium(V) oxide xerogel affords new complex compounds $(\text{C}_5\text{H}_8\text{N}_2\text{OS})_{0.35}\text{H}_2(\text{V}_{12}\text{O}_{31-\delta}) \cdot 8.8 \text{H}_2\text{O}$ and $(\text{C}_5\text{H}_8\text{N}_2\text{OS})_{0.35} \cdot \text{Cu}_{0.2}\text{H}_2(\text{V}_{12}\text{O}_{31-\delta}) \cdot 10.5 \text{H}_2\text{O}$, the inter-

layer distances in which are equal to 11.55 ± 0.05 and 14.30 ± 0.05 Å, respectively.⁸⁰ Intercalation of $C_5H_8N_2OS$ molecules was found to increase thermal stability of the xerogel (from 345 to 370 °C). As the temperature decreases from +50 to –50 °C, the electroresistivity increases sharply for these compounds, and the copper-containing xerogels always possess lower resistivities.

Upon interaction of 3,4-dihydroxyphenylalanine with $V_2O_5 \cdot nH_2O$ gel, a new hybrid material with the composition $(C_8H_9NO_2)_x \cdot V_2O_5 \cdot nH_2O$ was synthesised, which is characterised by a dark-blue colour and metallic lustre.^{81,82} The composite retains the laminar structure of the xerogel at $x < 0.02$, its interlayer distance is ~ 15 Å. A thin-film sample of this material possesses high stability in the electrochemical intercalation–deintercalation of Li^+ and is completely recovered even after 60 oxidation–reduction cycles. It was found that the intercalation of the alanine derivative into the $V_2O_5 \cdot nH_2O$ xerogel lowers the activation energy of conductivity from 0.35 to 0.20 eV.

Compounds of the $V_2O_5 \cdot x(ML_2X) \cdot nH_2O$ type ($M = Fe, Co, L$ is cyclopentadienyl, $X = Cl, Br, I$) were obtained by interaction of 5×10^{-3} M aqueous solution of ML_2X with vanadium(V) oxide xerogel.⁵ The interlayer distance in these compounds depends neither on the water content in the initial xerogel nor on the nature of the anion and amounts to ~ 13.22 Å. For the intercalation compounds with organometallic complexes, the main mechanism of formation consists of the exchange between the cations of the intercalant and the protons of hydrated polyvanadium acid. The formula of the iron-containing compounds was established as $V_2O_5 \cdot 0.4Fe(C_5H_5)_2 \cdot nH_2O$ ($n < 0.5$). Heating of the intercalation compounds in air up to 100 °C results in the loss of absorbed water. The structure of iron- and cobalt-containing complexes remains virtually unchanged up to 200 and 340 °C, respectively. Analysis of the widths of reflections in the diffractograms showed that the coherence length is noticeably increased for these compounds, in particular, for the cobalt-containing ones. Pentadienyl rings are oriented perpendicular to the layers of the basic structure and scaly-like stratifying occurs.

Complexes $V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcH]_{0.27}$, $V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcMe_2]_{0.22}$ and $V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcCH_2NHMe_2^+]_{0.16}$ were obtained by intercalation of the $V_2O_5 \cdot nH_2O$ xerogel with ferrocene, 1,1'-dimethylferrocene or (ferrocenylalkyl)ammonium halides, respectively, using their ethanolic solutions.⁸³ These complex compounds are formed mainly due to a redox reaction between iron and the V^{5+} ions and partly due to an ion exchange. The interlayer distances for the xerogels intercalated with ferrocene or with its alkylamino derivatives are virtually the same (13.2–13.5 Å) (Table 6), which suggests parallel orientation of the alkylammonium cation with respect to the vanadium–oxygen layers (Fig. 7). X-Ray spectroscopic and ESR studies have

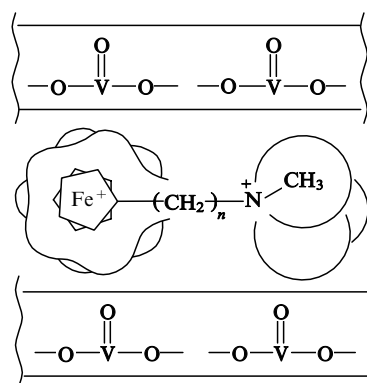


Figure 7. Schematic representation of the arrangement of (ferrocenylalkyl)ammonium compounds in the interlayer space of the $V_2O_5 \cdot nH_2O$ xerogel.⁸³

revealed that the Fe^{3+} ions are localised near the V^{4+} ions. Analogous conclusions have been drawn⁸⁴ from the study on the intercalation of diferrocenyl compounds containing bridging alkyl groups $[Fc(CH_2)_nFc; n = 1, 2]$ into the interlayer space of the $V_2O_5 \cdot nH_2O$ xerogel. In this case, intercalation is also caused by a redox reaction between iron and the V^{5+} ions. The guest molecules in $V_2O_5 \cdot (H_2O)_{0.8} \cdot (Fc^+CH_2CH_2Fc^+)_{0.23}$ are oriented nearly parallel to the vanadium–oxygen layers. Orientation of a cobaltocenium ion in the interlayer space of the complex compound $V_2O_5[Co(C_5D_5)_2]_{0.2} \cdot (H_2O)_{0.5}$ has been studied by ^2H NMR.⁸⁵ It was found that the C_5 axes are directed parallel to the vanadium–oxygen framework.

The possibility of intercalation of vanadium(V) oxide xerogel with various macrocyclic compounds as, for instance,

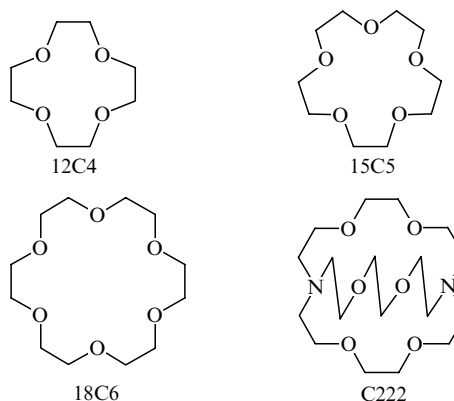
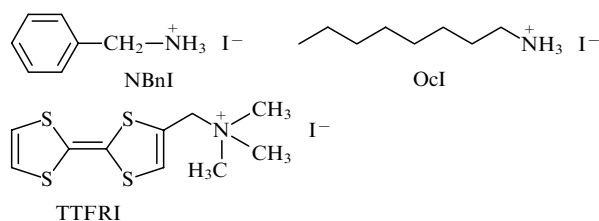


Table 6. Compositions and interlayer distances for intercalation compounds based on the $V_2O_5 \cdot nH_2O$ xerogel.^{83–86}

Intercalation compound	d_{001} / Å	Intercalation compound	d_{001} / Å
$V_2O_5 \cdot (H_2O)_{1.6}$	11.6	$V_2O_5(18C6)_{0.19} \cdot 0.83 H_2O$	17.1
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcH]_{0.27}$	13.4	$V_2O_5(C222)_{0.12} \cdot 0.39 H_2O$	17.4
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcMe_2]_{0.22}$	13.4	$Li_{0.26}V_2O_5(12C4)_{0.35} \cdot 0.15 H_2O$	16.3
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcCH_2NHMe_2^+]_{0.16}$	13.5	$Li_{0.26}V_2O_5(15C5)_{0.27} \cdot 0.03 H_2O$	17.3
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcCH_2NMe_3^+]_{0.15}$	13.2	$K_{0.26}V_2O_5(18C6)_{0.07} \cdot 0.39 H_2O$	16.2
$V_2O_5 \cdot (H_2O)_{0.8} \cdot [FcCH_2CH_2NH_3^+]_{0.21}$	13.4	$V_2O_5(Bn)_{0.17} \cdot 0.61 H_2O$	13.5
$V_2O_5 \cdot (H_2O)_{0.8} \cdot [FcCH_2CH_2NMe_3^+]_{0.14}$	13.5	$V_2O_5(Bn)_{0.31} \cdot 0.35 H_2O$	13.8
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcCH_2NHMe_2^+]_{0.18}$	13.0	$V_2O_5(OC)_{0.11} \cdot 0.89 H_2O$	12.4
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [FcCH_2CH_2NH_3^+]_{0.22}$	13.4	$V_2O_5(OC)_{0.25} \cdot 0.29 H_2O$	12.4
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [PhCH_2NHMe_2^+]_{0.29}$	14.2	$V_2O_5(OC)_{0.33} \cdot 0.29 H_2O$	20.5
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [PhCH_2NMe_3^+]_{0.24}$	14.1	$V_2O_5(OC)_{0.46} \cdot 0.10 H_2O$	24.0
$V_2O_5 \cdot (H_2O)_{0.6} \cdot [n-C_8H_{17}NH_3^+]_{0.33}$	26.0	$V_2O_5(TTFR)_{0.06} \cdot 1.32 H_2O$	12.5
$V_2O_5(12C4)_{0.44} \cdot 0.54 H_2O$	20.4	$V_2O_5(TTFR)_{0.16} \cdot 1.15 H_2O$	13.8
$V_2O_5(15C5)_{0.22} \cdot 0.65 H_2O$	16.9		



where 12C4 is 12-crown-4, 15C5 is 15-crown-5, 18C6 is 18-crown-6, C222 is cryptand-2,2,2, NBnI is benzylammonium iodide, OcI is octylammonium iodide, and TTFRI is *N,N,N*-trimethylmethyliumtetrathiafulvalene iodide, was discussed.^{86–89}

The formation of a hybrid product based on crown ethers proceeds by a complexation mechanism. Cyclic guest molecules interact as the ligands with protons or metal ions (Li^+ , Na^+) localised in the interlayer space of the xerogel with simultaneous partial replacement of water molecules. The compositions and the interlayer distances of the compounds obtained are given in Table 6. IR spectroscopic studies have revealed that the absorption band characterising $\delta(\text{H}-\text{O}-\text{H})$ vibrations is shifted from its position for the initial matrix (1620 cm^{-1}) to 1635 and 1644 cm^{-1} for $18\text{C}6/\text{V}_2\text{O}_5$ and $12\text{C}4/\text{V}_2\text{O}_5$, respectively. This indicates strengthening of the energy of binding between the water molecules and vanadium–oxygen layers in the intercalation compounds. It is obvious that intercalation of macrocyclic compounds into the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel decreases the mobility of the protons and the ionic component of conductivity. Application of hybrid materials based on crown ethers for ion-selective membranes and sensors was proposed.⁸⁹

Intercalation compounds of the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel with tetrathiafulvalene (TTF) and benzidine (Bzd) are of interest as promising novel materials. In essence, they can be assigned to ‘molecular bronzes’. Intercalation proceeds by a charge transfer mechanism. Irreversible intercalation of TTF into the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel in a water–ethanolic solution leads to the formation of a complex compound $(\text{TTF})_x \cdot \text{V}_2\text{O}_5$ ($x < 1.8$)⁹⁰ in which the interlayer distance amounts to $13.7\text{ \AA}$. This compound is insoluble in water, contains a large amount of strongly bound water and up to $\sim 25\%$ of vanadium ions in a tetravalent state. Electronic conductivity of $(\text{TTF})_x \cdot \text{V}_2\text{O}_5$ depends on the stoichiometric composition of these complexes. The conductivity for specimens with $x = 0.17$ and 1.5 is larger than that for V_2O_5 by factors 46 and 15, respectively.

Black flake-like precipitate of compounds $(\text{Bzd})_x \cdot \text{V}_2\text{O}_5$ with a maximum Bzd content ($x = 1$) is formed in an irreversible reaction of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel dispersed in water with an ethanolic solution of Bzd over a few seconds.⁹⁰ In the structurally similar compound $(\text{TTF})_x \cdot \text{V}_2\text{O}_5$, saturation with respect to intercalant is not achieved even at $x = 2.9$. The diffractogram of compound $(\text{Bzd})_x \cdot \text{V}_2\text{O}_5$ was found to contain 001 reflections corresponding to an interlayer distance of $15.6\text{ \AA}$. The benzidine molecules in the xerogel are inclined with respect to the vanadium–oxygen layers. Electronic conductivity of the complex compound $(\text{Bzd})_x \cdot \text{V}_2\text{O}_5$ ($\sigma = 2.8 \times 10^{-6}\text{ }\Omega^{-1}\text{ cm}^{-1}$) differs only slightly from that of the original xerogel.

The conditions for the preparation of intercalation products of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ gel with methyl-, heptyl- and benzylviologens have been described.^{91,92} As a result of ion exchange, the organic components are situated between the layers of the xerogel and orientation of their molecules depends on the type of viologen. With respect to the vanadium–oxygen layers, the molecules intercalated into the interlayer space of the xerogel are parallel (as a monolayer) in the case of methyl- and benzylviologens and perpendicular in the case of heptylviologen.

With intercalation of octyl-, benzyl- and TTF-ammonium iodides,⁸⁶ which is accompanied by a partial reduction of V^{5+} to V^{4+} , the conductivity of the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel increases by 1.5–2 orders of magnitude. The compositions and interlayer

distances for the compounds obtained are given in Table 6. The electroconductivity of the octyl-containing hybrids $\text{V}_2\text{O}_5(\text{Oc})_x \cdot n\text{H}_2\text{O}$ depends on the x value and on the orientation of organic molecules in the interlayer space. At $x \leq 0.2$, the alkyl chains are situated parallel, while, at $x > 0.5$, they are mainly perpendicular to the vanadium–oxygen layers. The electroconductivity of the specimens with transversal geometry of the intercalant is limited by the mobility of charge carriers, *i.e.*, the electrons. Their mobility is associated with overcoming a high potential barrier on moving across the vanadium–oxygen layers. As a consequence, an increase in the interlayer distance leads to decrease in conductivity of the octyl-containing complex.

Mechanical activation of vanadium(V) oxide xerogel accelerates significantly the initial intercalation step as was established⁹³ with an example of *n*-hexadecyltrimethylammonium bromide. The interlayer distance in the compound obtained under equilibrium conditions equals $14.45\text{ \AA}$. This value is very close to the value of quadruplicate diameter of the alkyl chains ($14.52\text{ \AA}$) and is twice as large as the parameter b of the crystal lattice of *n*-hexadecyltrimethylammonium bromide. It thus follows that the latter compound is situated parallel to the layers of the laminar structure of the xerogel.

Photo- and electrophotoreactive nanocomposite materials can be obtained using organic dyes as intercalated substances. The study on the kinetics of intercalation of methylene blue (MB^+) into $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ gel by absorption spectroscopy in the range $500\text{--}800\text{ nm}$ has shown that the driving force of the process is the reduction of methylene blue by the V^{4+} species (see Ref. 94). Interaction of MB^+ with the gel can be described by the following scheme:



Reduction of methylene blue is followed by protonation, reoxidation by oxygen and dimerisation of the dye. The rate constant for the transformation of protonated methylene blue into the dimer is $100\text{ mol litre}^{-1}\text{ s}^{-1}$.

Compounds based on the layered oxides VTO_5 ($\text{T} = \text{P, As, S}$, and others) with a structure of vanadyl phosphate VOPO_4 (Ref. 95) are relative to the above-considered intercalation compounds. In the phases intercalated by pyridine, this coordinates to vanadium and is situated perpendicular to the VTO_5 layers. Reduction of vanadium(V) virtually does not occur and the layers of the original matrix are retained. Cations of relatively large sizes, *e.g.*, ferrocenylalkylammonium, can be intercalated into a layered structure of $\text{VOPO}_4 \cdot \text{H}_2\text{O} \cdot \text{EtOH}$.^{84,96}

The results of the study on the intercalation of $\text{VOPO}_4 \cdot \text{H}_2\text{O} \cdot \text{EtOH}$ with ferrocene and its alkyl derivatives (1,1'-dimethyl-, ethyl-, *n*-butyl-) as well as by cobaltocenium cations, carried out in ethanol, have been reported.⁹⁷ The interlayer distances in the compounds obtained are increased with respect to the interlayer distance of the initial phosphate ($d_{001} = 7.5\text{ \AA}$) and reach $8.8\text{--}10.3\text{ \AA}$. Intercalated molecules of ferrocene and its derivatives were found to be situated perpendicular to the VPO_5 layers.

Layered hydrates of mixed oxides $\text{VAsO}_5 \cdot 3\text{H}_2\text{O}$ and $\text{VPO}_5 \cdot 2\text{H}_2\text{O}$ interact with alkylammonium iodides in an aqueous medium or in organic solvents with formation of compounds with the general formula $(\text{RNH}_3)_x \text{V}_x^{\text{IV}} \text{V}_{1-x}^{\text{V}} \text{TO}_5 \cdot \text{H}_2\text{O}$ ($\text{R} = \text{C}_n\text{H}_{2n+1}$, $n = 3\text{--}8$; $x = 0.4\text{--}0.6$; $\text{T} = \text{As, P}$). It is of note that the parameter d_{001} depends linearly on the number of carbon atoms in the alkyl radical $\text{C}_n\text{H}_{2n+1}$. A layered structure of the initial hydrates of mixed oxides $\text{VTO}_5 \cdot n\text{H}_2\text{O}$ is retained in these intercalation compounds.

Mixtures of aliphatic alcohols ranging from ethanol to *n*-heptanol are intercalated into the lattice of non-hydrated vanadyl sulfate VOSO_4 with the formation of the inclusion compounds.⁹⁸ Intercalation compounds of $\text{VOPO}_4 \cdot n\text{H}_2\text{O}$ with glycerol have been obtained.⁹⁹ These substances are unstable; on keeping in air, glycerol reduces vanadium to a tetravalent state and the specimen changes its colour from yellow to green. Incorporation of the

glycerol molecules into the interlayer space of vanadium(V) phosphates leads to disordered compounds.

The process of intercalation of aniline derivatives into $\text{VOPO}_4 \cdot n\text{H}_2\text{O}$ has been studied.^{100, 101} It was found that their intercalation into the interlayer space of vanadyl phosphate occurs only due to protonation of amino groups or oxidation of the iodide ion accompanied by reduction of V^{5+} to V^{4+} .

V. Nanotubular forms of intercalation compounds

A search for various nano-structured functional materials is accompanied by the development of studies into the synthesis and investigation of properties of non-carbon nanotubes (nanotubulenes, NTs).¹⁰² Vanadium(V) oxide-based nanotubulenes have been synthesised not long ago.¹⁰³ For their preparation, a sol–gel method was found to be effective, which allows one to obtain the xerogel with explicitly pronounced quasi-one-dimensional structure of the layers. By combination of the sol–gel method with hydrothermal treatment in air at 180 °C for 5 h, a nanowire with the composition $\text{V}_2\text{O}_5 \cdot 0.3\text{H}_2\text{O}$ and with a length of several tens of micrometers and a width of several tens of nanometers was synthesised.^{104, 105}

An extensive body of experimental data on the chemistry of intercalation compounds based on the $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel served as a basis for searching new methods for synthesis of nanotubular forms of vanadium(V) oxide. Obviously, the possibility of changing the distance between the vanadium–oxygen layers in the layered structure of the xerogel upon intercalation of molecules of various organic substances in the interlayer space was used in the design of vanadium–oxide NT: in this case, the organic guest molecules act as a template and determine the structure of multi-layered nanotubular composites.

It was suggested^{106–108} that primary amines $\text{C}_n\text{H}_{2n+1}\text{NH}_2$ ($4 \leq n \leq 22$) or diamines $\text{H}_2\text{N}(\text{CH}_2)_n\text{NH}_2$ ($14 \leq n \leq 20$) be used as structure-forming templates. For instance, ethanolic solutions of vanadium(V) triisopropyl oxide ($\text{Pr}^i\text{O})_3\text{VO}$ and an amine taken in the molar ratio 2 : 1, were stirred for 1 h followed by hydrolysis. After ageing of this system for 12–96 h, an orange composite was obtained, which transformed into a black monophasic product after hydrothermal treatment in an autoclave at 180 °C for 2–7 days. The product was isolated in the form of nanotubes with a length of up to 15 μm , an outer diameter of 15–150 nm and an inner diameter of 5–50 nm. The walls of the tubes consisted of 2–30 layers of crystalline vanadium oxide with the amine or diamine molecules intercalated in the space between the layers. The distance between the layers was proportional to the length of alkylamine and changed in the range from 17 to 38 Å. The general formula of these compounds can be written as $\text{VO}_x\text{O}_{y/2} \cdot (\text{C}_n\text{H}_{2n+4}\text{N})_y$. In the case of diamines, the tubes had thicker walls and smaller inner diameters than in the case of amines. The structure of the vanadium–oxygen layers comprised tetrahedra of VO_4 and tetragonal pyramids of VO_5 . The tubes of vanadium oxide remained stable after removal of the amines and were destroyed upon thermal treatment above 250 °C.

Unlike mesoporous metal oxides with laminar structures, the composites under consideration are characterised by a tubular morphology and well-structured walls. According to the published data,¹⁰⁴ the ‘volumes’ of vanadium–oxygen layers are very flexible, they can be stretched in a line and can be involved in numerous exchange reactions. It was reported¹⁰⁹ that the synthesis of NT with the use of vanadium(V) oxychloride and oxide as precursors occurs in two stages. In the first step, VOCl_3 or V_2O_5 was mixed with a primary amine $\text{C}_n\text{H}_{2n+1}\text{NH}_2$ ($11 \leq n \leq 20$) in an inert atmosphere, then hydrolysed in an acetate buffer (pH 7) or in water. The next step consisted of hydrothermal treatment at 180 °C for 7 days. According to data from elemental analysis, the compositions of the NT synthesised from VOCl_3 or V_2O_5 correspond to the general formulae $\text{VO}_{2.45 \pm 0.05} \cdot (\text{C}_n\text{H}_{2n+4}\text{N})_{0.27 \pm 0.01}$ ($11 \leq n \leq 16$) and $\text{VO}_{2.43 \pm 0.03} \cdot (\text{C}_n\text{H}_{2n+4}\text{N})_{0.27 \pm 0.01}$ ($11 \leq n \leq 20$), respectively. Morphological

Table 7. Morphologic characteristics of the vanadium-oxide nanotubulenes (the template is $\text{C}_n\text{H}_{2n+1}\text{NH}_2$).¹⁰⁹

Precursor	<i>n</i>	Outer diameter NT /nm	Inner diameter NT /nm	Number of layers	Length NT / μm
($\text{Pr}^i\text{O})_3\text{VO}$	$4 \leq n \leq 22$	15–150	5–50	2–30	1–15
VOCl_3	11	50–100	15–35	10–20	1.5–5
	16	80–100	20–35	11–14	0.8–1.5
V_2O_5	11	70–140	20–35	9–13	2–12
	12	50–90	15–35	7–13	1–3
	16	70–100	20–45	6–11	1–2
	20	60–90	20–45	6–10	1–3

characteristics of the vanadium oxide NT obtained from different precursors and templates are given in Table 7. It should be mentioned that the ends of the NT obtained by this method are open and characterised by a multi-layer morphology formed by the ‘volumes’ of vanadium–oxygen layers.

Changes in the pH of the V_2O_5 gel by addition of ammonia allows one to synthesise NT with definite structural characteristics.¹¹⁰ In neutral or weakly acidic media, tubes with an interlayer distance proportional to the length of the amine are formed. Nanotubulenes obtained at pH 9–10 have unique wall structures; these are built of the VO_x layers alternating regularly with intercalated molecules of the amine or ammonia (the interlayer distances VO_x – VO_x are equal to 2.0 and 0.9 nm, respectively). Nanotubulenes formed with the use of ammonia are characterised by a significantly larger outer diameter (> 250 nm) and by a smaller length (2–5 μm) as compared with the NT synthesised at pH 4–8. The general formula of the new NT was suggested to be $[(\text{NH}_4)_y\text{VO}_x][(\text{C}_n\text{H}_{2n+1}\text{NH}_3)_z\text{VO}_x]$. An excess amount of the amine in the NT is easily replaced by sodium, potassium, magnesium, calcium, strontium, iron, cobalt, nickel or copper cations.¹¹¹ This method of modification of VO_x -nanotubulenes may become effective for improving properties of the initial composite. This procedure does not change the tubular morphology and only decreases the interlayer distance from 2.8 nm (for $\text{C}_{12}\text{H}_{25}\text{NH}_3\text{VO}_x$) to 0.9–1.2 nm depending on the cation.

A new manganese-containing intercalation compound with tubular morphology with the general composition $\text{Mn}_{0.1}\text{VO}_{2.5+\delta} \cdot n\text{H}_2\text{O}$ was synthesised¹¹² by ion exchange starting from the layered precursor $\text{V}_2\text{O}_5 \cdot \delta(\text{C}_{12}\text{H}_{25}\text{NH}_3)$. For the NT obtained, the section diameter and the length reached 100 nm and 1300 nm, respectively. These NT contained such defects as partial destruction of the layers and their zigzag-like shape. The structure of the layers is tetragonal with unit cell parameters $a = 6.157(3)$ and $c = 10.52(3)$ Å. This compound was assayed as a cathode material in the electrochemical intercalation of lithium. It was found that 0.5 moles of lithium per mole of V_2O_5 are reversibly intercalated into these NT at a potential of ~ 2 V. The specific discharge capacity of the battery amounted to 140 A h kg^{-1} .

It was proposed¹¹³ to use derivatives of *trans*-(1*R*,2*R*)- and *trans*-(1*S*,2*S*)-1,2-diaminocyclohexane as templates in the synthesis of helical chiral VO_x -nanotubulene structures. In the case of the *R,R*-enantiomer, a left-handed helix was always formed, while in the case of *S,S*-enantiomer it was right-handed.

Carbon NT can be used as templates for obtaining nano-structured vanadium oxide.^{114, 115} The synthetic procedure includes covering of a carbon NT with V_2O_5 gel and subsequent removal of carbon by calcination at 700 °C. The carbon NT are pretreated with boiling HNO_3 for 24 h for creation of acidic centres on the surface. The diameters and the lengths of the NT synthesised according to this procedure amounted to 20–55 nm and 2–3 μm , respectively. Electron diffraction studies of the specimens have revealed their orthorhombic structures with unit cell parameters $a = 11.44$, $b = 3.54$ and $c = 4.35$ Å.

Unfortunately, most investigations into the VO_x -nanotubulenes are concerned mainly with synthetic procedures and studies on the morphology of specimens. Only a few publications (see, e.g., Ref. 116) contain data on the physicochemical properties and evaluate the prospects for the application of vanadium-oxide NT as oxidation catalysts,¹¹⁵ a cathode material for reversible lithium batteries^{117–120} and a semiconducting material for the preparation of field-controlled transistors.¹²¹

VI. Applications of intercalation compounds

Most studies on the application of vanadium(V) oxide xerogels have focused on their use in the design of chemical power sources.¹²² Compared to the crystalline vanadium oxides, the xerogels form very mobile layered structures in which various cations and molecules of organic substances can easily be intercalated and deintercalated. The advantages of xerogels include the ion-electronic type of conductivity and the possibility of displacing water molecules by hydrophilic organic solvents. Studies on the cathodic behaviour of superfine powders, films and nanocomposites of the intercalation compounds in the electric power sources with lithium anode merit special attention.^{123–125} In a 1 M solution of LiClO_4 in propylenecarbonate (PC), the exchange of water molecules with molecules of the organic solvent occurs without application of a voltage; this is accompanied by an increase in the interlayer distance up to 21.5 Å. However, the solvent is further displaced by lithium and $\text{Li}_{0.4}\text{V}_2\text{O}_5$ is formed. In the discharge step, the formation of compounds $\text{Li}_{1.1}\text{V}_2\text{O}_5$ and $\text{Li}_{1.6}\text{V}_2\text{O}_5$ was detected. The layered structure of the xerogel is destroyed in the final step of intercalation of Li^+ . The steady-state potential for the film with the composition $\text{V}_2\text{O}_5 \cdot 2.2\text{H}_2\text{O}$ in a 1 M solution of LiClO_4 in PC amounts to 3.20–3.85 V relative to metallic lithium.¹²⁶ The parameter d_{001} of the xerogel $\text{Li}_x\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ changed from 11.6 to 16.7 Å on keeping the specimen in a solution of LiClO_4 , decreased to 10.4 Å ($x = 0.2$) upon cathodic lithiation and then remained constant up to $x = 0.7$ in $\text{Li}_x\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$.

According to the reported data,¹²⁷ intercalation of PC results in compounds $\text{V}_2\text{O}_5 \cdot 0.1\text{H}_2\text{O} \cdot 0.3\text{PC}$ with the parameter $d_{001} = 22.0$ Å, which decreases to 11.0 Å for the ratio $\text{Li}:\text{V} = 0.01$ in the xerogel. Intercalation of Li^+ is accompanied by simultaneous insertion of PC, which weakens the interaction between the protons of the interstitial water and oxygen of the xerogel. Kinetic studies on a compound with the composition $\text{Li}_{0.3+x}\text{V}_2\text{O}_5 \cdot 0.2\text{H}_2\text{O} \cdot \text{PC}$ have revealed¹²⁸ that the chemical diffusion coefficient of lithium ions (D_{Li}) decreases from 10^{-8} to $10^{-9} \text{ cm}^2 \text{ s}^{-1}$ as the x value increases from 0 to 0.2. The above-mentioned values of D_{Li} are higher than the value of $10^{-11} \text{ cm}^2 \text{ s}^{-1}$, characteristic of the crystalline V_2O_5 in the region $0 < x < 1$. As the content of lithium ions increases ($0.2 < x < 1.3$), their mobility decreases and the D_{Li} value becomes equal to $5 \times 10^{-11} \text{ cm}^2 \text{ s}^{-1}$ at $x = 1.3$. Using a chemical or electrochemical method, up to 4 moles of lithium per mole of V_2O_5 can be intercalated. With this material, the specific cell capacity of 1600 W h kg^{-1} can be reached, which is significantly higher than for any other material based on vanadium oxide.¹²⁹

It was mentioned^{130,131} that the degree of intercalation of lithium ions into the films of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogel depends on the morphology of films, which can be modified by adding carbon (in the form of a powder) in the course of the synthesis of the gel. The degree of lithium intercalation is also affected by the electronic conductivity of the xerogel, which can be increased by adding silver (in the form of a powder) or copper to the gel.^{132,133} Thin films with a molar ratio $\text{M}:\text{V} = 0.005–5$ ($\text{M} = \text{Ag}, \text{Cu}$) have been obtained from this type of composite. An increase in the electronic conductivity of the xerogel by 2–3 orders of magnitude was thus achieved. The amount of lithium intercalated into the composite reaches 4 moles per mole of V_2O_5 ; lithium is intercalated reversibly at a very high rate. For $\text{M} = \text{Cu}$, the capacity of

the cathodes does not drop even after 450 charge–discharge cycles.¹³³

Nanocomposites with the compositions $(\text{PPyr})_x\text{V}_2\text{O}_5$ ($x = 0.4–0.9$), $(\text{PAni})_{0.4}\text{V}_2\text{O}_5$ and $(\text{PTh})_x\text{V}_2\text{O}_5$ ($x = 0.3–0.8$, PTh is polythiophene) were tested as cathode materials in lithium power sources.^{63,134} The best characteristics as regards reversibility of the intercalated cations were obtained for the polyaniline-containing composite.^{135–138} Its capacity with respect to Li^+ is 40% higher than that for the original material, viz., $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$. Intercalation of a PAni derivative, namely, poly[*N*-(3-sulfo-propyl)aniline] (PSPAni) resulted in a new composite $(\text{PSPAni})_{0.3} \cdot \text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ exhibiting a specific discharge capacity of cathode equal to 307 A h kg^{-1} and reduction kinetics faster than for the initial xerogel.^{139,140} The electrochemical characteristics of the composites $(\text{C}_6\text{H}_4\text{N})_x\text{V}_2\text{O}_5$ ($x = 0.35–0.40$), annealed in oxygen at 150 °C and treated with hydrogen peroxide to oxidise the reduced vanadium have been reported.¹³⁵ The intercalation of Li^+ remains reversible in the composite even after profound reduction corresponding to intercalation of 3 moles of lithium; the lithium diffusion is deeper than in the case of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$. At a current density of 10 $\mu\text{A cm}^{-2}$, the potential changes over the range from 3.8 to 1.8 V and the specific discharge capacity becomes equal to 370 A h kg^{-1} . On the 15th day after the synthesis, the composite material $(\text{C}_6\text{H}_4\text{N})_{0.6}\text{V}_2\text{O}_5 \cdot 0.3\text{H}_2\text{O}$ not subjected to oxidative treatment had an electroconductivity of $0.09 \Omega^{-1} \text{ cm}^{-1}$ and $d_{001} = 14.14$ Å.¹³⁶ The specific discharge capacity of this compound, equal to 161 A h kg^{-1} , increased to 302 A h kg^{-1} after its annealing in an oxygen atmosphere at 80 °C for 5 h. This value of capacity corresponds to intercalation of 2.7 moles of lithium per mole of the composite material.^{136,141} As the temperature of annealing of the specimen increases, the electrochemical activity of PAni in the composite material decreases.

The use of the nanocomposites PPy–vanadium(V) oxide xerogel as a cathode material for power sources with a lithium anode has been discussed.^{63,66,142} Supercritical dessication of the xerogels (under cryogenic conditions) allows one to obtain materials with a large specific surface area (150–257 $\text{m}^2 \text{ g}^{-1}$) and a density of 0.1–0.2 g cm^{-3} (see Ref. 142). Intercalation of lithium into these composites depends strongly on the concentration of the oxidant [for instance, $\text{Fe}(\text{NO}_3)_3$] used in their synthesis.⁶⁶ For the compound $(\text{PPyr})_{0.8}\text{V}_2\text{O}_5$ obtained without an oxidant, the specific capacity equals 240 A h kg^{-1} upon intercalation of 3 moles of lithium per mole of composite. In the synthesis performed under conditions where $\text{Pyr}:\text{V} = 1$ and $\text{Fe}:\text{V} = 0.05$, the composite obtained had the specific discharge capacity 180 A h kg^{-1} upon intercalation of 2.8 moles of lithium. With an increase in the PPy content to 8.5 moles per mole of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ and the $\text{Fe}:\text{V}$ ratio to 2, the specific capacity of the xerogel decreased to 25 A h kg^{-1} and the amount of intercalated lithium decreased to 1.8 moles.

Hydrated intercalation compounds with the composition $\text{M}_x\text{V}_2\text{O}_5 \cdot \delta \cdot n\text{H}_2\text{O}$, where M is an alkali metal ion, were used in the design of new compact power sources, namely, reserve batteries of bipolar construction with aqueous electrolytes.¹²² Such sources are needed for aerological investigations of the surface atmospheric layers. The process of intercalation of Mg^{2+} , Zn^{2+} and Al^{3+} cations into the vanadium(V) oxide xerogel in both the propylenecarbonate-based and aqueous electrolyte can be used in the design of high-energy batteries. Such power sources will be less dangerous and cheaper than the lithium batteries.

Intercalation compounds based on vanadium(V) oxide xerogel are of interest as solid electrolytes⁷⁵ conducting M^{z+} cations and as electrochromic materials;¹⁴³ they change their colour in the intercalation–deintercalation of protons or lithium ions. Relatively simple technology for obtaining films of these substances allows one to produce electrochromic displays of large area. For instance, the film of polyvanadium acid deposited on the conducting layer of indium and tin oxides changes colour from yellow to green at the voltage ± 1.5 V.¹⁴⁴ The time constant of such an

electrochromic device amounts to 2–20 s depending on the power of the current source; the duration of memory is 20 h, the number of cycles may reach 8×10^4 . The film varies in colour from yellowish-green to grayish-violet according to the amount of intercalated lithium.

$\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ xerogels are of interest as precursors for the synthesis of superfine powders and films of oxide vanadium bronzes^{125, 145–148} and vanadates^{27, 149} used as cathode materials in power sources. The bronze $\text{Na}_{0.33}\text{V}_2\text{O}_5$ with monoclinic syngony was obtained^{150, 151} by annealing the $\text{Na}_{0.33}\text{V}_2\text{O}_5 \cdot 1.6\text{H}_2\text{O}$ xerogel at 550 °C. Electrochemical intercalation of Li^+ and Na^+ ions into the β -phase of $\text{Na}_{0.33}\text{V}_2\text{O}_5$ obtained by the sol–gel method is achieved using solutions of the corresponding salts in PC. This leads to a significantly higher content of these ions as compared with the specimens synthesised by a solid-phase method.¹⁴⁶ In addition, the compound obtained by the sol–gel method possesses the higher (by two orders of magnitude) lithium diffusion coefficient. According to the data from cyclic voltammetry, the β -phase prepared by the sol–gel method has higher electrochemical activity. The oxide vanadium bronze with the composition $\text{Fe}_{0.12}\text{V}_2\text{O}_5$ prepared also by the sol–gel method was recommended as a cathode material in accumulators with a lithium anode. The discharge curve for this source has three plateaux corresponding to total capacity of 3.5 moles of lithium per mole of $\text{Fe}_{0.12}\text{V}_2\text{O}_5$. The specific discharge capacity of the bronze after the 40th cycle amounted to 200 A h kg^{-1} upon cycling in the range 3.8–2.0 V.

Usually, the oxide compounds obtained upon complete dehydration of vanadium xerogels have a large surface and easily undergo intercalation with Li^+ ions. For instance, 0.8 moles of lithium are intercalated into the oxide $\text{Al}_{0.11}\text{V}_2\text{O}_{5.15}$ at a current density of $20 \mu\text{A cm}^{-2}$ with the potential varying in the interval from 3.4 to 3.1 V. The chemical diffusion coefficient for Li^+ in $\text{Li}_x\text{Al}_{0.11}\text{V}_2\text{O}_{5.15}$ equals 10^{-10} – $10^{-11} \text{ cm}^2 \text{ s}^{-1}$. It increases in the interval $0.05 < x < 0.2$ and reaches a maximum at $x = 0.25$, then decreases in the range $0.25 < x < 0.50$ and remains virtually unchanged at $x > 0.50$. The current–voltage curve suggests the possibility of cycling the compound; this is characterised by the three peaks at about 3.35, 3.15 and 2.25 V. Similar studies have been performed on the mixed oxide $\text{Fe}_{0.11}\text{V}_2\text{O}_{5.16}$ (see Ref. 149). Electrochemical intercalation with lithium yielded the compound $\text{Li}_x\text{Fe}_{0.11}\text{V}_2\text{O}_{5.16}$ ($0 < x < 2.4$). As in the case of $\text{Li}_x\text{Al}_{0.11}\text{V}_2\text{O}_{5.15}$, the chemical diffusion coefficient for Li^+ ions depends strongly on x . The Fe^{3+} cations localised in the V_2O_5 octahedra act as stabilisers of the host lattice. As a result, the appearance of phases of the $\text{Li}_x\text{V}_2\text{O}_5$ type upon intercalation of lithium slows down.

Polyvanadate xerogels deposited onto inert plates were used¹⁵² as precursors for obtaining films of oxide vanadium bronzes with the composition $\text{M}_x\text{V}_2\text{O}_5$ ($\text{M} = \text{Na}, \text{Ag}, \text{Ba}$). After annealing at 550 °C of thin layers of compounds $\text{M}_x\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ prepared from $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ by ion exchange in the 0.1 M aqueous solution of MCl, compounds $\text{Na}_{0.33}\text{V}_2\text{O}_5$ and $\text{Ag}_{0.33}\text{V}_2\text{O}_5$ with the β -phase structure of oxide vanadium bronze are formed. The electroconductivity of β -phase films is strongly anisotropic and depends on the nature of the cation M^+ . For $\text{Na}_{0.33}\text{V}_2\text{O}_5$, $\sigma_{\parallel} = 8$ and $\sigma_{\perp} = 4 \times 10^{-2} \Omega^{-1} \text{ cm}^{-1}$ at room temperature, while for $\text{Ag}_{0.33}\text{V}_2\text{O}_5$ the corresponding values are 3 and $1.5 \times 10^{-2} \Omega^{-1} \text{ cm}^{-1}$, respectively. The characteristic times of electron mobility are approximately the same for both these compounds and are equal to 10^{-11} s . The mobilities of Na^+ and Ag^+ ions are characterised by the times $\tau = 5 \times 10^{-12}$ and $\tau = 2 \times 10^{-11} \text{ s}$, and by the activation energies 0.12 and 0.08 eV, respectively. A higher mobility of electrons ($\tau = 10^{-10} \text{ s}$) is observed in the case of $\text{Ba}_{0.16}\text{V}_2\text{O}_5$.

The results of X-ray and thermal studies on the oxide vanadium bronzes with the compositions $\text{Ba}_{0.17}\text{V}_2\text{O}_5$, $\text{Ni}_{0.17}\text{V}_2\text{O}_5$, $\text{Al}_{0.11}\text{V}_2\text{O}_5$ and $\text{Fe}_{0.11}\text{V}_2\text{O}_5$ prepared by the sol–gel method were reported.²⁶ It was noted that, unlike the solid-phase procedure, the sol–gel method allows one to synthesise thin layers of bronzes $\text{M}_x\text{V}_2\text{O}_5$ of the α type with rhombic structures. The

orientation of these layers depends on the nature of the intercalated cation. The layers situated parallel to the support surface can be parallel (Fe^{3+} and Al^{3+}), perpendicular (Ba^{2+}) or either parallel or perpendicular (Ni^{2+}) to the planes of the V_2O_5 layers. With the cesium cation, bronze of a hexagonal syngony with the composition $\text{Cs}_{0.35}\text{V}_2\text{O}_5$ and the unit cell parameters $a = 13.34(1)$ and $c = 3.610(1) \text{ \AA}$ is formed under the same conditions.¹⁵³

From the mixed (as regards the intercalated cation) xerogels, films of oxide vanadium bronzes of the β type, with compositions $\text{Li}_{0.11}\text{Na}_{0.23}\text{V}_2\text{O}_5$, and $\text{Li}_{0.23}\text{Na}_{0.14}\text{V}_2\text{O}_5$ were obtained by an analogous method.¹⁵⁴ Electroconductivities of these bronzes are also strongly anisotropic. At room temperature, $\sigma_{\parallel} = 5.98 \times 10^{-2}$ and $\sigma_{\perp} = 5.48 \times 10^{-5} \Omega^{-1} \text{ cm}^{-1}$ for the first bronze and $\sigma_{\parallel} = 0.138$, $\sigma_{\perp} = 1.08 \times 10^{-4} \Omega^{-1} \text{ cm}^{-1}$ for the second one. The activation energy of the conductivity of the films is close to 0.08 eV at $\sim 100 \text{ K}$ and increases to 0.11 eV as the content of sodium ion decreases.

VII. Conclusion

In recent years, intercalation compounds based on the xerogels of complex and simple vanadium oxides have been the most extensively studied. Different views on the nature of hydrated vanadium(V) oxide existed for a long time but are currently united due to the progress in the studies on the structures of films and the mechanisms of intercalation of cations and organic molecules. In this respect, the results obtained in determining the content and types of the hydrogen–oxygen groups by ^1H NMR are of considerable importance.

The preparation of ordered nano-, meso-, micro- and macrostructures of intercalation compounds is typical of modern experimental research. Synthetic procedures, chemical composition and morphology of the xerogel are usually reported, but the data concerning physicochemical and physical properties are scarce and concern mainly the cathodic behaviour of these substances in chemical power sources. Studies on the electronic structure and the reactivities of the nanocomposites consisting of vanadium–oxygen layers and intercalated organic components are lacking. A new direction for applications of the intercalation compounds is becoming evident, which consists of their use as nanoreactors in the synthesis of polymers⁶¹ or nanotubular carbon structures.¹⁵⁵

New publications dealing with intercalation compounds based on V_2O_5 xerogels have appeared after completion of this review. Studies on the refinement of a bilayer structure of vanadium(V) oxide xerogel are of interest.¹⁵⁶ Investigations into the preparation of bulk¹⁵⁷ and film¹⁵⁸ materials with mesoporous structures have begun. A superlight macroporous crystalline intercalation compound of $\text{V}_2\text{O}_5 \cdot n\text{H}_2\text{O}$ was synthesised that contains intercalated hexadecylamine molecules ($d = 33.4 \text{ \AA}$) with alkyl chains perpendicular to the planes of the vanadium–oxygen layers.¹⁵⁹ All this evidences progress in the studies on the class of compounds under consideration.

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Reactions of alkenes with nitrogen oxides and other nitrosating and nitrating reagents

A V Stepanov, V V Veselovsky

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Abstract. Reactions of alkenes with nitrogen oxides and other nitrosating and nitrating reagents are considered. The bibliography includes 134 references.

I. Introduction

Reactions of alkenes with nitrogen oxides and other nitrosating and nitrating reagents have attracted attention during the entire history of contemporary organic chemistry. The fundamental studies carried out in this area are of independent significance and have contributed considerably to the arsenal of organic synthesis by providing new preparative methods and accessible highly reactive synthetic blocks.

In this review, we consider the transformations of alkenes in reactions with NO, NO₂, their synthetic equivalents and sources of NO⁺, NO₂⁺ and NO₂⁻ ions. Aside from differences originating from the specific nature of each of these reagents, their reactions with alkenes have certain common features which manifest themselves in the similarity of the intermediates and products formed. Particular attention is paid to reactions which result in aliphatic and alicyclic nitro compounds, since the uses of these compounds in organic synthesis are the most diverse (see., *e.g.*, the reviews ^{1–8}).

The transformations discussed here have been reported in the last 10–15 years. Earlier examples can be found in other reviews.^{9–12} In particular, reactions of alkenes with N₂O₃, N₂O₅ and HNO₃ have been considered in detail in those reviews; however, there have been few publications on these reagents recently,^{13,14} since, as a rule, their reactions have only limited application in preparative synthesis. One should note, however, a recently developed original solid-phase method for the synthesis of 2-arylnitroethenes from styrenes under microwave radiation in the presence of Fe(NO₃)₃ · 9 H₂O or an NH₄NO₃–clay system.¹⁵

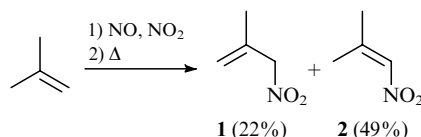
Likewise, we do not consider reactions of alkenes with NOCl discussed in detail previously,¹⁶ since this reagent has rarely been used for alkene functionalisation in recent years.¹⁷

II. Reactions of alkenes with NO

Although the NO molecule has an unpaired electron, it is characterised by its low activity toward potential acceptors of free radicals.¹⁸

At present, evidence is available that NO cannot add directly to alkenes. It was reported back in 1957 that meticulously purified NO can be kept in contact with liquid alkenes for a few days without noticeable interactions.¹⁹ It was reported later that pure NO did not react with functionally substituted alkenes (allyl benzyl ether, acetylcyclohexene) or with 1,4-diphenylbuta-1,3-diene.²⁰ It was also found that alkenes with electron-donating substituents at a double bond (butyl vinyl ether and silyloxycyclohexene) undergo changes in the presence of NO but no nitrogen-containing compounds are formed.

On the other hand, there are rather many examples where nitrogen-containing products are obtained in NO–alkene systems. In the study mentioned above,¹⁹ isobutene reacted with NO (from a gas cylinder) containing an admixture of NO₂ to give nitroisobutene **1** and a labile compound with unknown structure, which decomposed during high-vacuum distillation to give nitroalkene **2**.

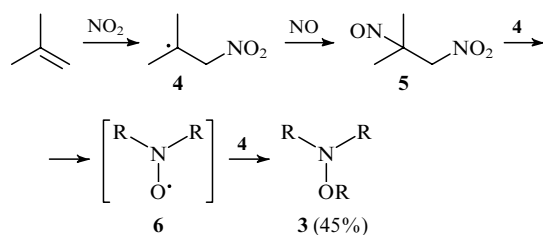


Brown¹⁹ emphasised that traces of NO₂ in NO are a prerequisite for the reaction. It was assumed that it is NO₂ that triggers the free radical process which continuously regenerates NO₂. This hypothesis was confirmed by the well-known ability of free radicals (including alkyl radicals) to convert NO into NO₂.²¹ According to more accurate data reported later,²² the reaction in the NO–isobutene system yields a very labile hydroxylamine **3** as the main product. The latter is presumably formed as a result of successive reaction of NO with three nitro-*tert*-butyl radicals **4** (which result from the addition of NO₂ present in NO to the alkene) *via* the nitro nitroso compound **5** and the iminoxyl radical **6**.

A V Stepanov, V V Veselovsky N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 19991 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 135 88 54. E-mail: step@ioc.ac.ru (A V Stepanov), ves@ioc.ac.ru (V V Veselovsky)

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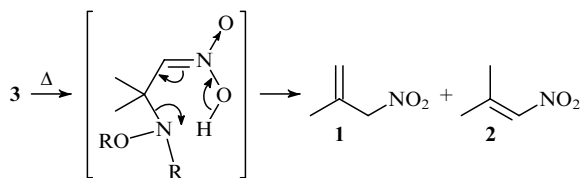
Uspekhi Khimii 72 (4) 363–378 (2003); translated by S S Veselyi



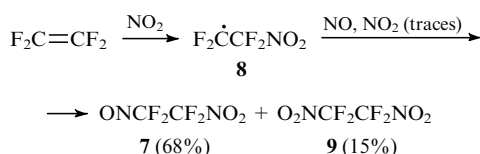
$\text{R} = \text{CMe}_2\text{CH}_2\text{NO}_2$.

It should be noted that the radical **6** was detected in an ESR study of this reaction.²³ In addition, nitro-*tert*-butyl radicals **4** were also identified. It was noted that the addition of oxygen to the reaction medium accelerated the process considerably; this confirms the activating role of NO_2 , the concentration of which in the reaction mixture increases due to the oxidation of NO.

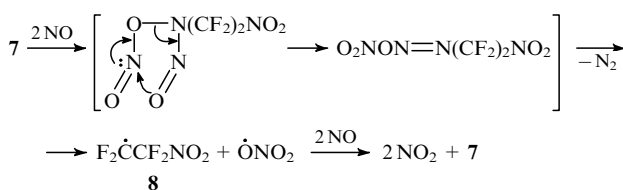
On moderate heating, hydroxylamine **3** gives a mixture of nitroisobutenes **1** and **2** in the ratio 1 : 4 and in an overall yield of 85%. It is assumed that the reaction occurs *via* a six-membered transition state.²²



The relatively stable 1-nitro-2-nitroso-1,1,2,2-tetrafluoroethane **7**, which is akin to the intermediate **5** postulated by Phillips and Coyne,²² is the major product formed in the NO – tetrafluoroethylene system.²⁴



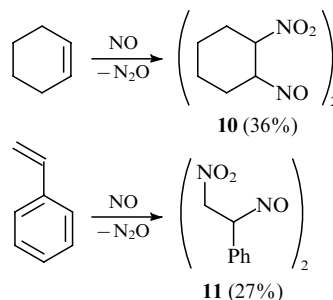
The suggested reaction mechanism also involves initiation of the chain process by NO_2 radicals, which are more reactive than NO. The resulting radical **8** is subsequently recombined with NO to give the nitro nitroso compound **7**. This mechanism is confirmed by the fact that no 1,2-dinitrosotetrafluoroethylene was present in the reaction products; the presence of the latter would have meant that the process was initiated by direct addition of NO to the alkene. The authors noted that the reaction was accelerated considerably on addition of NO_2 to the reaction mixture and suggested the possible ways of its formation. In particular, the reaction of perfluoronitronitrosoethane **7** with an excess of NO may give two NO_2 molecules per molecule of the nitroso compound.



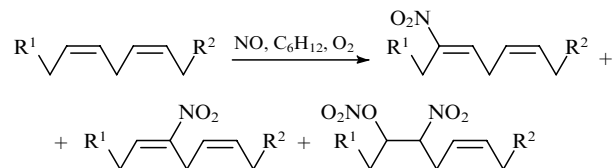
When the concentrations of NO_2 and NO become comparable, the recombination of NO_2 with the radical **8**, which terminates the chain process and gives the side dinitro compound **9**, acquires a progressively significant role.

The formation of NO_2 is also possible as a result of disproportionation $3\text{NO} \rightarrow \text{NO}_2 + \text{N}_2\text{O}$, which is favoured by an increase in pressure.

For example, it was found²⁵ that thoroughly purified NO reacted at a noticeable rate with cyclohexene or styrene only at pressures above 5 atm; a GC/MS study of the gaseous reaction products revealed the presence of N_2O . At 7 atm, the corresponding dimeric nitro nitroso compounds **10** and **11** were isolated as the main reaction products; their structures were established by X-ray diffraction analysis. However, when this reaction was carried out with raw NO under atmospheric pressure, analysis of the gas mixture also showed that a small amount of N_2O was present.²⁶



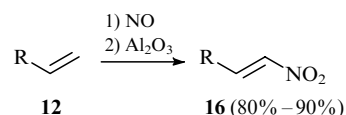
The fact that the presence of NO_2 plays a key role in the reaction of NO with alkenes is also confirmed by results of other studies^{27,28} where linoleic and arachidonic acids and their esters were used as substrates (as models of unsaturated lipids). The air equilibrated reactions were carried out in cyclohexane or benzene. Complex product mixtures were obtained; based on spectroscopic data, nitroalkenes and nitro nitrates were the main components of these mixtures. It was noted that this process was virtually not observed if the reaction mixture did not contact air.



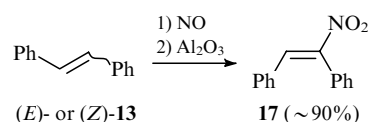
$\text{R}^1 = (\text{CH}_2)_3\text{Me}$, $\text{R}^2 = (\text{CH}_2)_6\text{CO}_2\text{Et}$; $\text{R}^1 = (\text{CH}_2)_6\text{CO}_2\text{Et}$, $\text{R}^2 = (\text{CH}_2)_3\text{Me}$.

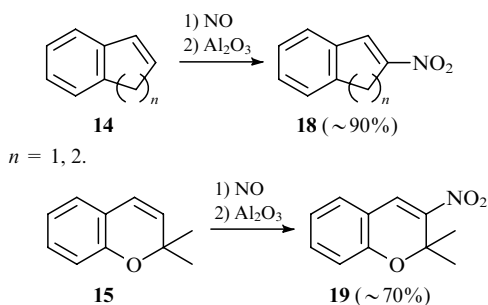
It is evident from the examples described above that reactions in alkene – NO systems are not straightforward; as a rule, they give mixtures of products. What is more, their results depend on the purity of nitrogen oxide used. However, studies of the nature of processes in this system have made it possible to develop an efficient method for converting mono- and disubstituted alkenes of the type **12** – **15** into conjugated nitro derivatives.^{29–31}

According to the standard procedure, a solution of an alkene in dichloroethane is stirred under NO, then acidic alumina is added to the reaction mixture, which is refluxed for a short time. The yields of the corresponding vinylnitro compounds **16** – **19** reach 90%. It was found later that treatment with Al_2O_3 can be excluded by performing the reaction in the presence of H-zeolites.³²



$\text{R} = \text{Alk}, \text{Ar}, (\text{CH}_2)_3\text{X}$; $\text{X} = \text{CH}_2\text{Ac}, \text{OSiMe}_2\text{Bu}^t, \text{OAlk}$.

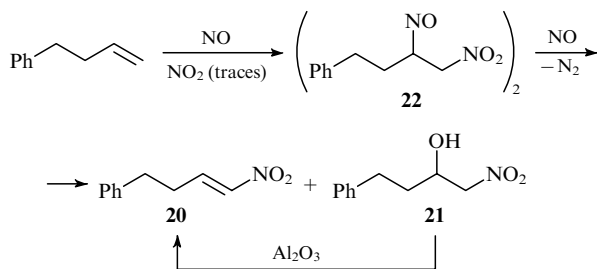




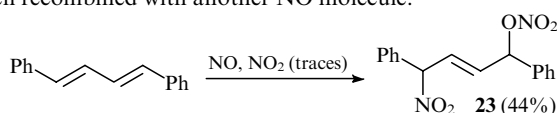
A detailed study of the characteristic features of this process using 4-phenylbut-1-ene as an example made it possible to reveal certain regularities. It was found that complete conversion of the alkene requires four equivalents of NO. A mixture ($\sim 4:1$) of the vinylnitro compound **20** and the nitro alcohol **21** is formed initially (Al_2O_3 is used for the dehydration of the latter). Analysis of the reaction products revealed its stoichiometry:



Using a lesser amount of NO, Hata *et al.*³⁰ isolated the dimer of an intermediate nitro nitroso compound **22**, which reacts with NO to give nitroalkene **20** with liberation of one equivalent of N_2 .

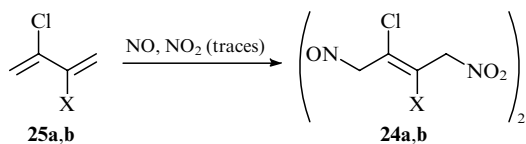


As noted above, there is evidence that thoroughly purified NO does not react with 1,4-diphenylbuta-1,3-diene.²⁰ This observation contradicts earlier data,³³ according to which the reaction of NO with 1,4-diphenylbuta-1,3-diene gives the nitro nitrate **23**. However, it was assumed that the chain radical process is initiated by direct addition of NO to the diene to give an allyl radical, which then recombined with another NO molecule.

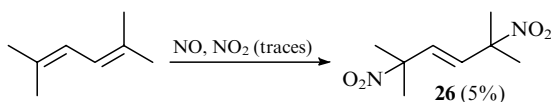


The accumulation of NO_2 , which gives rise to the dinitro derivative **23**, is rationalised as follows: the nitroso compound formed initially can sequentially add two NO molecules to give the $\cdot\text{ONO}_2$ radical. The latter reacts with NO to give two molecules of nitrogen dioxide, which competes with NO as the initiator of the radical chain process.

The suggested mechanism also offers an explanation of the formation of dimeric nitroso compound **24a,b** from 2-chloro- (**25a**) and 2,3-dichlorobuta-1,3-diene (**25b**) under similar conditions. In addition, this reaction gives polymers which, according to IR spectroscopic data, contain NO_2 and ONO_2 functional groups. Complete conversion of 2,5-dimethylhexa-2,4-diene afforded a quite stable dinitro compound **26** and a polymeric product.³³



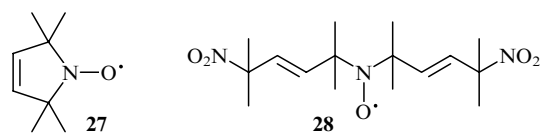
$\text{X} = \text{H} \text{ (a, 15\%)}, \text{Cl} \text{ (b, 40\%)}$.



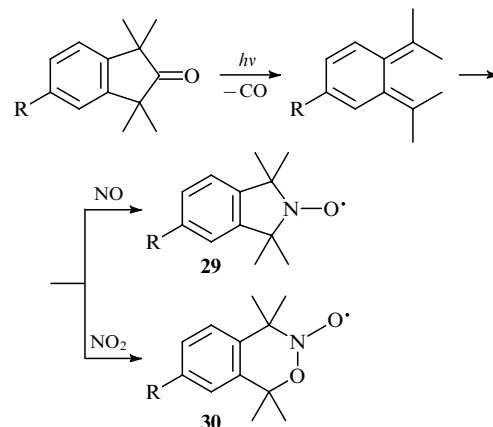
It should be noted that the reactions of NO with di(poly)enes are currently considered as a promising way to solve the problem of *in vivo* monitoring of this biologically important molecule³⁴ using the ESR method. In particular, it was found³⁵ that absorption of NO with such conjugated polyenes as vitamins A and D₃, as well as β -carotene, results in the appearance of distinct signals of iminoxyl radicals in ESR spectra. It was noted that NO_2 addition products could not be detected in the reaction mixtures.

Treatment of 2,5-dimethylhexa-2,4-diene with nitrogen(II) oxide also resulted in the appearance, in the ESR spectrum, of signals of an iminoxyl radical,^{36,37} which is assumed to have the cyclic structure **27**. However, attempts to isolate it failed.³⁸

However, as was shown later,²⁰ the signals in the ESR spectrum recorded in this case are due to the presence of the iminoxyl radical **28**, which is formed upon initiation of the process by nitrogen(IV) oxide present in NO as an admixture, and the formation of a nitroallyl radical intermediate.



The idea of using dienes as efficient NO traps in biological objects was implemented using *o*-quinodimethanes, which can be obtained by photolysis of the corresponding indanones.^{39,40}

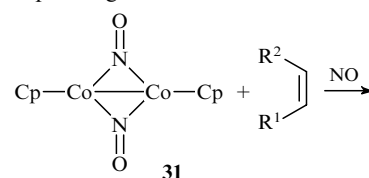


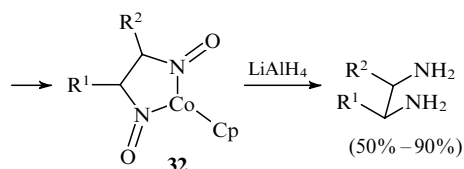
$\text{R} = \text{CO}_2\text{H}, \text{Et}_3\text{N}^+\text{CH}_2.$

Stable iminoxyl radicals **29** formed upon reactions of quinodimethanes with NO can be reliably detected by ESR. Hydrophilic properties required for the use of these compounds in biological systems are provided by incorporation of substituents ($\text{R} = \text{CO}_2\text{H}, \text{Et}_3\text{N}^+\text{CH}_2$). It is of interest that the ESR spectra of reaction mixtures also contain traces of radicals **30** resulting from the addition of NO_2 to dienes.

In conclusion, let us note certain special methods that make it possible to obtain NO addition products of alkenes.

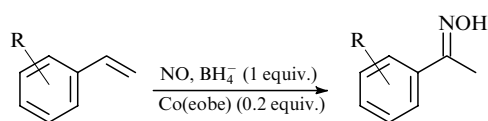
For example, the addition of the NO-containing cobalt(II) complex **31** to mono- and disubstituted alkenes has been reported.⁴¹ The resulting adducts **32** can be reduced to the corresponding diamines.



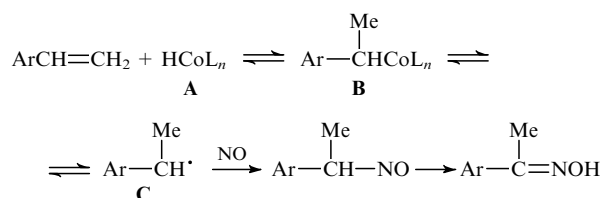


$R^1, R^2 = \text{H, Alk, Ar}; R^1 - R^2 = (\text{CH}_2)_n; n = 3, 4.$

The ability of NO to add to alkenes by catalysis with Co(II) complexes is well known. The method involves the initial addition of the hydride complex **A** generated *in situ* to an alkene, dissociation of the resulting metal–carbene adduct **B** to release the alkyl radical **C** and recombination of the latter with NO. The resulting nitroso compound quickly rearranges into an oxime.⁴² In this case, the involvement of coordination-bound NO in the process can be ruled out,⁴³ since the addition of a stronger ligand, *viz.*, pyridine, does not inhibit the reaction.

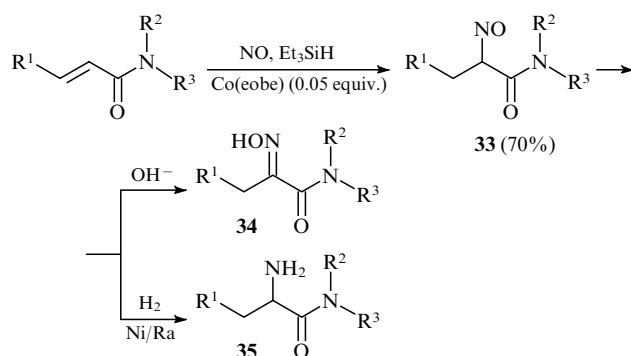


$R = \text{Alk, OAlk, Hal}; \text{Co(eobe)} = \text{EtO}_2\text{C}-\text{C}_6\text{H}_4-\text{Co}(\text{O})_2-\text{C}_6\text{H}_4-\text{CO}_2\text{Et}.$



The efficiency of this approach was first demonstrated with the transformation of substituted styrenes into the corresponding oximes as an example.^{42, 43} In polar aprotic solvents, the reaction occurs slowly and in moderate yields (40%–60%). The best results were obtained in a mixture of dimethoxyethane and Pr^iOH . In this case, acetophenone oxime was obtained in 83% yield.

The method also proved to be efficient for the nitrosation of α, β -unsaturated amides. In this case, the Co(II) hydride complex was generated using Et_3SiH . The resulting nitroso compounds **33** can be transformed into oximes **34** or reduced with Raney nickel into amino acid derivatives **35**.⁴⁴

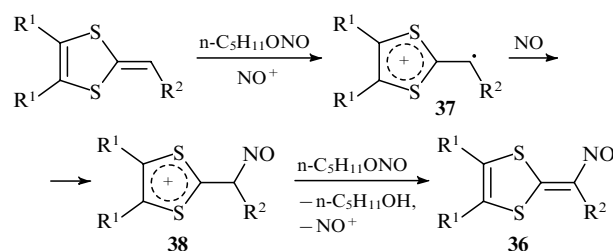


$R^1 = \text{H, Alk}; R^2, R^3 = \text{Alk, Ar, ArCH}_2.$

III. Reactions of alkenes with alkyl nitrites

Alkyl nitrites react only with double bonds incorporated in readily polarisable conjugated systems. In particular, it was found that dithiafulvenes react with *n*-pentyl nitrite in CH_2Cl_2 to give the

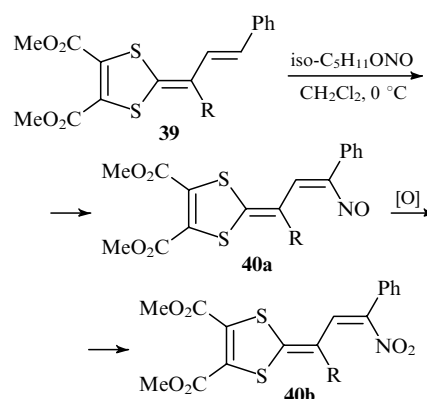
corresponding nitroso compounds **36** in 60%–70% yields.^{45–47} Diselenafulvenes react with alkyl nitrites in a similar way.⁴⁸



$R^1 = \text{CO}_2\text{Me, Ar, Me, SMe}; R^2 = \text{Ar, COMe, CHO}.$

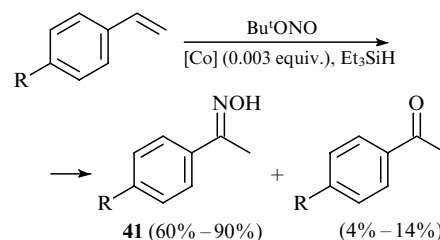
The proposed reaction mechanism⁴⁵ involves the generation of the NO^+ cation from nitrite; however, owing to the low electrophilicity of the cation, it can only participate in electron transfer; in such a case, it is oxidised into NO. The alkene is converted into the radical cation **37**. Recombination of the latter with NO followed by the reaction of the resulting cation **38** with a second nitrite molecule gives the nitro compound **36** and pentanol; the nitronium ion is regenerated.

Dithiafulvene derivatives **39** are even more reactive with respect to nitrites; under mild conditions, they give unstable nitroso compounds **40a**, which are readily oxidised with atmospheric oxygen into the corresponding nitro derivatives **40b**.⁴⁹



$R = \text{Me, CF}_3, \text{CN}.$

Nitrosation of less reactive substrates with alkyl nitrites can only be carried out under catalysis with Co(II) complexes; this method turned out to be more efficient and more convenient in preparative synthesis than the Co(II)-catalysed reaction of alkenes with NO (see Section II). This is obviously due to the higher electrophilicity of the NO^+ cation in comparison with NO and also due to the fact that this reaction is carried out under homogeneous conditions. For example, nitrosation of substituted styrenes in the presence of catalytic amounts of a porphyrin–Co(II) complex and Et_3SiH as a reducing agent gives oximes **41** with an admixture of the corresponding acetophenones.⁵⁰

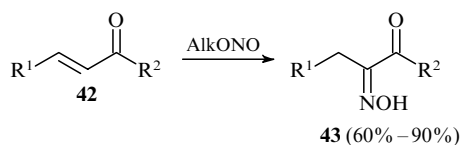


$R = \text{H, Me, Cl, CO}_2\text{Me, NO}_2.$

The use of Fe(III) acetylacetonate as a catalyst has also been reported.⁵¹ In this case, mono- and dialkyl-substituted alkenes

gave dimers of the corresponding nitroso compounds in ~ 50% yields.

The use of Co(II)-based catalysts for the nitrosation of linear alkenes **42** with electron-withdrawing substituents by alkyl nitrites was found to be very efficient. The reaction gives oximes **43** in high yields.⁵⁰ Dienes **44** as substrates give the corresponding conjugated oximes.⁵⁰ It was noted that the yields of oximes **43** can be increased noticeably using PhSiH₃ as the reducing agent.^{52, 53}

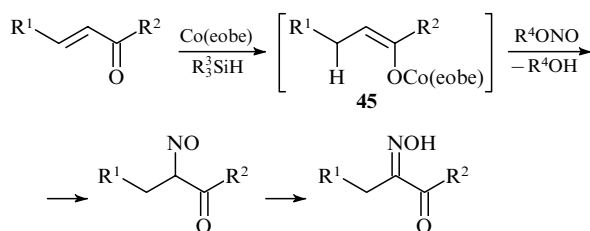


R¹ = H, Alk; R² = H, Alk, OAlk.



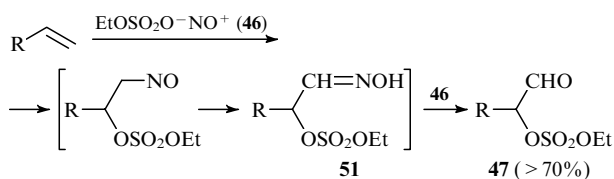
R¹ = H, Bu^t, NR₂², OAlk, OAr; R² = Alk.

Styrenes probably react with nitrites according to a mechanism similar to that suggested for the reaction with NO, whereas the conversions of α,β-unsaturated carbonyl compounds presumably involve cobalt enolate **45**.⁵³

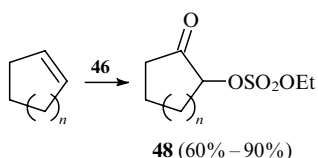


R¹ = H, Alk; R² = Alk, Ph, NMePh, OAlk, OBn; R³ = Et, Ph; R⁴ = Alk.

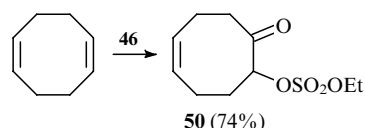
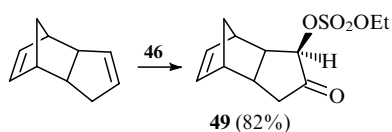
There is yet another method for using alkyl nitrites for the nitrosation of alkenes.^{54, 55} Thus, a highly reactive intermediate is generated from EtONO upon treatment with SO₃; it is believed to have an ionic structure, viz., EtOSO₂O[−]NO⁺ (**46**). The reaction of an excess of the reagent **46** with various alkenes affords sulfates of α-hydroxy aldehydes (**47**) or ketones (**48–50**).



R = H, Alk.

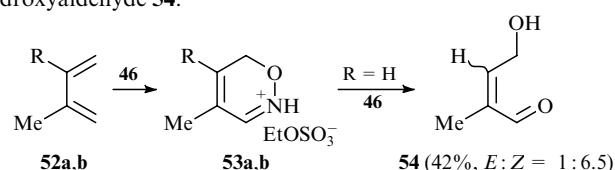


n = 1, 2, 4.



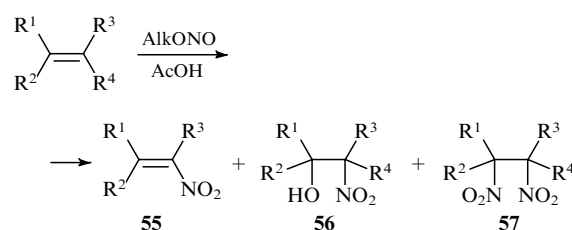
The reagent **46** also serves as an oxidant which converts the intermediate oximes **51** into the corresponding carbonyl compounds. The proposed reaction mechanism is confirmed by the fact that it is possible to isolate dimers of nitroso intermediates using one equivalent of the reagent **46** with respect to the alkene. This reaction was found to be chemoselective. In particular, only the least hindered double bond is involved in the cyclopentadiene dimer; in the case of cyclooctadiene, the monoadduct **50** can be obtained in high yield.

The reaction of isoprene (**52a**) or dimethylbutadiene (**52b**) with a stoichiometric amount of the reagent **46** ends in the formation of the corresponding oxazonium salts **53a,b**. The reaction of the salt **53a** with an excess of the reagent affords hydroxyaldehyde **54**.



R = H (a), Me (b).

In conclusion, we would like to note the ability of alkyl nitrites to generate reactive species in acidic media, which react with alkenes. For example, treatment of acyclic di-, tri- and tetrasubstituted alkenes with pentyl or butyl nitrite in AcOH gives mixtures of products **55–57**, the composition of which varies depending on the substrate structure.⁵⁶

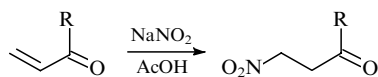


R ¹	R ²	R ³	R ⁴	Yield (%)		
				55	56	57
Ph	Ph	H	H	27	25	—
Ph	Me	H	H	—	33	—
Me	CO ₂ Me	H	H	—	20	—
Et	Et	Me	H	—	23	43
Me	Me	Me	Me	—	6	30

IV. Reactions involving nitrous acid salts

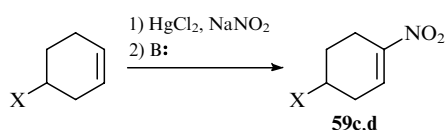
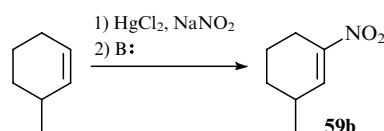
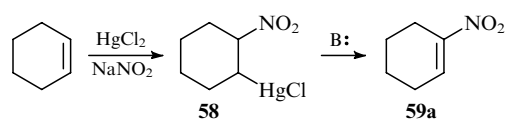
Nitrous acid salts can serve as sources of various neutral species (NO, NO₂, N₂O₃, N₂O₄) and ions (NO₂[−], NO₂⁺) resulting from disproportionation of unstable nitrous acid formed.⁵⁷ Each of these species can, in one way or another, react with alkenes.

For example, the NO₂[−] anion can undergo Michael-type addition to vinyl ketones on treatment of the latter with NaNO₂ in AcOH, giving β-nitro derivatives in satisfactory yields.⁵⁸

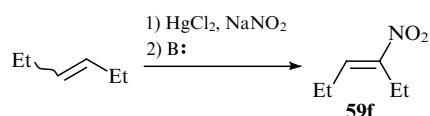
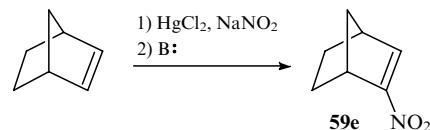


R = Me (82%), Et (46%), Prⁱ (42%), Prⁿ (57%), Buⁿ (65%), n-C₅H₁₁ (68%).

Furthermore, procedures based on the reaction of NO₂[−] and a carbocation generated from an alkene are also known. For example, chloromercuriation of mono- and disubstituted alkenes in the presence of NaNO₂ gives adducts of the type **58**, which can be transformed without isolation into the corresponding nitroalkenes **59a–f** in ~80% yields upon treatment with a base.⁵⁹ Mercury perchlorate can be used instead of HgCl₂.⁶⁰ It should be noted that reactions with hex-3-enes stereoselectively give the *E*-nitro derivative **59f** irrespective of the configuration of the starting alkene.



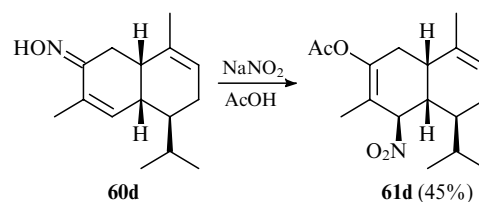
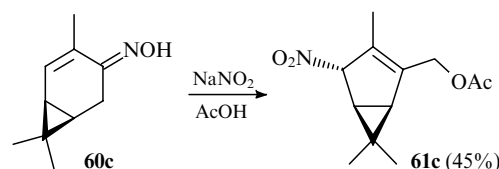
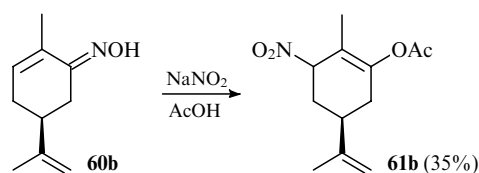
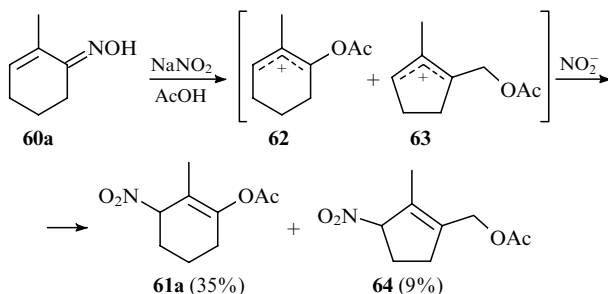
X = CN (**c**), CO₂Me (**d**).



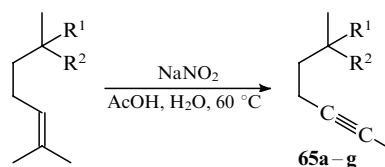
B: is a base

The conversion of conjugated oximes **60a–d** into nitro acetates **61a–d** on treatment with NaNO₂ in acetic acid was explained by reactions of allylic cations of the types **62** and **63** with NO₂[−] (see Ref. 61). In this case, the system NaNO₂–AcOH (HNO₂) plays a double role, *viz.*, it also cleaves oximes to give carbenium intermediates.

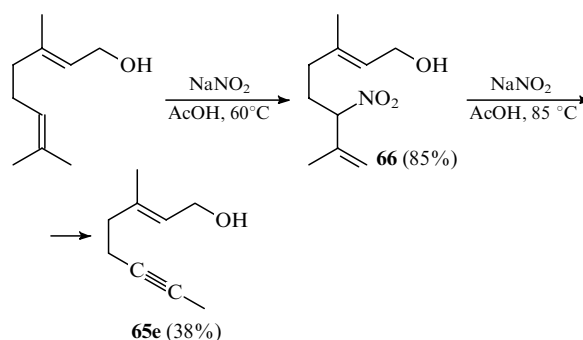
Oxime **60a** gave, in addition to the main product **61a**, the minor cyclopentene **64** corresponding to the carbocation **63**. The predominant pathway of the reaction with the carene derivative **60c** results in the nitro derivative **61c**.



In 1985, Abidi⁶² reported an unusual transformation of the isopropylidene fragment of linear monoisoprenoid derivatives into a methylethynyl fragment, which occurred upon treatment with NaNO₂ in aqueous acetic acid (see also the subsequent papers by Abidi^{63,64}). It should be noted here that later studies of this reaction (formal methane elimination) with the same and related substrates^{65,66} could not reproduce the previously reported^{62–64} high yields (60%–90%) of the corresponding methylacetylenes **65a–g**. For example, the yield of the acetylene **65e** from geraniol was no higher than 35%.⁶⁵

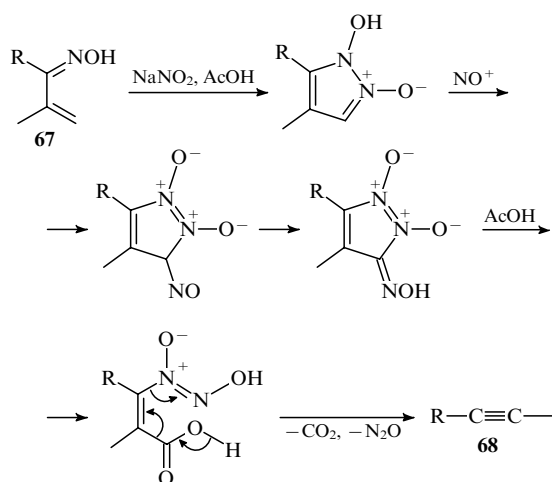


R¹ = H, R² = (CH₂)₂OH (**a**), CH₂CHO (**b**); R¹ = CH=CH₂, R² = OH, OAc, OMe (**c**); R¹, R² = (*E*)-CHCHO (**d**), (*E*)-CHCH₂OH (**e**), (*E*)-CHCH₂CH₂C(O)Me (**f**), (*E,E*)-CHCH₂CH₂C(Me)=CH₂CH₂OH (**g**) *etc.*



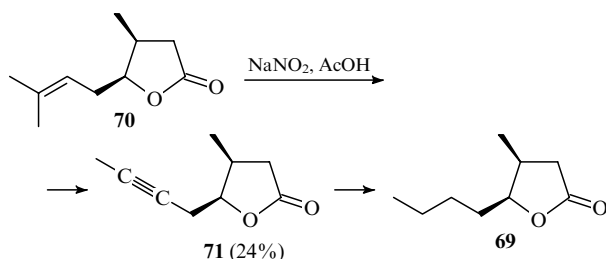
It was found that this reaction initially yields the nitro derivative **66**. Its treatment with sodium nitrite in acetic acid affords acetylene **65e** with evolution of an equivalent amount of CO₂.

Attempts to rationalise the mechanism of this process^{65,66} led to the assumption that oximes of the type **67** are precursors of acetylenes **65**. It is well known that nitrosation of oximes of conjugated aliphatic ketones can give pyrazole derivatives that can subsequently undergo conversions indicated in the scheme.⁶⁷ In fact, oximes **67** (obtained by an independent synthesis) gave the corresponding alkynes **68** in up to 20% yields upon treatment with NaNO₂ in acetic acid.⁶⁶

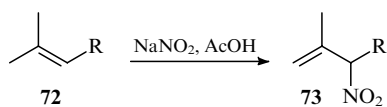


R = CH₂Ph, (CH₂)₉Me, CH₂CH(Me)CH₂CH₂OAc,
CH₂CH(Me)OCOPh.

Although the conversion of isoprenoids into methylacetylenes of the type **65** on treatment with NaNO_2 in acetic acid occurs in low yields, this was used in the synthesis of a natural lactone **69**, the key stage of which involves the conversion of a butanolide **70** into acetylene **71**.⁶⁸

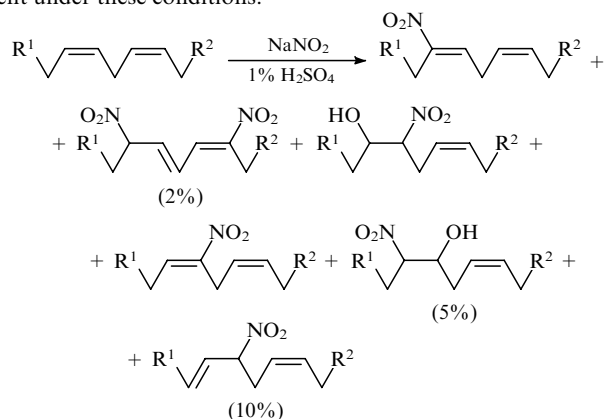


Of particular interest is the conversion of geraniol into a nitro derivative **66**, because there is only a limited number of ways for the selective functionalisation of linear isoprenoids.⁶⁹ As was shown later, this reaction is of rather general character and can involve various isoprenoids **72**, including those with additional functional groups.^{70–74} The nitro derivatives **73** obtained by this method have a large synthetic potential and can be used in directed syntheses of natural terpenes.^{70, 72–75}

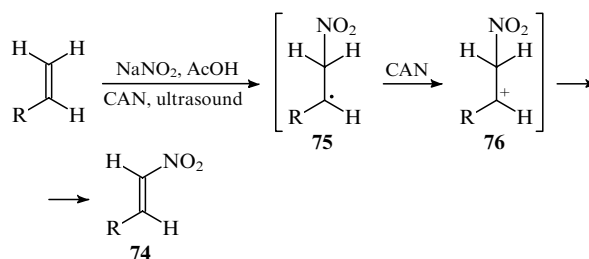
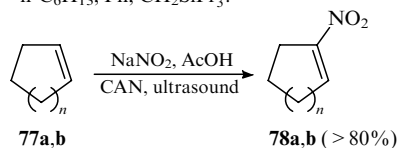
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It is of note that the mechanisms of reactions of alkenes under the action of metal nitrites in acidic media are still a matter of discussion. This is due to the diversity of the reactive species formed. Presumably, the pathway which the process follows, and hence the decisive role of a particular species in conversions of specific olefins, depends on the nature of the unsaturated substrate as well. For instance, unlike the trisubstituted alkenes **72**, ethyl linoleate gives a mixture of diverse products upon treatment with NaNO_2 in an acidic medium.⁷⁶ Their formation is explained by the simultaneous occurrence of at least three processes: a free-radical process involving NO_2 , an ionic process involving NO^+ or NO_2^+ and a direct reaction with N_2O_3 or

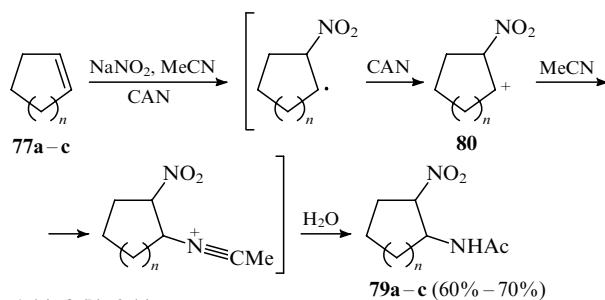
N₂O₄.⁷⁶ It was also assumed that nitric acid present in the system in a small concentration can serve as a nitrosating or nitrating agent under these conditions.⁷⁷


$$\begin{aligned} \text{R}^1 &= (\text{CH}_2)_3\text{Me}, \text{R}^2 = (\text{CH}_2)_6\text{CO}_2\text{Et}; \\ \text{R}^1 &= (\text{CH}_2)_6\text{CO}_2\text{Et}, \text{R}^2 = (\text{CH}_2)_3\text{Me}. \end{aligned}$$

Conversions of alkenes upon treatment with the $\text{NaNO}_2\text{--AcOH}$ system in the presence of cerium(IV) ammonium nitrate (CAN) is of interest from the viewpoint of preparative synthesis.^{78,79} The reaction occurs particularly efficiently under sonication.⁷⁹ α,β -Unsaturated nitro compounds **74** were obtained in high yields by this method. A scheme explaining the conversions of linear alkenes, taking the regio- and stereoselectivity of the reactions into account, was suggested. Initially, NO_2 adds to double bonds in alkenes to give alkyl radicals **75**; the latter are oxidised with cerium(IV) ammonium nitrate into carbocations **76**, which eliminate a proton to give more thermodynamically favourable α,β -unsaturated nitro compounds **74** with a *trans*-configuration. Under these conditions, cycloalkenes **77a,b** give nitro derivatives **78a,b**.


$$R = n\text{-C}_6\text{H}_{13}, \text{Ph}, \text{CH}_2\text{SiPr}_3^i$$
 $n = 1$ (**a**), 2 (**b**).

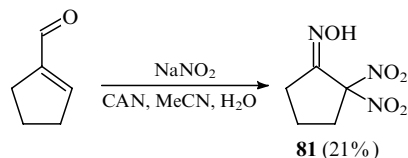
The formation of the carbocation intermediate **76** is confirmed by the fact that the reaction of cycloalkenes **77a–c** in acetonitrile gives nitroacetamides **79a–c**, which are presumably



$n = 1$ (a), 2 (b), 3 (c).

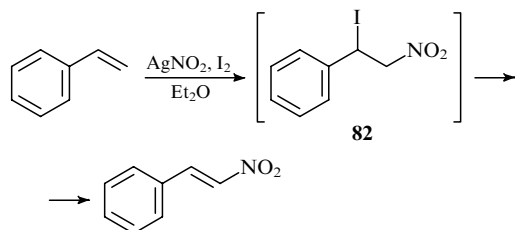
formed due to the stabilisation of the carbocation **80** upon the addition of MeCN.⁸⁰

Quite an unexpected result was obtained under similar conditions with cyclopentenecarbaldehyde as the substrate: the reaction yielded dinitrooxime **81**. It was shown using labelled $\text{Na}^{15}\text{NO}_2$ that the latter is the only source of nitrogen atoms incorporated into compound **81**.⁸¹

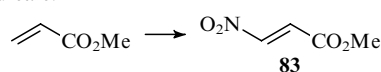


There is yet another approach to the use of nitrous acid salts as sources of reactive intermediates: nitrile halides, *e.g.*, nitrile iodide, are generated *in situ* from the salts under the action of halogens. Nitrile iodide was first generated using the reaction of AgNO_2 with I_2 .^{82,83} Theoretically, it may be assumed that the heterolysis of nitrile iodide occurs with formation of either NO_2^+ ions and I^- , or NO^+ and I^- ; furthermore, homolysis into free radicals is also possible (see Ref. 82 and references cited therein).

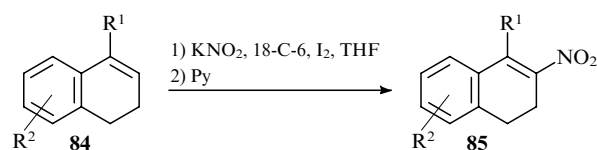
The reaction of AgNO_2 with I_2 in the presence of an alkene, *e.g.*, styrene, results in the labile nitro iodide **82**, which readily undergoes dehydroiodination on treatment with a base to give ω -nitrostyrene.⁸² This regioselectivity of the process suggests that the reagent formed cannot react with the alkene as iodonium nitrite INO_2 .



With methyl acrylate as the substrate, a terminal nitro derivative **83** was obtained after treatment of the reaction mixture with a base; it may be concluded on this basis that INO_2 in this process is not an equivalent of NO_2^+ but rather a source of NO_2 radicals.



The use of more accessible sodium and potassium nitrites instead of AgNO_2 was a further development of this method.^{84–86} For example, treatment of a series of mono- and disubstituted alkenes with NaNO_2 and I_2 in an $\text{EtOAc}-(\text{CH}_2\text{OH})_2-\text{H}_2\text{O}$ mixture afforded the corresponding α,β -unsaturated nitro compounds in high yields.⁸⁴ The use of phase-transfer catalysis in order to intensify the process was also described. In particular, dihydronaphthalene derivatives **84** reacted with potassium nitrite and iodine in the presence of a crown ether (18-C-6) to give (after treatment with pyridine) nitro derivatives **85** in 50%–90% yields.⁸⁵ It was noted that the reaction occurred much faster under sonication.



$\text{R}^1 = \text{H}, \text{Ph}; \text{R}^2 = \text{H}, \text{OMe}.$

It is also of note that nitro derivatives can be obtained using the $\text{NaNO}_2-\text{I}_2-\text{CuO}-\text{HBF}_4$ system. The efficiency of this approach was demonstrated by the conversion of substituted

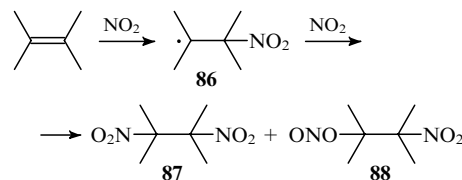
styrenes into nitrostyrenes; additional treatment with a base was not required under these conditions.⁸⁶

V. Reactions of NO_2 with alkenes

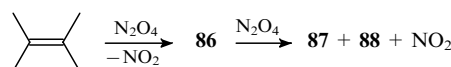
The reactions of NO_2 with alkenes have mostly been considered in the reviews published previously;^{8–12} therefore, this chapter only discusses the latest publications not included in those reviews.

To date, a number of mechanisms have been suggested for reactions of NO_2 with alkenes. Which one predominates depends on the reaction conditions. In fact, according to kinetic data, if the process is carried out in non-polar solvents, the reaction becomes second-order with respect to NO_2 with an increase in its concentration.⁸⁷ At low NO_2 concentrations, the formation of the alkyl radical **86** (pathway *a*) is the rate-determining step. Subsequently, the radical **86** recombines with the second NO_2 molecule to give dinitro compound **87** and nitro nitrite **88**. In more concentrated solutions, dimerisation of NO_2 increases the concentration of N_2O_4 , which obviously can also add to the alkene to give the radical **86** (pathway *b*), thus increasing the reaction order. Furthermore, one may not rule out the possibility that the alkyl radical **86** reacts with N_2O_4 to give the same products, *viz.*, **87** and **88**.⁸⁸

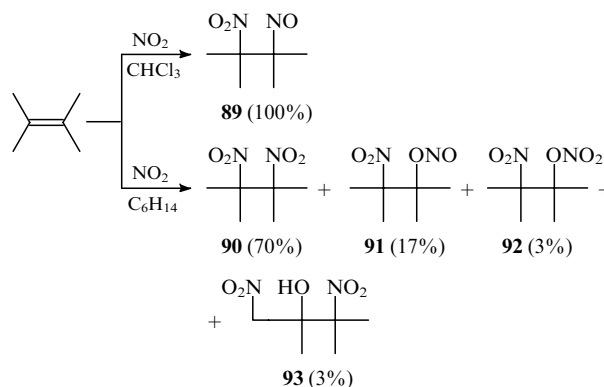
Pathway *a*



Pathway *b*

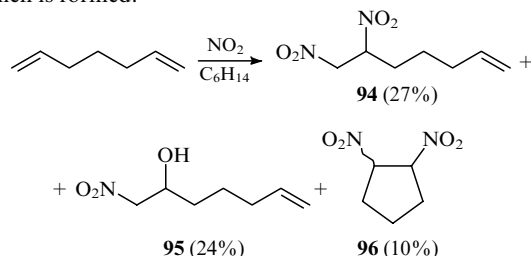


If the reaction is carried out in a more polar medium, another process starts to play a considerable role; it occurs by a heterolytic mechanism due to the presence of nitrosyl nitrate (NO^+NO_3^-) in solutions of NO_2 or N_2O_4 .^{89,90} The possibility of the existence of this compound was substantiated by calculations.^{91,92} The fact that alkenes can react with nitrosyl nitrate by a heterolytic mechanism follows from the formation of the corresponding nitro nitroso compounds.^{93,94} For example, treatment of 2,4-dimethylhexene with a solution of NO_2 in CHCl_3 results only in the nitro nitroso adduct **89**, whereas in hexane, this alkene gives a mixture of compounds **90**–**93**, which are formed in the reaction occurring by a homolytic mechanism.⁹⁴ The formation of the dinitro alcohol **93** results from the ability of nitrogen dioxide to abstract hydrogen from the carbon atom adjacent to the double bond to give an allylic radical. This process starts to play a significant role at very low NO_2 concentrations.⁹⁵ For example, a study of reactions of NO_2 with unsaturated fatty acids mainly

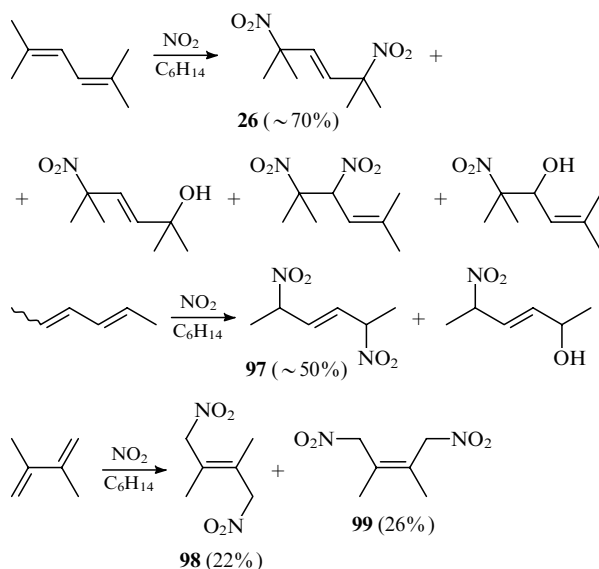


revealed allylic nitration products and the corresponding allyl hydroperoxides.^{96, 97}

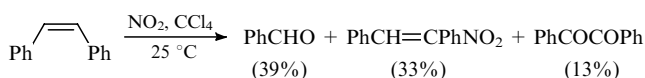
It should be noted that treatment of hexa-1,5-diene with a dilute solution of NO_2 in hexane gives not only the dinitro compound **94** and the nitro alcohol **95** but also the isomeric 1,2-dinitrocyclopentanes **96**.⁹⁸ The formation of the latter suggests that two NO_2 molecules can add to the diene independently; this is accompanied by intramolecular recombination of the biradical which is formed.



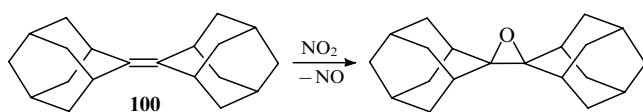
Conjugated dienes mostly give dinitro derivatives **26**, **97–99** under these conditions.⁹⁸ A small amount of compound **26** is also formed in the reaction of 2,5-dimethylhexa-2,4-diene with NO_2 .³³



NO_2 manifests considerable oxidising properties with respect to some substrates. For example, (*Z*)-stilbene reacts with NO_2 in CCl_4 to give benzaldehyde as the main reaction product formed due to oxidative fragmentation.⁹⁹



One should also note the interesting version of epoxidation of the sterically hindered tetrasubstituted alkene **100** on treatment with NO_2 .¹⁰⁰ The latter is reduced to NO . Using the smooth oxidation of NO to NO_2 , this reaction can be carried out either with a stoichiometric or a catalytic amount of NO_2 in the presence of oxygen.

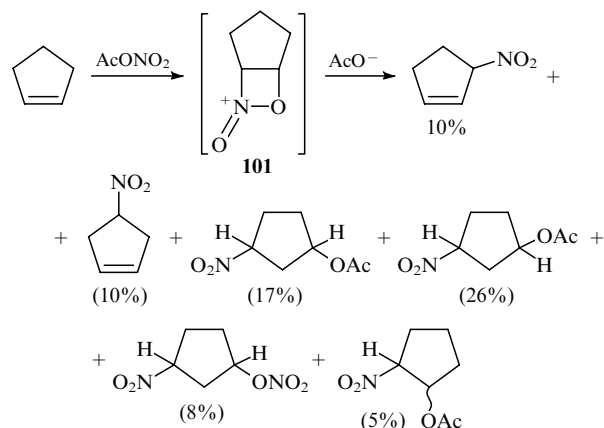


VI. Reactions of the NO_2^+ cation and its equivalents with alkenes

The NO_2^+ cation is generated from acetyl nitrate, which is usually obtained *in situ* from Ac_2O and concentrated nitric acid. It should be noted that the previously suggested mechanism of electrophilic

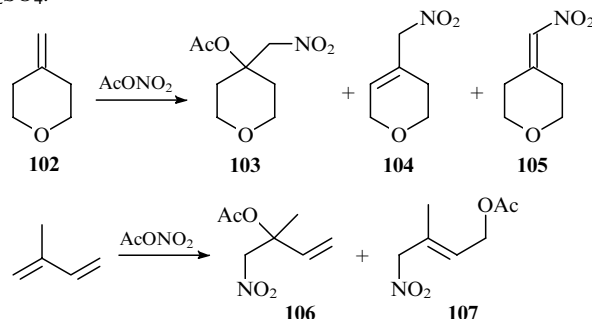
addition of NO_2^+ to a double bond to give a classical carbocation does not often allow one to explain the diversity of the resulting products and their structures (see, *e.g.*, Ref. 92 and references cited therein).

For example, the reaction of cyclopentene with AcONO_2 results in a mixture of at least six compounds. This mixture does not contain conjugated 1-nitrocyclopent-1-ene, the most thermodynamically favourable compound, the formation of which, due to deprotonation of the corresponding α -nitrocarbocation, could be expected.⁹² Analysis of these results made it possible to assume that this process can occur through initial [2 + 2]-cycloaddition of NO_2^+ to the double bond to give the cyclic cationoid intermediate **101**. Its subsequent reaction with the acetate anion, rearrangement and deprotonation of the intermediates result in a wide range of products. This hypothesis was also confirmed by semiempirical calculations for the ethylene- NO_2^+ system, according to which the cyclic ion of the type **101** corresponds to one of the potential energy minima.^{92, 101–103}



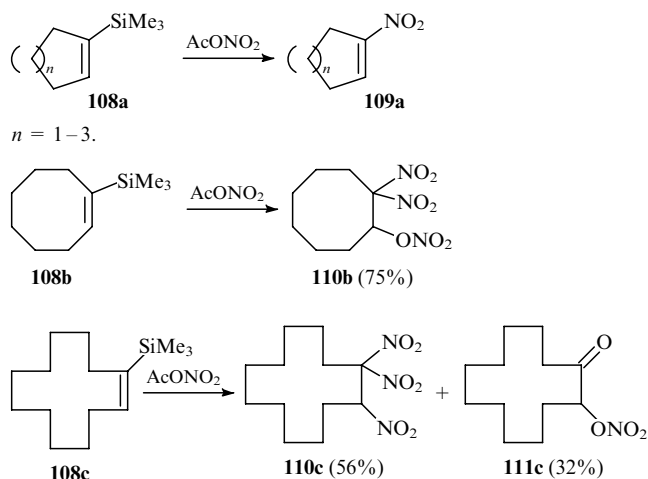
In fact, reactions of various alkenes with NO_2^+ generally yield allylic rather than conjugated nitro compounds. In particular, allylic nitro derivatives were isolated from a mixture of products obtained upon treatment of a derivative of an antibiotic milbemycin with acetyl nitrate.¹⁰⁴

Nitration of 4-methylidenetetrahydropyran **102** with nitric acid in Ac_2O gave the nitro acetate **103** as the major product; the ratio of the allylic (**104**) and vinylic (**105**) regioisomers in the reaction mixture was 2 : 1.¹⁰⁵ The reaction of acetyl nitrate with isoprene afforded a mixture of 1,2- (**106**) and 1,4-addition (**107**) products; the tertiary acetate **106** smoothly isomerises into the primary acetate **107** on treatment with a catalytic amount of H_2SO_4 .^{106, 107}

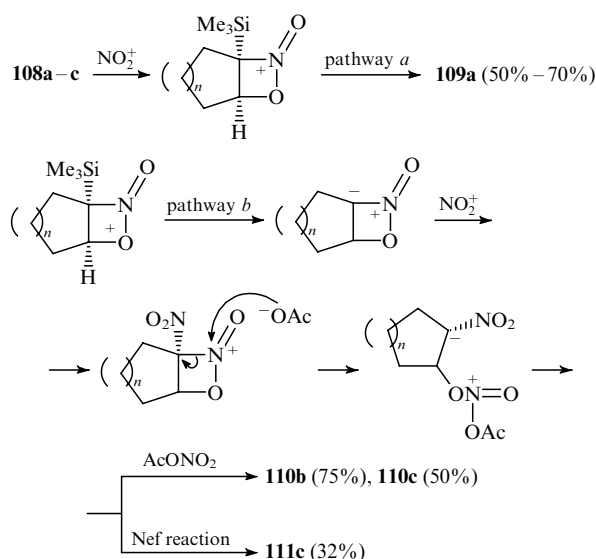


One of the most convincing confirmations of the four-centred addition mechanism of NO_2^+ to alkenes was obtained in a study of the reaction of acetyl nitrate with 1-trimethylsilylcycloalkenes **108a–c**, which resulted in different products depending on the ring size.¹⁰⁸ For instance, cyclopentene, cyclohexene and cycloheptene derivatives **108a** only give unsaturated nitro compounds **109a** in good yields (50%–70%). Under similar conditions, 1-trimethylsilylcyclooctene (**108b**) gives the dinitro nitrate **110b**;

the cyclododecadecene derivative **108c** gave the dinitro nitrate **110c** and the ketone **111c**.

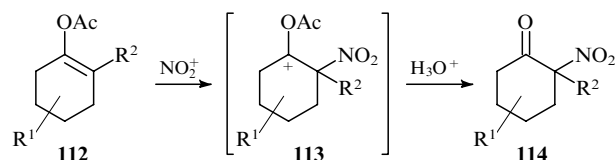


In these reactions, the trimethylsilyl substituent serves as the directing group in the addition of NO_2^+ to the double bond. The trimethylsilyl group is a better leaving group than hydrogen; this ensures the eventual formation of the conjugated nitro alkene **109a** (pathway *a*). It is believed¹⁰⁸ that the spatial arrangement of the trimethylsilyl substituent in large rings is unfavourable for the E_2 elimination. As a result, it is eliminated by the E_1 mechanism; the resulting carbanion is then converted to the products **110b,c** and **111c** (pathway *b*) on treatment with acetyl nitrate.



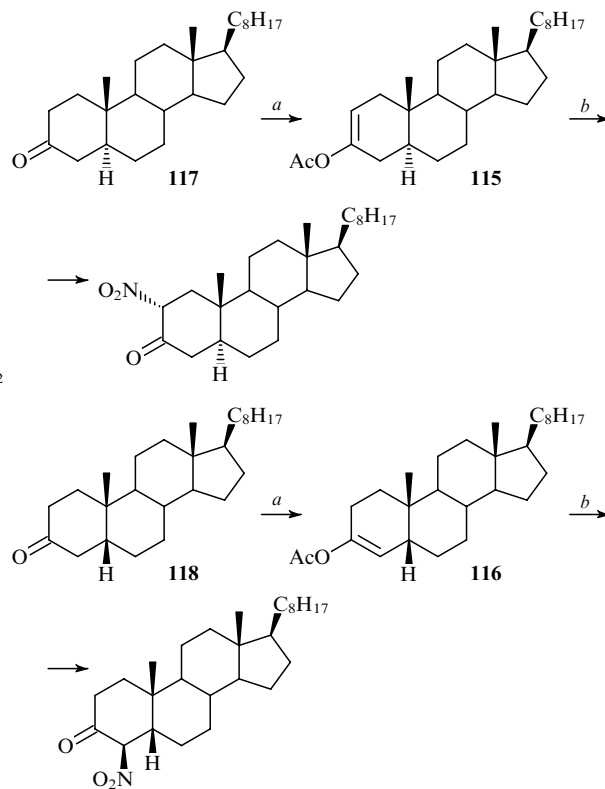
More examples are known in which acetyl nitrate reacts selectively with unsaturated substrates containing functional substituents at the double bond.

For example, the reaction of AcONO_2 with alkyl-substituted 1-acetoxycyclohexenes **112**, which occurs through deacetylation of the cation **113**, affords α -nitrocyclohexanones **114** in 70%–90% yields.¹⁰⁹ The yields of the corresponding ketones were subsequently increased to 80%–100% using trifluoroacetyl nitrate.¹¹⁰



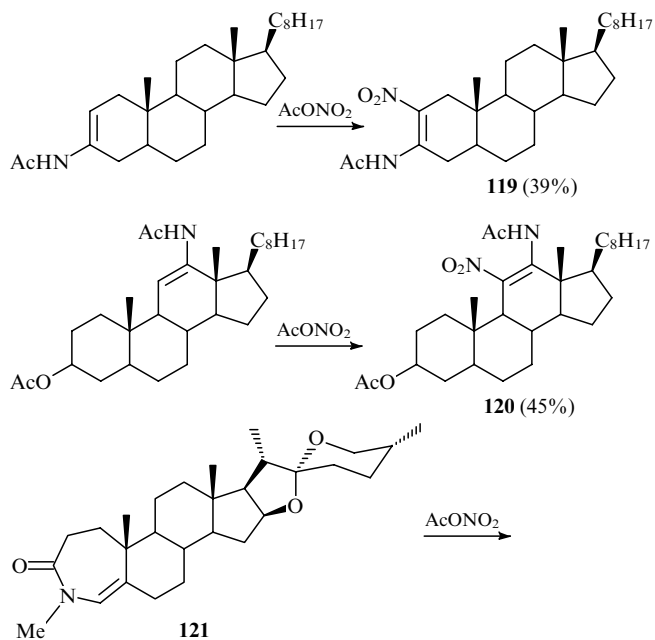
$\text{R}^1 = \text{Alk}, \text{R}^2 = \text{H}, \text{Me}.$

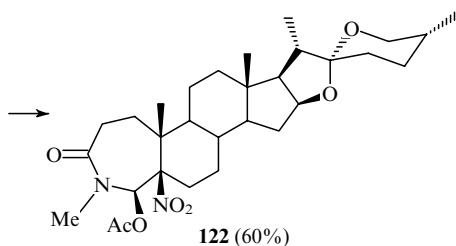
A similar reaction of enol acetates **115** and **116** was used for the regio- and stereoselective incorporation of a nitro group into isomeric ketosteroids **117** and **118**,¹¹¹ the direction of their enolisation is governed by the type of fusion of rings A and B.



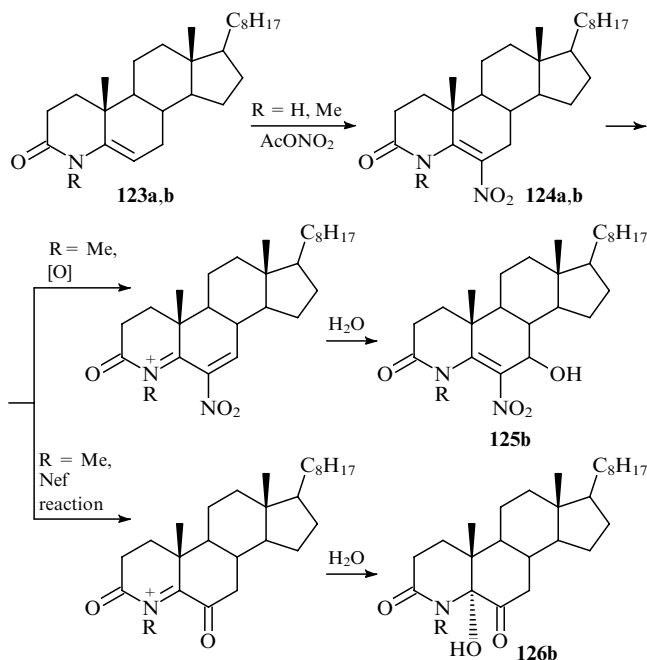
a — $\text{Ac}_2\text{O}, 4\text{-MeC}_6\text{H}_4\text{SO}_3\text{H}$; *b* — $\text{CF}_3\text{CO}_2\text{NO}_2, \text{CH}_2\text{Cl}_2.$

In enamides of the steroid series, the AcHN group directs the attack of the nitronium cation to the β -position with respect to the double bond, giving the nitro enamides **119** and **120**.¹¹² The enamide **121** gives the nitro acetate **122** under the same conditions.¹¹³



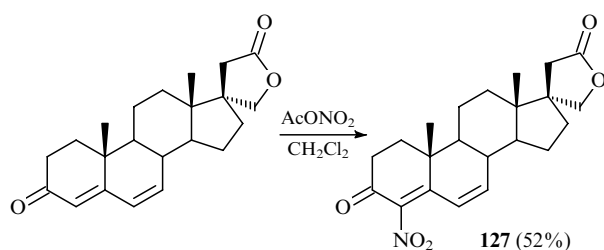


The nitration of the enamides **123a,b** gives different products, depending on the substituent R at the nitrogen atom.¹¹⁴ The unsubstituted amide **123a** yields the nitro alkene **124a** as the main product (55%), whereas the methylated derivative **123b** gives a mixture of the nitro alcohol **125b** and hydroxy ketone **126b** in moderate yield (20%). The difference between the reactivities of the amides **123a,b** is explained by the fact that the nitro compound **124a** can be stabilised due to the formation of an intramolecular hydrogen bond. The methyl derivative **124b** is unstable and undergoes further conversions as a result of the Nef reaction and allylic oxidation. In the case of the amide **124a**, both of the processes also occur, but the yield of the minor products is no higher than 15%.



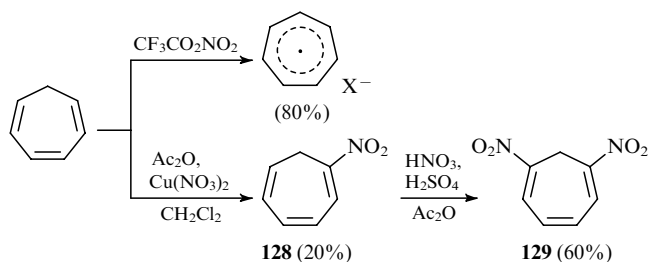
R = H (a), Me (b).

Probably, a unique example of a reaction of acetyl nitrate with a diene system conjugated with a carbonyl group has been reported by German chemists.¹¹⁵ The nitration of a pregnane ketosteroid, *viz.*, a canrenone derivative, unexpectedly resulted in a 4-nitro compound **127**, whereas the 6,7-double bond in the original dienone remained intact.



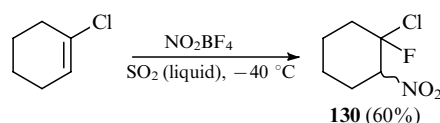
Furthermore, the unusual behaviour of cycloheptatriene is also noteworthy. Its conjugated system is oxidised on treatment with CF_3CONO_2 to give a tropylium cation.¹¹⁶ On the other hand, the reaction of cycloheptatriene with copper nitrate in Ac_2O gives

the 1-nitro derivative **128** in low yield.¹¹⁷ The role of copper ions is probably to inhibit the oxidation process. Subsequent nitration of the mononitro derivative **128** with acetyl nitrate gave the dinitro compound **129**.

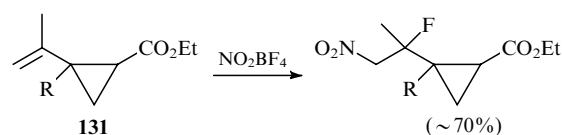


Nitronium tetrafluoroborate is yet another source of NO_2^+ known for a long time. As noted in an earlier review,¹¹⁸ its reaction with alkyl-substituted alkenes is not straightforward due to the formation of very reactive cationoid intermediates and can be accompanied by polymerisation. We will consider certain examples of reactions of alkenes with NO_2BF_4 which have not been covered in the review by Guk *et al.*¹¹⁸ or in later reviews.

Obviously, the nature of the products formed in the reactions of alkenes with NO_2BF_4 depends on the structure and environment of the cationoid centre, which appears in a reacting molecule in the first step of the process. For example, the reaction of 1-chlorocyclohexene with NO_2BF_4 yields exclusively products of the formal NO_2F addition, *viz.*, compound **130** (with the ratio of the *cis* and *trans* isomers equal to 4:1).¹¹⁹

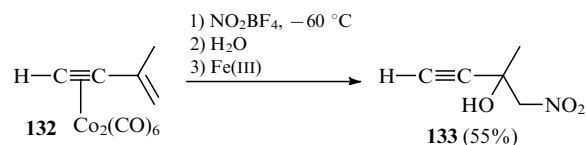


Isopropenyl derivatives of cyclopropanecarboxylic acid **131** react with NO_2BF_4 in a similar way.¹²⁰ Surprisingly, this does not cause a skeletal rearrangement typical of carbocations with the cyclopropyl substituent.



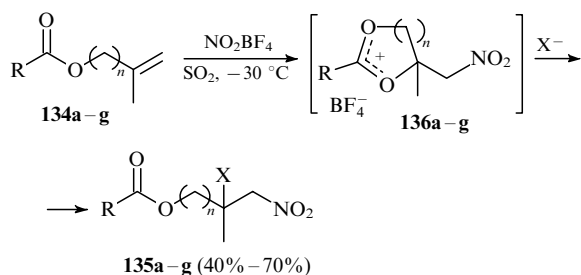
R = H, Me.

A different pattern is observed in the reaction of nitronium tetrafluoroborate with the isopropenylacetylene–octacarbonyl–dicobalt complex **132**. The alkynedicobaltoctacarbonyl residue in this compound stabilises the carbenium ion formed due to the NO_2^+ attack on the double bond.¹²¹ Subsequent hydrolysis of the reaction mixture and oxidation of the cobalt carbonyl complex gives the nitro alcohol **133**.



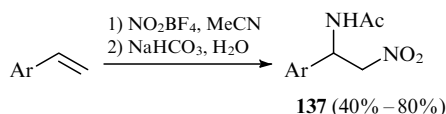
Furthermore, reactions of allylic esters (**134a–d**)¹²² and homoallylic esters (**134e–g**)¹²³ with nitronium tetrafluoroborates followed by hydrolysis have been reported; they gave mixtures of 2-fluoro nitro alkane (X = F) and β -nitro alcohol (X = OH) derivatives **135a–g**. In this case, the overall yield and composition of the products depend on the bulk of the acyl substituent R. The reaction presumably occurs *via* cyclic cationoid intermediates **136a–g**, which are split by fluoride or hydroxide ions to give the

final products. The formation of these intermediates was detected using low-temperature NMR spectroscopy.¹²³

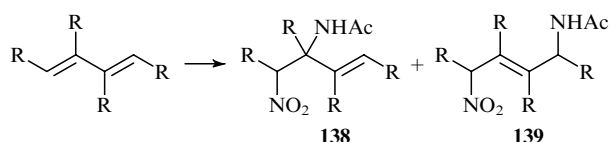


Compound 134	R	n	Product ratio 135a–g (X = F/X = OH)
a	Me	1	95/5
b	Et	1	70/30
c	Pr ⁿ	1	65/35
d	Pr ⁱ	1	75/25
e	Me	2	95/5
f	Pr ⁿ	2	75/25
g	Pr ⁱ	2	55/45

Acetonitrile may serve as the nucleophile which completes the reaction of alkenes with NO_2BF_4 . For example, low-temperature treatment of substituted styrenes with nitronium tetrafluoroborate in MeCN followed by decomposition with saturated aqueous NaHCO_3 afforded the corresponding nitro acetamides **137** obviously formed by the Ritter reaction.¹²⁴

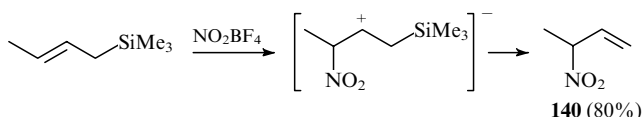


Conjugated dienes undergo similar conversions to give 1,2- (**138**) and 1,4-addition (**139**) products in approximately 1 : 1 ratios (the overall yield is 70%–90%). In this case, nitronium tetrafluoroborate was generated by *in situ* anodic oxidation of N_2O_4 in the presence of LiBF_4 .¹²⁵

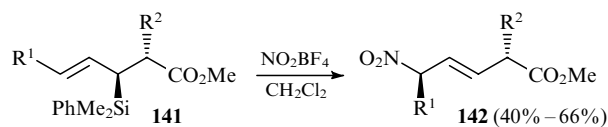


R = H, Me.

Finally, the reaction of NO_2BF_4 with allylsilanes deserves attention. In particular, it was found that treatment of *trans*-but-2-enyltrimethylsilane with nitronium tetrafluoroborate results in the allylic nitro compound **140**, which is formally a reaction product by the S_{E}' mechanism.¹²⁶ It is believed that compound **140** is formed by electrophilic addition of the NO_2^+ cation to the double bond followed by elimination of the trimethylsilyl group from the carbenium intermediate.

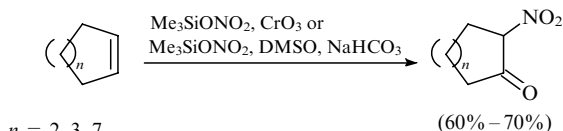


Subsequently,¹²⁷ potential synthetic applications of this approach were demonstrated. It was found that treatment of chiral (*E*)-crotylsilanes **141** with NO_2BF_4 converts them to allylic nitro derivatives **142**. The reaction occurs with high diastereoselectivity (*de* > 90%), since the stereochemistry of the forming chiral centre is controlled by the configuration of the asymmetric centre with the silyl substituent.

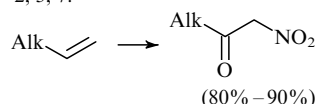


$\text{R}^1 = \text{Alk}$; $\text{R}^2 = \text{H}, \text{Me}, \text{All}, \text{OMe}$.

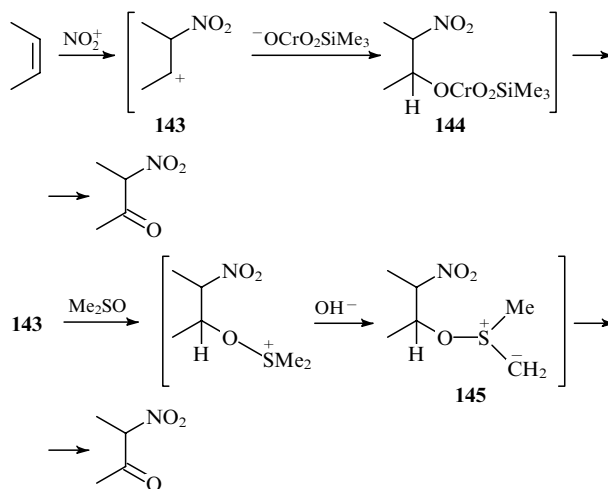
The NO_2^+ cation can also be generated from $\text{Me}_3\text{SiONO}_2$, which reacts with linear or cyclic alkenes in the presence of CrO_3 or DMSO to give α -nitro ketones in high yields.^{128, 129}



$n = 2, 3, 7$.

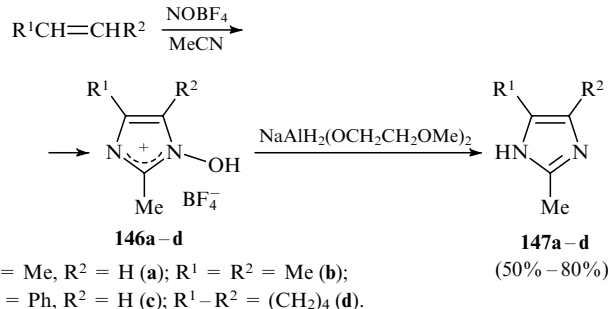


It is believed that the reaction of $\text{Me}_3\text{SiONO}_2$ with CrO_3 generates $\text{NO}_2\text{OCrO}_2\text{SiMe}_3$ *in situ*; the latter is a source of NO_2^+ and of an oxidant, *viz.*, the $^-\text{OCrO}_2\text{SiMe}_3$ anion. The latter reacts with the carbenium ion **143**, which is originally formed upon the attack of the NO_2^+ cation on the double bond to give intermediate **144**. A similar intermediate was postulated in the oxidation of alcohols with chromium-containing reagents. An analogous role is played by DMSO, which reacts with the carbocation **143** *via* an oxysulfonium salt to give the ylide **145**, a well-known intermediate in the Moffatt–Swern oxidations.



VII. Reactions of alkenes with NO^+

Reactions of NO^+ with alkenes are accompanied by further transformations of reactive β -nitroso carbocations formed initially, and the nature of the products depends on the structure of the substrate. For example, reactions of terminal and internal alkenes with nitrosonium tetrafluoroborate in acetonitrile give *N*-hydroxyimidazolium tetrafluoroborates **146a–d**.¹³⁰ Substi-

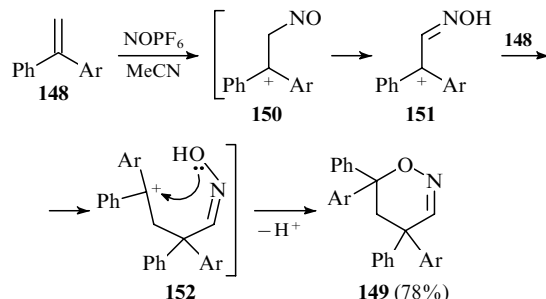


$\text{R}^1 = \text{Me}, \text{R}^2 = \text{H}$ (**a**); $\text{R}^1 = \text{R}^2 = \text{Me}$ (**b**);

$\text{R}^1 = \text{Ph}, \text{R}^2 = \text{H}$ (**c**); $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_4$ (**d**).

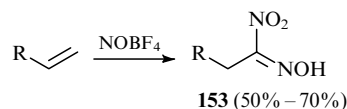
tuted imidazoles **147a–d** can be obtained in high yields by hydride reduction of the tetrafluoroborates **146**.

Arylalkenes react with nitrosonium tetrafluoroborate or hexafluorophosphate in a different way. In particular, 1-(4-methoxyphenyl)-1-phenylethylene (**148**) gave substituted 1,2-oxazine **149** in acetonitrile in high yield.¹³¹ It is assumed that the reaction occurs *via* carbocationic intermediates **150–152**.



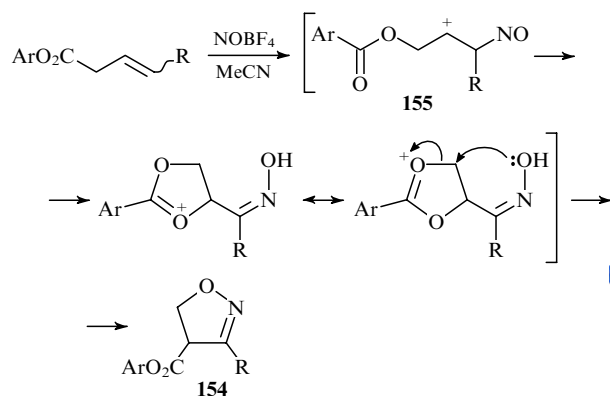
Ar = 4-MeOC₆H₄.

Vinylpyridines react with NOBF₄ in an unusual way to give nitrolic acids **153**,¹³² the mechanism of their formation under these conditions has not been elucidated so far.



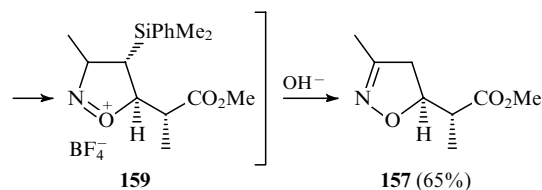
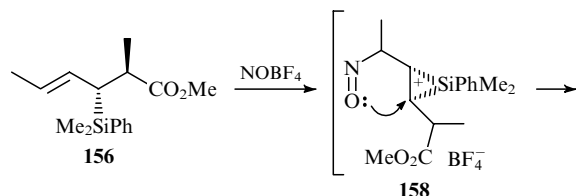
R = 2-, 3-, 4-pyridyl.

The reaction of allylic esters with NOBF₄ turned out to be a convenient method for the preparation of substituted 4,5-dihydroisoxazoles **154**.¹³³ The process occurs *via* the β-nitroso carbocation **155**, which is subsequently stabilised due to involvement of the arenecarboxylate residue.



R = H, Me, CH₂Br.

The transformation of the substituted crotylsilane **156** on treatment with NOBF₄ results in 4,5-dihydroisoxazole derivatives **157**.¹³⁴ Presumably, the reaction is stereocontrolled by the formation of a bridged cation **158** (σ,π-C–Si-conjugation), which is opened with total reversal of the configuration of the chiral centre at C(3) [C(5) in the product]. Heterocyclisation of the intermediate **158** gives the oxonium salt **159**, which is then deprotonated and protodesilylated by a base. The process occurs with high enantioselectivity and has high synthetic potential.



Thus, the results considered above demonstrate the wide prospects of nitrosation and nitration of alkenes for the synthesis of diverse functional derivatives, many of which are of interest as building blocks in organic synthesis.

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^b — *Russ. J. Org. Chem. (Engl. Transl.)*

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of specific receptors of aspartic and glutamic acids may have therapeutic significance.

Studies of metabotropic glutamate receptors (mGluRs) which control the transmission of electrical signals from nerve cells mediated by interacting membrane proteins suggest that they are activated by L-glutamic acid in an 'extended' conformation.¹⁷ An analysis of the biological role of these receptors is complicated due to insufficient activity, selectivity and bioaccessibility of presently known agonists and antagonists of mGluRs. Carbo- and heterocyclic compounds containing a fragment of the acid **2** are potential selective antagonists of glutamate receptors and interesting subjects for the study of structure–activity relationships.^{18–22}

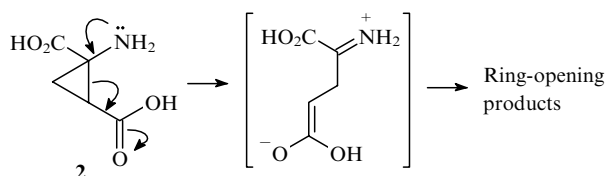
It is known also that (±)-*cis*-1-aminocyclopropane-1,2-dicarboxylic acid is an agonist of the *N*-methyl-D-aspartate receptor.²³

The present review is devoted to surveying the methods for the synthesis of derivatives of 1-aminocyclopropane-1,2-dicarboxylic acid including miscellaneous carbo- and heterocyclic compounds and peptides. Special attention is given to the methods for the preparation of individual stereoisomers of these compounds, some of which possess pharmacological activity.

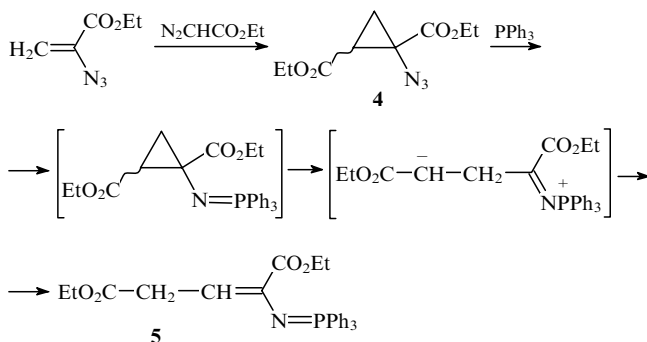
II. Methods for the synthesis of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives

A problem in the synthesis of compound **2** is associated with the fact that the acid itself and its esters, which contain a free amino group, are unstable compounds.¹ The data from the first synthesis of acid **2** (see Ref. 24) were not confirmed by the results of subsequent investigations.^{2, 25–27}

The ability of the cyclopropane fragment to be involved in conjugation and to transfer the effects of the attached functional groups²⁸ favours push–pull reactions in 2-aminocyclopropane-carboxylic acid. Acid **2** undergoes spontaneous ring-opening as a result of which the unshared electron pair of the nitrogen atom takes part in the formation of a double bond giving rise to imines.^{29, 30}



Thus an attempt to synthesise amino acid **2** by reaction of triphenylphosphine with a mixture of *cis*- and *trans*-1-azidocyclopropane-1,2-dicarboxylates (**4**) obtained by cycloaddition of ethyl diazoacetate to α -azidoacrylate resulted in diethyl 2-triphenylphosphiniminopent-2-ene-1,5-dioate (**5**).²⁵



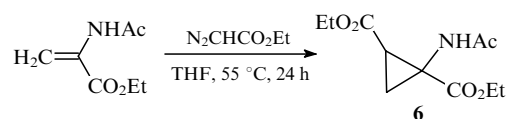
However, recently a series of stable compounds containing a functionalised cyclopropane ring were successfully prepared. The known methods for the synthesis of acid **2** and its derivatives can be divided into several groups, viz., 1,3-dipolar cycloaddition of

diazo compounds at unsaturated bonds, syntheses based on reactions of acetylenedicarboxylates with nitrogen-containing compounds, addition of sulfur ylides to dipolarophiles and intramolecular cyclisation.

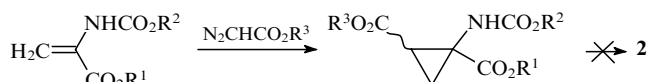
1. 1,3-Dipolar cycloaddition of diazo compounds to unsaturated bonds

Addition of diazo compounds to alkenes, alkynes and heterocycles is a classical approach³¹ widely employed in the synthesis of cyclopropane-containing amino acids.^{3, 13, 32–38} This reaction first yields dihydropyrazoles which are decomposed upon heating or irradiation with evolution of nitrogen and closure of the cyclopropane ring.

The possibility of preparing acid **2** derivatives by addition of diazoacetates to protected α,β -dehydroalanine has been demonstrated.³⁹ *N*-Acetyl- α,β -dehydroalanine ethyl ester reacts with ethyl diazoacetate to give diethyl *N*-acetyl cycloaspartate (**6**) (yield 12.5%); however, the attempts to establish the configuration of the resulting stereoisomer failed.

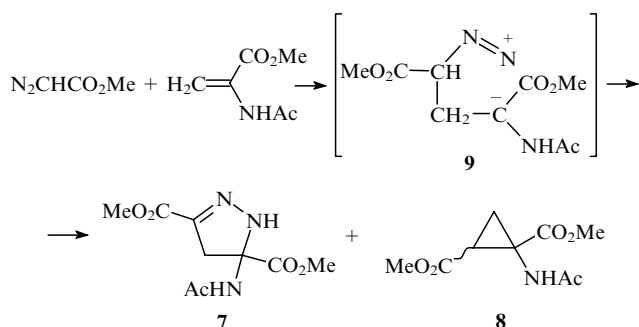


Cycloaddition of diazoacetates to a dehydroalanine derivative with subsequent deprotection has been undertaken by Stammer,¹ but acid **2** could not be isolated in a free state.



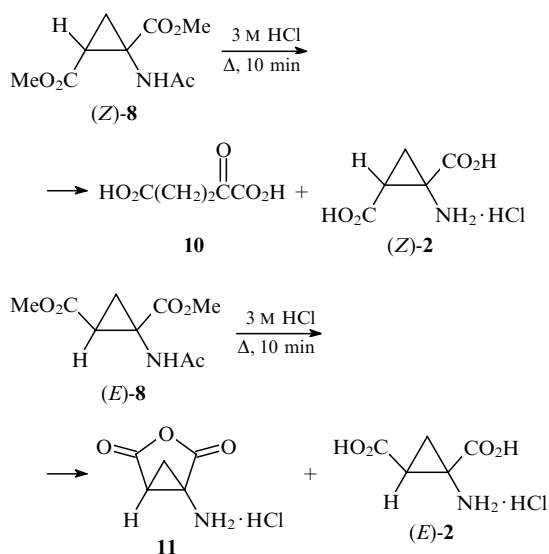
The low yields of acid **2** derivatives and difficulties in the isolation of the target product have stimulated further studies of reactions of alkyl diazoacetate with *N*-protected α -aminoacrylates.⁴⁰

It was found⁴¹ that methyl diazoacetate reacts with methyl 2-acetylaminocrylate in dichloromethane at room temperature to give dihydropyrazole **7** (yield 60%) and a mixture of *Z* and *E* isomers of dimethyl 1-acetylaminocyclopropane-1,2-dicarboxylates (**8**) (total yield 30%). Presumably, the ring closure occurs *via* the zwitterion **9**.

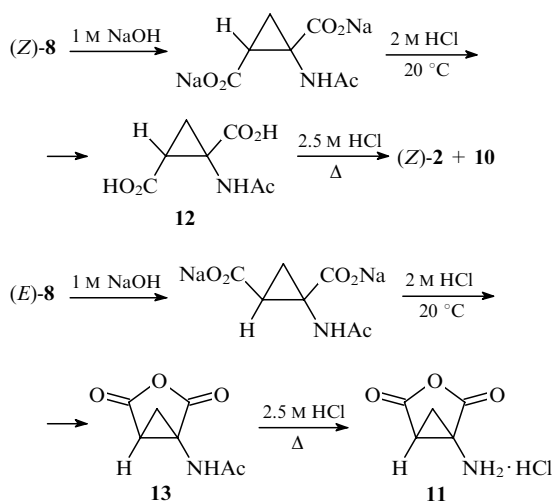


When the reaction is carried out in chloroform, the yields of cyclopropane derivatives increase to 70%.⁴² With a twofold excess of methyl diazoacetate, the ratio of *Z*- and *E*-isomers was 1 : 3 in dichloromethane and 1 : 1 in chloroform.

It has been shown⁴³ that hydrolysis of the *Z* isomer **8** with 3 M HCl is accompanied by the formation of 2-ketoglutaric acid (**10**) (yield 60%) and (*Z*)-1-aminocyclopropane-1,2-dicarboxylic acid hydrochloride (**2**) (yield 8%). The *E* isomer **8** gives the more stable hydrochloride of anhydride **11** and the hydrochloride of the *E* isomer of acid **2** (yields 60% and 6%, respectively) under identical conditions.

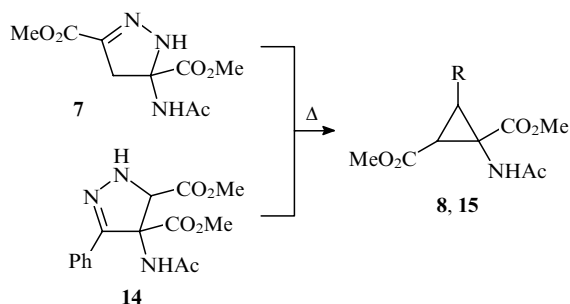


Removal of methyl protective groups in *Z* and *E* isomers of compound **8** by treatment with 1 M NaOH (22 °C, 10 h) and subsequent acidification of disodium salts to pH 5–6 give (*Z*)-1-acetylamino-cyclopropane-1,2-dicarboxylic acid (**12**) and (*E*)-1-acetylamino-cyclopropane-1,2-dicarboxylic acid (**13**) anhydride, respectively.



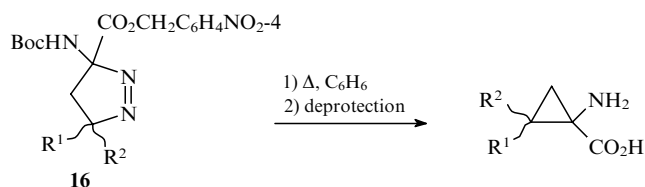
Further acidification to pH 2 and boiling of the *Z* isomer **12** affords compound (*Z*)-**2** (yield 15%) and an acyclic product **10**, whereas anhydride **11** hydrochloride is the only hydrolysis product of the *E* isomer under identical conditions.

Dihydropyrazoles **7** and **14** decompose on boiling in DMF for 40–60 min to give the corresponding *N*-acetylamino-cyclopropane-1,2-dicarboxylates **8** and **15** in 50% and 40% yields, respectively.⁴⁴



R = H (**8**), Ph (**15**).

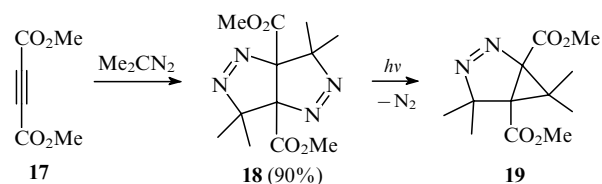
Cycloaddition of diazo compounds to *N*-*tert*-butoxycarbonyl- α,β -dehydroalanine *p*-nitrobenzyl ester yields dihydropyrazoles **16**. Decomposition of compounds **16** and subsequent removal of protective groups gave cyclopropane-containing amino acids that were further used for the preparation of peptides which are of interest for their use as renin inhibitors, analgetics and sweeteners.⁴⁵



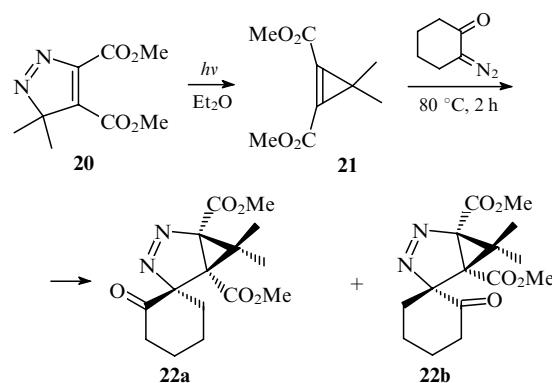
R¹, R² = H, Alk, Ar; Boc = CO₂Bu^t.

Heterocyclic compounds containing a fragment of 1-amino-cyclopropane-1,2-dicarboxylic acid provide illustrative examples of systems with a stabilised cyclopropane fragment. In addition, their rearrangements afford products manifesting useful properties. Therefore, the development of methods for the synthesis of these compounds is attracting the attention of investigators.

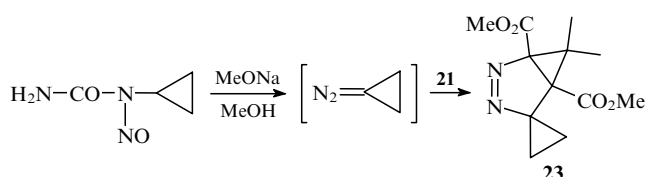
Reaction of 2-diazopropane with dimethyl acetylenedicarboxylate (**17**) gives the adduct **18** in high yield; photoirradiation of the latter results in the evolution of nitrogen and its conversion into dihydropyrazole **19**, a bicyclic derivative of the acid **2**, which represents a convenient synthon for the synthesis of cyclopropenes and dienes.⁴⁶



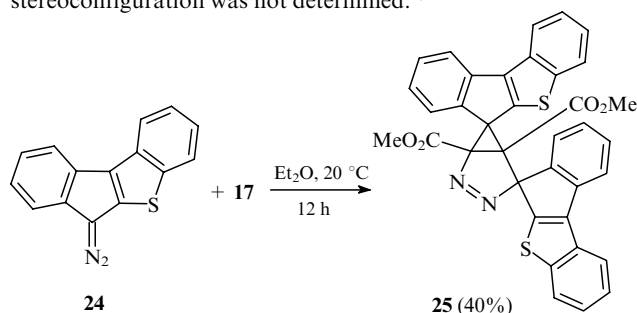
1,2-Bis(methoxycarbonyl)-3,3-dimethylcyclopropene (**21**) obtained by photolysis of 3*H*-pyrazole **20** reacts with α -diazocyclohexanone in benzene to give isomeric tricyclic adducts **22a** and **22b** in a 3 : 1 ratio (total yield 70%).⁴⁷



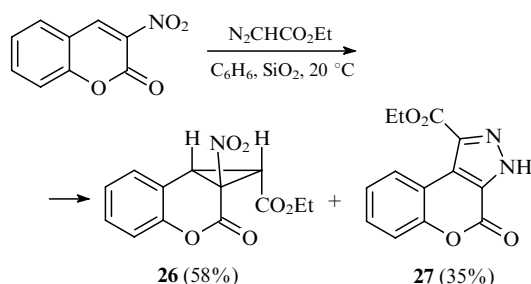
A reaction of cyclopropene **21** with diazocyclopropane generated *in situ* from *N*-nitroso-*N*-cyclopropylurea under the action of sodium methoxide in methanol afforded a spirocyclic adduct **23** in 48% yield.⁴⁸



Diazoindeno[2,3-*b*]benzothiophene **24** adds to acetylenedicarboxylate **17** to give a stable polycyclic dihydropyrazole **25**; its stereoconfiguration was not determined.⁴⁹

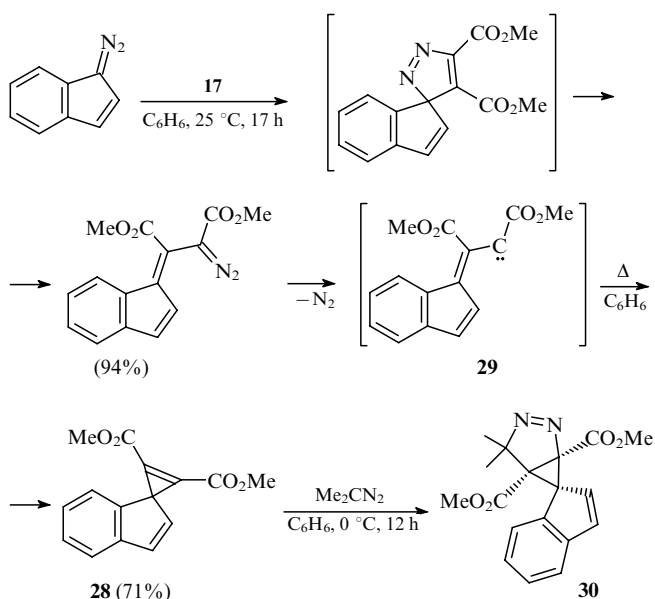


Cycloaddition of ethyl diazoacetate to 3-nitrocoumarin in the presence of silica gel yields a mixture of ethyl 4,5-benzo-1-nitro-2-oxo-3-oxabicyclo[4.1.0]hept-4-ene-7-carboxylate (**26**) and chromeno[3,4-*c*]pyrazolecarboxylate **27**.



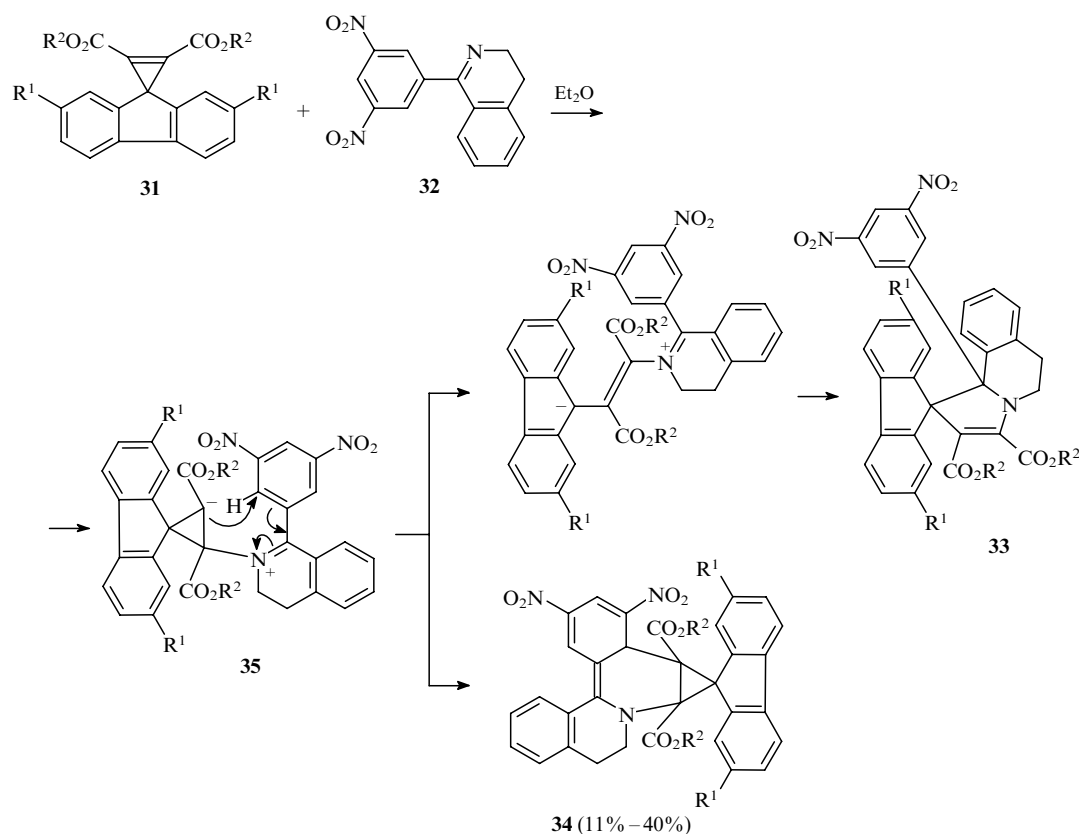
According to the ^1H NMR spectroscopic data, compound **26** is an *endo*-isomer with a *cis*-arrangement of the two protons in the cyclopropane ring and incorporates a nitro analogue of compound **2**.⁵⁰

Spirocyclopropene **28** obtained by addition of diazoindene to dimethyl acetylenedicarboxylate (**17**) with subsequent elimination of a nitrogen molecule and cyclisation of the vinylcarbenium intermediate **29** reacts with 2-diazopropane to give a spiro derivative **30**.⁵¹



The reaction of substituted spirocyclopropenefluorenes **31** with 1-(3,5-dinitrophenyl)-3,4-dihydroisoquinoline (**32**) in anhydrous diethyl ether was studied.⁵² In addition to the expected products (tetrahydroindolizines **33**), this reaction gave novel spiroazanorenefluorenes **34** formed upon intramolecular 1,6-cyclisation of the intermediate **35** (Scheme 1).

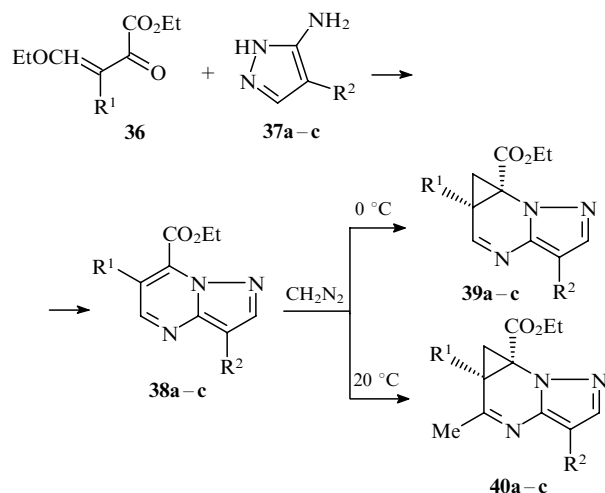
Scheme 1



$\text{R}^1 = \text{H}; \text{R}^2 = \text{Me, Et, Pr}^i, \text{Bu}^t, \text{C}_6\text{H}_{13}; \text{R}^1 = \text{Br}, \text{R}^2 = \text{Me}; \text{R}^1 = \text{Cl}, \text{R}^2 = \text{Et}.$

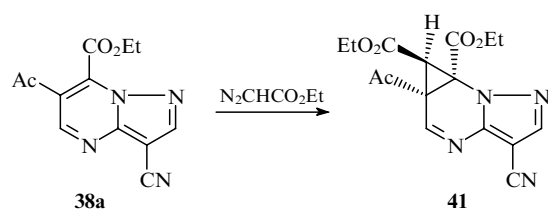
The structure of compounds **34** was established using X-ray diffraction analysis and NMR spectroscopy. Azanorcarene **34** ($R^1 = H$, $R^2 = Me$) was found to possess acidochromic properties. Its ethanolic solution has a green colour which changes to bright violet on addition of aqueous NaOH.

The addition of diazomethane to alkene fragments of heterocyclic systems was studied in the course of synthesis of substituted tricyclic nitrogen-containing compounds.^{53–55} Condensation of keto acid derivatives **36** with 5-aminopyrazoles **37a–c** gave pyrazolo[1,5-*a*]pyrimidines **38a–c** which react with diazomethane at 0 °C to give 6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]dihydropyrimidines **39a–c** in 61%–100% yields. At room temperature, this reaction gives exclusively 5-methylated derivatives **40a–c**.⁵³

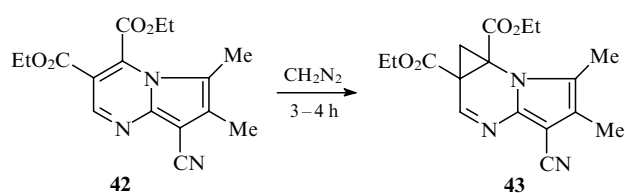


$R^1 = Ac, CO_2Et$; $R^2 = CN$ (a), $CONH_2$ (b), $CONHMe$ (c).

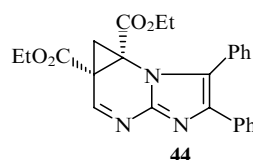
Compound **38a** ($R^1 = Ac$) reacts with ethyl diazoacetate in dioxane at 70 °C in the presence of copper as a catalyst to give 6-ethoxycarbonyl-6*H*-cyclopropa[*e*]pyrazolo[1,5-*a*]dihydropyrimidine **41**; its stereoconfiguration was assigned as *trans* based on the ^1H NMR spectroscopic data.⁵³



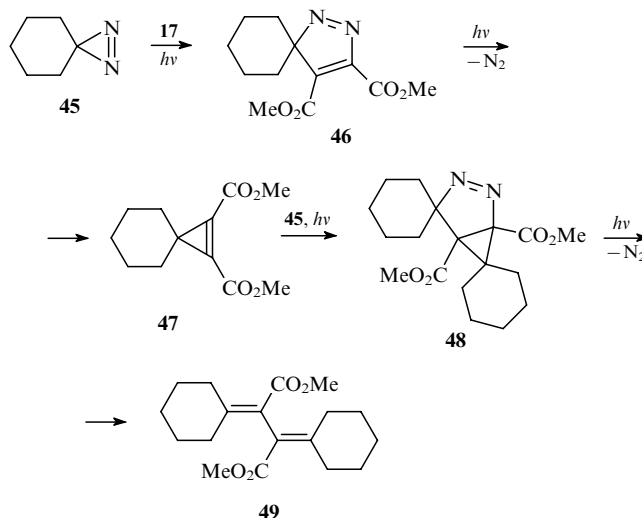
Cyclopropane derivatives of partially hydrogenated pyrrolo[1,2-*a*]pyrimidines, which can be used as catalysts in the synthesis of polyurethanes, have been synthesised. For example, diethyl 6,7-dimethyl-8-cyanopyrrolo[1,2-*a*]pyrimidine-3,4-dicarboxylate (**42**) reacts with an excess of diazomethane at room temperature to give the corresponding cyclopropane derivative of pyrrolopyrimidine **43** (yield 40%).⁵⁴



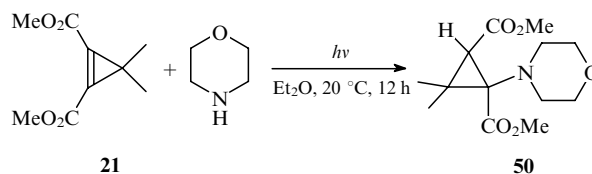
The cyclopropane derivative of imidazo[1,2-*a*]pyrimidine **44** was obtained analogously. This is representative of an interesting class of compounds which includes substances manifesting analgetic, antiinflammatory, antipyretic and anticonvulsive activities.⁵⁵



Selective irradiation ($\lambda = 250–350$ nm) of a spiro-fused diazirine **45** and of dimethyl acetylenedicarboxylate (**17**) in dry toluene gives pyrazole **46** which is further converted into a spiro-fused cyclopropane **47** with liberation of nitrogen. The addition of a second molecule of diazirine **45** to the product formed gives cyclopropadihydropyrazole **48** (yield 12%) after column chromatography on silica gel. Further irradiation is accompanied by the cyclopropane ring opening and elimination of nitrogen, as a result of which compound **48** is converted into diene **49**.⁵⁶



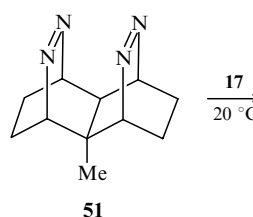
Reaction of cyclopropane **21** with morpholine in anhydrous diethyl ether under irradiation with a mercury lamp afforded morpholinocyclopropane **50**, a potential pyrethroid, as a mixture of two diastereomers as can be judged from ^1H NMR spectroscopic data (total yield 54%).⁵⁷

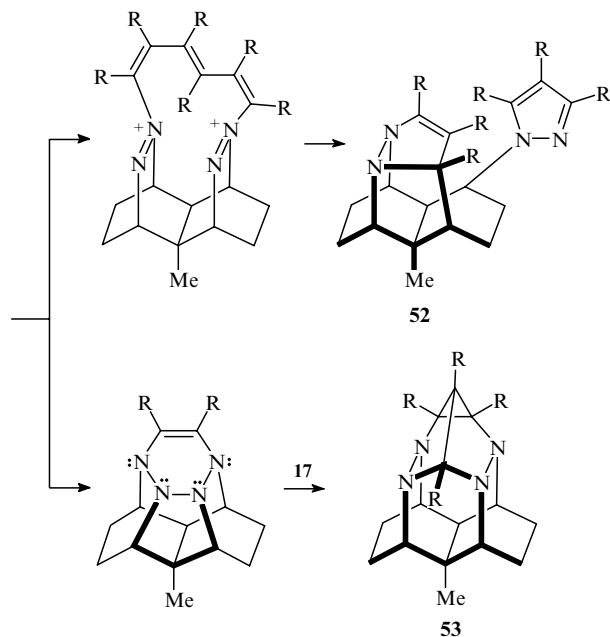


2. Reactions of acetylenedicarboxylates with other nitrogen-containing compounds

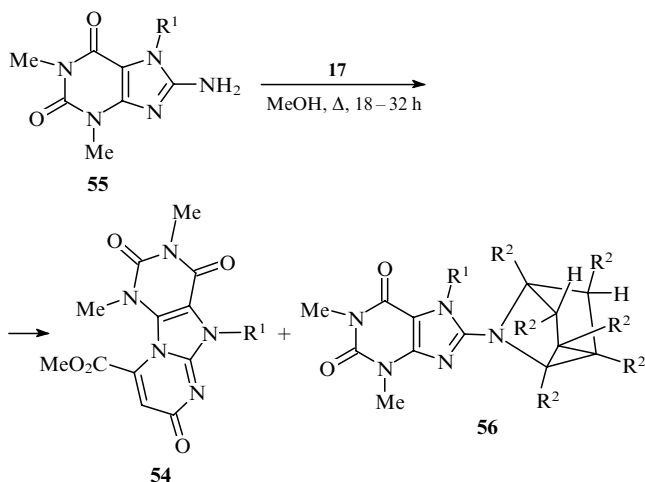
The 1-amino-1,2-dicarboxycyclopropane system can be formed as a result of reactions of electrophilic alkynes with bisdiazines.

The reactivities of cyclic bisdiazines in nucleophilic cycloaddition reactions were studied in the reaction of compound **51** with acetylenedicarboxylate **17** in CH_2Cl_2 in a nitrogen atmosphere.^{58, 59} In addition to a non-symmetrical 1 : 3 adduct **52**, this reaction yields a symmetrical 1 : 2 adduct **53** which incorporates 1,2-diaminocyclopropane-1,2,3-tricarboxylic acid.

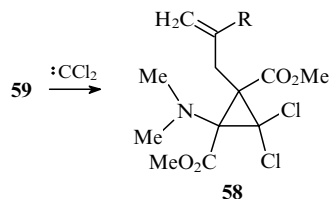
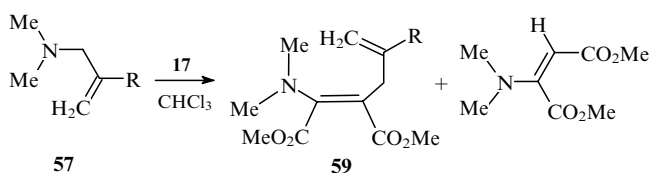




Pyrimido[1,2-*e*]purines **54** were prepared by the reaction of 7-alkyl-8-amino-1,3-dimethylxanthines (**55**) with acetylenedicarboxylate **17**. Along with compounds **54**, this reaction yields xanthines **56**, the addition products of two molecules of the alkyne **17** to the amino group of xanthine **55** followed by intramolecular cyclisation involving an additional molecule of compound **17**. The structure of compounds **56** was established by mass spectrometry and X-ray diffraction analysis.⁶⁰



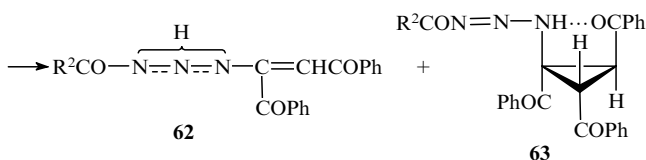
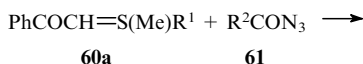
Reaction of allyl amines **57** with acetylenedicarboxylate **17** in chloroform gives 3,3-dichloro derivatives of 1-aminocyclopropane-1,2-dicarboxylic acid **58** as side products formed in low yields as a result of addition of dichlorocarbene, generated from chloroform, to the double bond of the enamine fragment of compound **59**.⁶¹



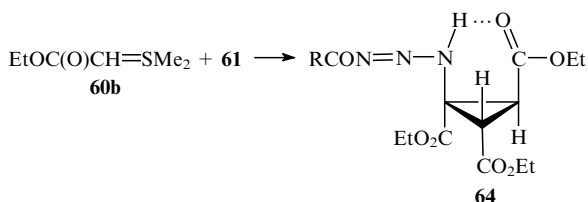
$\text{R} = \text{H}$ (18%), Me (10%).

3. Addition of stabilised sulfur ylides to dipolarophiles

Phenacylidenesulfuranes **60a** react with acyl azides **61** in benzene at 20 °C to give 2:1 adducts **62** and azido analogues of 1-aminocyclopropane-1,2-dicarboxylic acid **63**. Reaction of ethyl azidoformate (**61**, $\text{R}^2 = \text{OEt}$) with ethoxycarbonylmethylidenedimethylsulfurane (**60b**) gives exclusively the derivative **64** ($\text{R} = \text{OEt}$) with a *trans*-configuration of the cyclopropane ring protons and an intramolecular hydrogen bond (¹H NMR spectroscopic data). Reactions of compound **60b** with benzoyl azides **61** also yield the cyclopropane derivatives **64** rather than the 2:1 adducts.⁶²

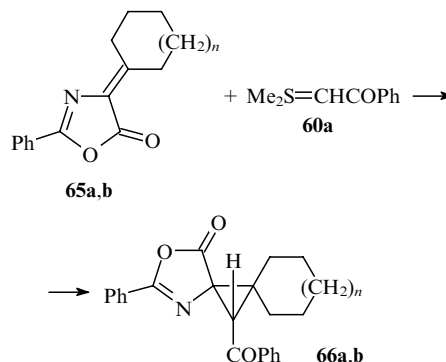


$\text{R}^1 = \text{Me, Ph; R}^2 = \text{OEt, 4-MeOC}_6\text{H}_4, 4\text{-MeC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4.$



$\text{R} = \text{OEt}$ (60%), 4-MeOC₆H₄ (25%), 4-MeC₆H₄ (57%), 4-ClC₆H₄ (32%).

Reaction of dihydrooxazolones with sulfur methylides was studied in order to prepare functionalised spirocyclopropanes that can be rearranged into non-natural amino acid derivatives upon heating.⁶³ 4-Cyclohexylidene- and 4-cycloheptylidene-2-phenyl-4,5-dihydrooxazol-5-ones **65a,b** react with phenacylidenedimethylsulfurane (**60a**, $\text{R}^1 = \text{Me}$) in dry THF at 0 °C to give spirofused cyclopropanes **66a,b** in 84% and 35% yields, respectively. ¹H NMR spectroscopic data suggest that in both cases the major isomer has a *trans*-configuration of the carbonyl groups.



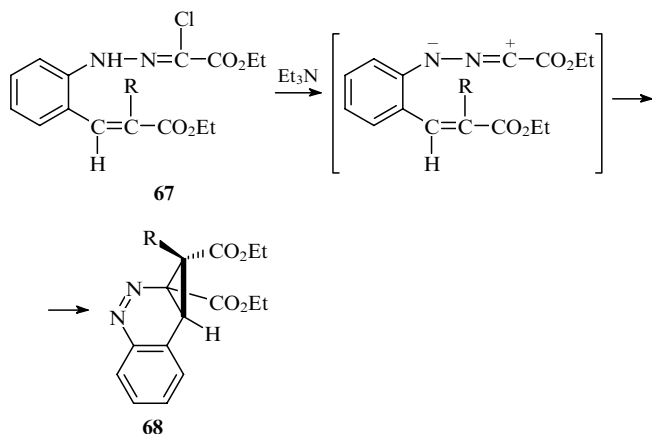
$n = 1$ (**a**), 2 (**b**).

Under identical conditions, reaction of dihydrooxazolone **65a** with ethoxycarbonylmethylidenedimethylsulfurane (**60b**) gives a

mixture of diastereomers (3 : 1) (^1H and ^{13}C NMR spectroscopic data) in a total yield of 97%.⁶³

4. Intramolecular cyclisation reactions

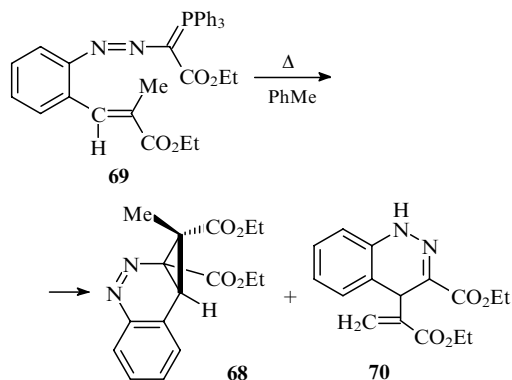
Substituted imines undergo [2+1]-cycloaddition at the C=C bond to give cyclopropanes. The derivatives **67** synthesised from *ortho*-substituted anilines by diazotisation and condensation with ethyl chloroacetate were used to prepare cyclopropacinnolines **68**. The *endo*-position of the R group in the resulting compounds was established by ^1H NMR spectroscopy.⁶⁴



R = Me, Et.

Compounds **68** are interesting in that they undergo rearrangements upon boiling to give heterocyclic structures with potential biological activity.^{65, 66}

Easily accessible azo-substituted phosphorus ylides are also subject to intramolecular cycloaddition at the double bond. Phosphorane **69** loses a PPh_3 group upon heating in toluene to give cyclopropacinnoline **68** (R = Me) and the product of its thermal rearrangement **70** (yields 10% and 43%, respectively).⁶⁷



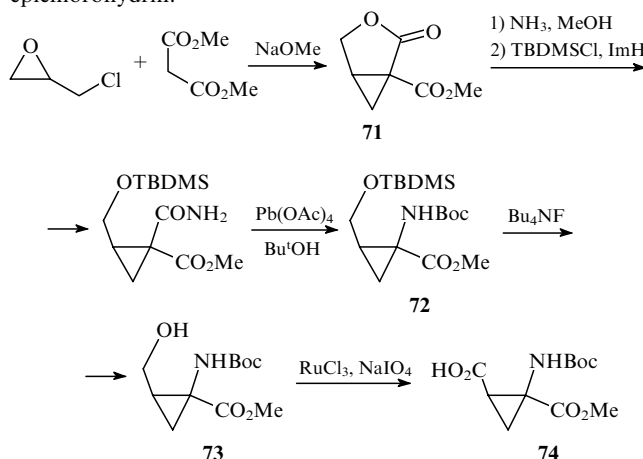
III. Methods for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid

The current demand for all four cycloaspartic acid **2** diastereomers is explained by the fact that their incorporation into peptide structures changes the conformations and, as a consequence, biological activities of the peptides as regards their binding to receptors. However, the methods for the synthesis of individual stereoisomers of derivatives of compound **2** are very few in number. Some recently developed procedures for their synthesis based on diastereoselective reactions using chiral starting compounds and catalysts are considered below.

1. Syntheses based on diastereoselective reactions

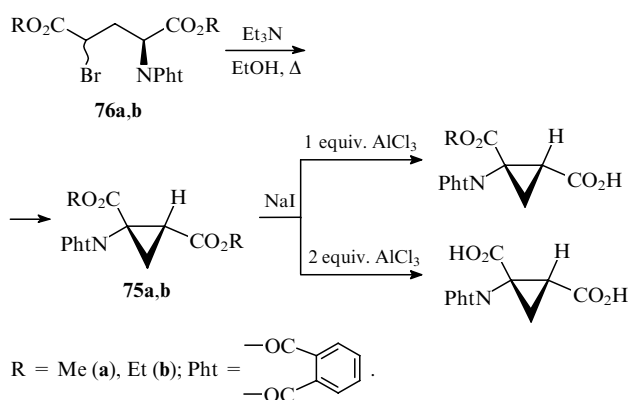
The preparation of a *trans*-isomer of an *N-tert*-butoxycarbonyl derivative of acid **2** has been described.⁶⁸ Methyl (1*RS*, 5*SR*)-2-

oxo-3-oxabicyclo[3.1.0]hexane-1-carboxylate (**71**) was synthesised by condensation of epichlorohydrin with dimethyl malonate in the presence of freshly prepared sodium methoxide as a catalyst. Ammonolysis of bicyclic lactone **71**, protection of the free hydroxy group by reaction with *tert*-butyldimethylsilyl chloride in the presence of imidazole and subsequent Hoffmann rearrangement with lead tetraacetate in *tert*-butyl alcohol yielded *N*-Boc-protected cyclopropane **72**; selective deprotection of its hydroxy group gave alcohol **73** in 85% yield. The next step included mild oxidation of the primary alcohol in a neutral medium by *in situ* generated RuO_4 with retention of the cyclopropane ring and the protected amino group. The monomethyl ester **74** with *trans*-configuration of the carboxy groups was obtained in 60% yield. This method can also be used for the preparation of isomers with definite absolute configuration starting from optically active epichlorohydrin.



TBDMS = $\text{Bu}^t\text{Me}_2\text{Si}$, ImH is imidazole.

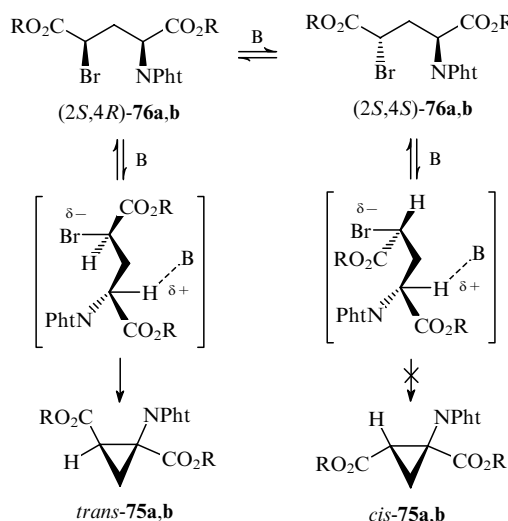
Dialkyl 1-phthalimidocyclopropane-1,2-dicarboxylates **75a,b** having a *trans*-configuration were prepared starting from dialkyl *N*-phthaloyl-4-bromoglutamates **76a,b** upon boiling in ethanol in the presence of triethylamine.⁶⁹ Under the action of 1 or 2 equiv. of AlCl_3 in the presence of NaI, esters **75a,b** are converted either into monoalkyl esters of 1-phthalimidocyclopropane-1,2-dicarboxylic acid or into a free diacid. According to X-ray diffraction analysis,⁶⁹ ^1H NMR and ^{13}C NMR spectroscopic and GC/MS data,⁷⁰ dialkyl esters **75a,b** represent individual isomers with a *trans*-configuration of ester groups relative to the cyclopropane ring, although the starting bromo derivatives **76a,b** were used as a mixture of diastereomers.



R = Me (a), Et (b); Pht =

HPLC studies have shown⁷⁰ that (2*S*,4*S*)-isomers of compounds **76** react with bases much more slowly than (2*S*,4*R*)-isomers. This reaction is accompanied by epimerisation at the C(4) atom of glutamic acid. It was suggested that the abstraction of the proton and the bromide ion follows a concerted mechanism and is similar to the E_2 mechanism. The reaction begins with an attack of the base on the proton at C(2) and the formation of a

transition state. As this reaction requires that the C(1)–C(5) atoms are coplanar in the transition state and that the *anti*-abstraction of the proton and bromide ion occur, the activation energies of the reactions of *threo*-isomers (2*S*,4*S*)-**76a,b** markedly exceed those of the *erythro*-isomers, presumably due to forced shielded positions of C(5)-carboxy and phthalimide groups in the transition state of *threo*-isomers. Therefore, the transformation of a mixture of diastereomers of compounds **76a,b** into derivatives of acid **2** is stereospecific and gives exclusively *trans*-isomers.



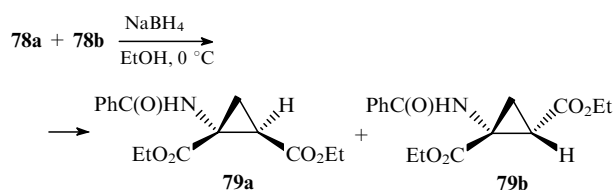
B = Et₃N, KOH.

An original method for the synthesis of derivatives of acid **2** based on diastereoselective cycloaddition of stabilised sulfur

ylides to substituted 4-methylideneoxazolidin-5-ones was proposed.²⁶

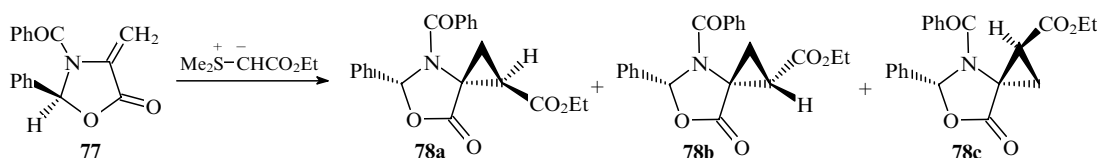
Treatment of compound **77** with ethyl dimethylsulfonioacetate in THF at 0 °C gives a mixture of three diastereomeric cyclopropane adducts separated by column chromatography. (1*R*,3*R*,6*R*)- and (1*S*,3*R*,6*R*)-isomers of 7-benzoyl-1-ethoxycarbonyl-4-oxo-6-phenyl-5-oxa-7-azaspiro[2.4]heptane (**78a** and **78b**) were isolated as a 9 : 1 mixture in a total yield of 55%, the yield of the diastereomerically pure product **78c** was 6%. The assignment of the stereoconfiguration of the isomers formed was carried out based on X-ray diffraction analysis and NMR spectroscopic data (Scheme 2).

Treatment of a mixture of isomers **78a,b** with sodium borohydride in ethanol results in the oxazolidinone ring opening, as a result of which a mixture of diastereomers of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives **79a** and **79b** is formed in a 9 : 1 ratio.

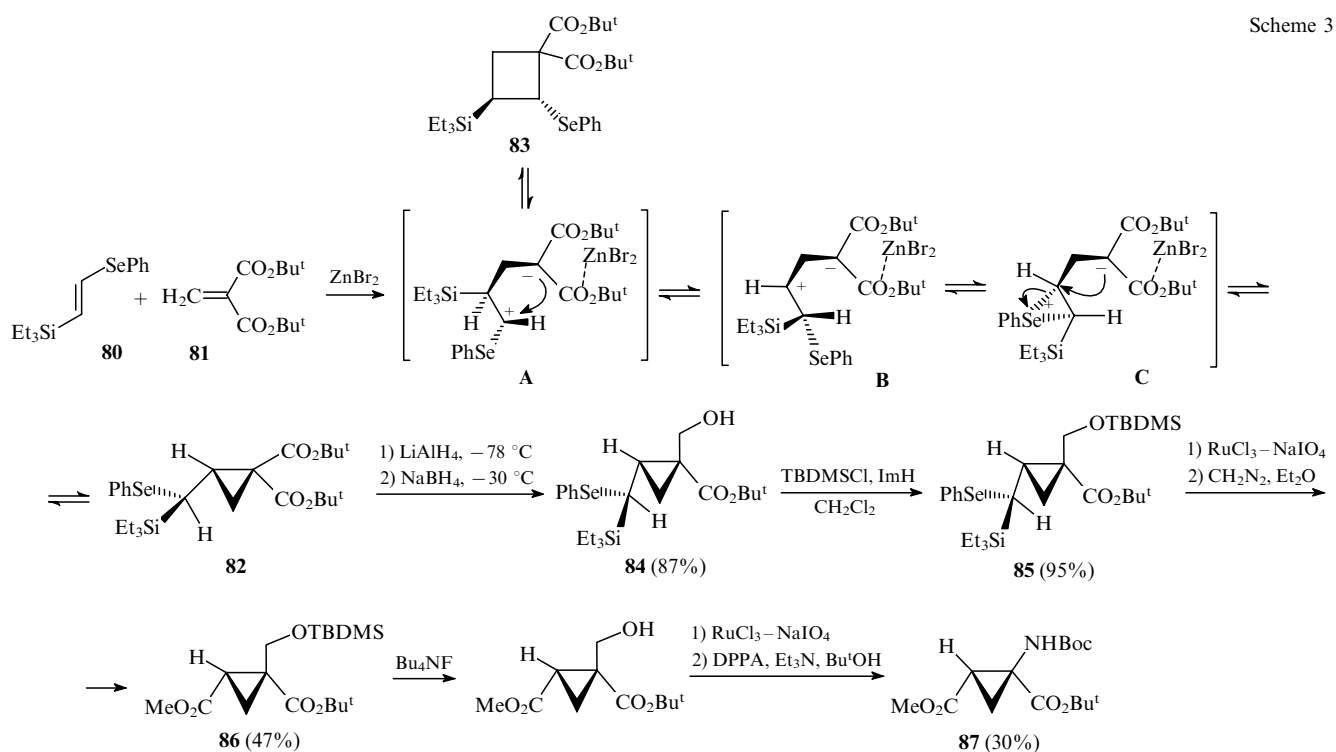


Attempts to hydrolyse the ester groups of the isomers **78a** and **78b** by treatment with 6 M HCl were unsuccessful, since this led to cyclopropane ring opening.²⁶

A method for the synthesis of (*E*)-2,3-methanoaspartic acid derivatives⁷¹ (Scheme 3) is based on the use of a chiral cyclopropane with substituents which can readily be converted into amino and carboxy functional groups. Reaction of 1-phenylseleno-2-triethylsilyl ethene (**80**) with di-*tert*-butyl methylidene-



Scheme 2



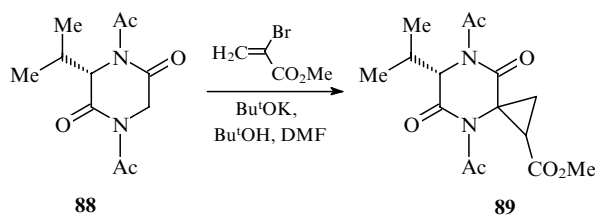
Scheme 3

DPPA = (PhO)₂P(O)N₃.

malonate (**81**) in the presence of ZnBr_2 in CH_2Cl_2 at $-30-0^\circ\text{C}$ gives a mixture of di-*tert*-butyl 2-[(phenylseleno)(triethylsilyl)methyl]cyclopropane-1,1-dicarboxylate (**82**) and protected cyclobutane **83** (7:3) in high yield. Presumably,⁷² the cycloaddition mechanism is similar to that proposed⁷³ for vinyl ketones. The nucleophilic selenide **80** attacks the electrophilic alkene **81** activated by a Lewis acid to give the zwitterion **A**; its cyclisation gives substituted cyclobutane **83**. Intermediate **A** undergoes rearrangement to the zwitterion **B**, which can be converted into an electron-stabilised intermediate **C** containing a selenium bridge. The latter is cyclised to compound **82**; its stereochemistry was established as (*S,S*) or (*R,R*) using ^1H and ^{13}C NMR spectroscopy (Scheme 3).

Stereoselective reduction of a less shielded ester group in compound **82**, which is in the *trans*-position relative to the substituent at C(2), gave an alcohol **84**. The product **85** formed after protection of the hydroxy group in the alcohol **84** was oxidised using the $\text{RuCl}_3\text{--NaIO}_4$ system. Treatment of the acid formed with diazomethane in ether resulted in compound **86**. Removal of the protective *tert*-butyldimethylsilyl group, oxidation of the primary alcohol to an acid and its subsequent reaction with diphenyl phosphorazidate accompanied by the Curtius rearrangement and addition of *tert*-butyl alcohol to the isocyanate formed afforded dialkyl ($\pm$)-(*E*)-1-[(*N*-*tert*-butoxycarbonyl)amino]cyclopropane-1,2-dicarboxylate (**87**); its stereochemistry was established by NMR.

The diastereoselective addition of diketopiperazine **88** to the double bond of methyl 2-bromoacrylate has been described.⁷⁴ Elimination of hydrogen bromide yields the cyclic dipeptide **89** incorporating protected acid **2**.



2. Syntheses based on the use of chiral compounds

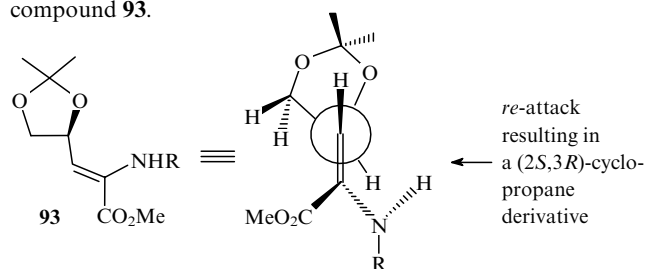
The methods for the synthesis of individual stereoisomers of cyclopropane-containing amino acids from optically active starting compounds are often more efficient than those based on stereoselective reactions. The use of commercially available optically active synthons allows one to reduce the number of synthetic

steps and to increase the yield and optical purity of the final product.

A method for the synthesis of methyl-(2*S*,3*R*)-*N*-benzyloxycarbonyl cycloasparaginate from chiral diols was proposed.^{75,76} The Wittig–Horner condensation of phosphonates **90a–c** with isopropylidene-D-glyceraldehyde (**91**) synthesised from D-mannitol yielded (*Z*)-dehydroamino acid derivatives **92a–c** containing one chiral centre (Scheme 4).

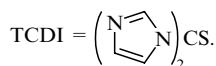
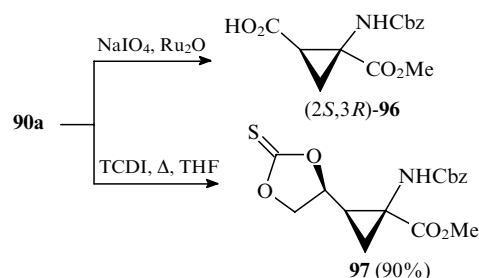
Addition of diazomethane to the double bond of intermediates **92a–c** gives dihydropyrazoles **93a–c**; their photochemical degradation affords optically pure cyclopropane derivatives **94a–c** in a quantitative yield (data from ^1H and ^{13}C NMR spectroscopy).

The diastereoselectivity of 1,3-dipolar cycloaddition at the double bond is explained⁷⁵ by the fact that diazomethane attacks preferably from the less shielded *re*-side of the C(2) atom of compound **93**.



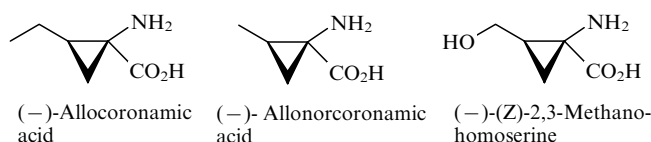
Removal of the isopropylidene protective group in compounds **94a–c** is carried out under mild conditions in order to prevent cyclopropane ring opening and epimerisation of the diols formed. Treatment of derivatives **94a–c** with 5% HCl in methanol for 4–4.5 h at room temperature affords chiral diols **95a–c** in quantitative yields; the assignment of their stereoconfigurations was made based on ^1H NMR spectroscopic data. Hydrolysis performed for a longer time caused epimerisation of chiral centres of cyclopropane to yield (2*R*,3*S*)-enantiomers of the diols **95**.

Oxidation of the diol **95a** with sodium periodate in the presence of ruthenium oxide at room temperature gives a dicarboxylic acid monoester (2*S*,3*R*)-**96** in 63% yield.^{75,76}

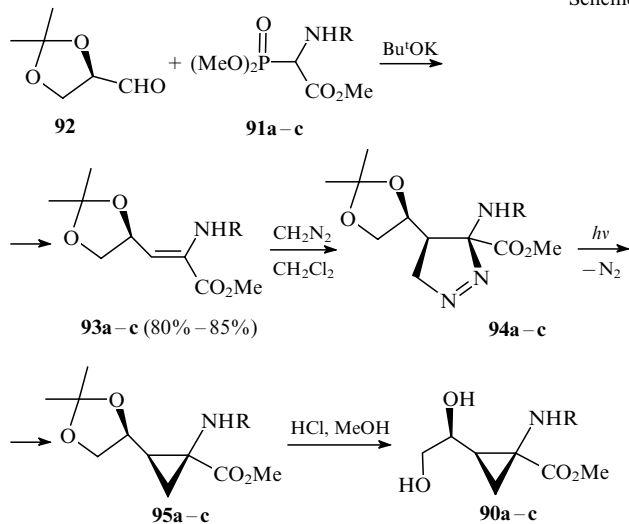


Reaction of compound **95a** with thiocarbonyldiimidazole gave (2*S*,3*R*)-thiocarbonate **97**; its absolute configuration was established unambiguously using X-ray diffraction analysis.

Other cyclopropane-containing amino acids, *viz.*, (–)-allo-coronamic and (–)-allonorcoronamic acids and (–)-(*Z*)-2,3-methanohomoserine,^{75,76} were synthesised starting from the diols **95**, which demonstrates the efficiency of the latter as enantiomeric synthons in the stereocontrolled synthesis of natural compounds containing a cyclopropane fragment and methano analogues of proteinogenic amino acids.

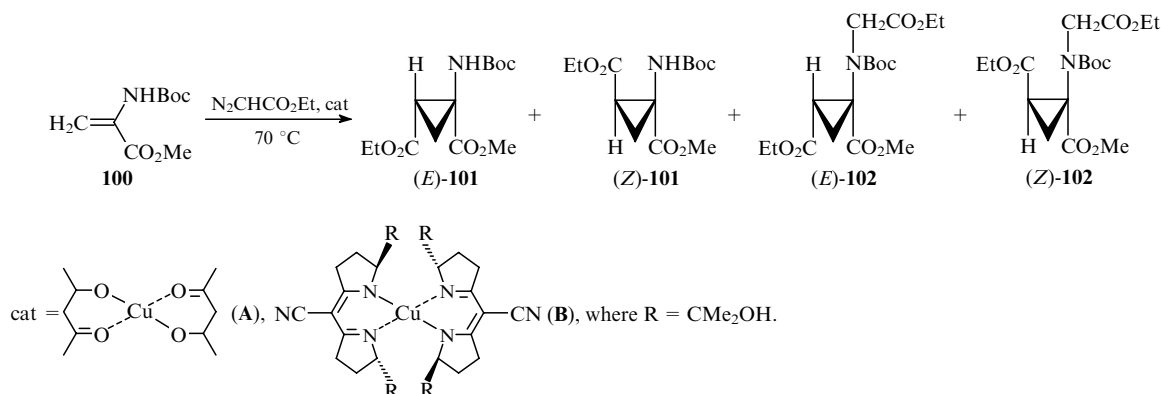


Scheme 4



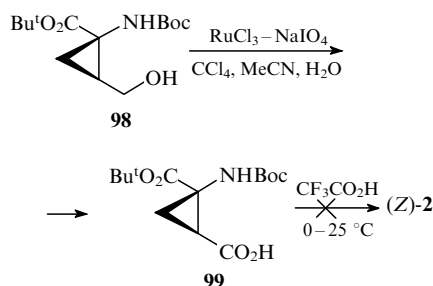
R = Cbz (**a**), Boc (**b**), Ac (**c**); Cbz = $\text{C}_6\text{H}_5\text{CH}_2\text{OC(O)}$;

Scheme 5



Enantiomerically pure amino acids, which can undergo chemical transformations without loss of their optical activities, can be used as the starting compounds in the synthesis of 2,3-methano amino acid derivatives.

Thus the 2,3-cyclohomoserine derivative **98** with protected amino and carboxy groups was oxidised with $\text{RuCl}_3\text{--NaIO}_4$ to give compound **99** (yield 51%). However, attempts at deprotection of the amino group led to the destruction of the cyclopropane ring.²



3. The use of metal complexes

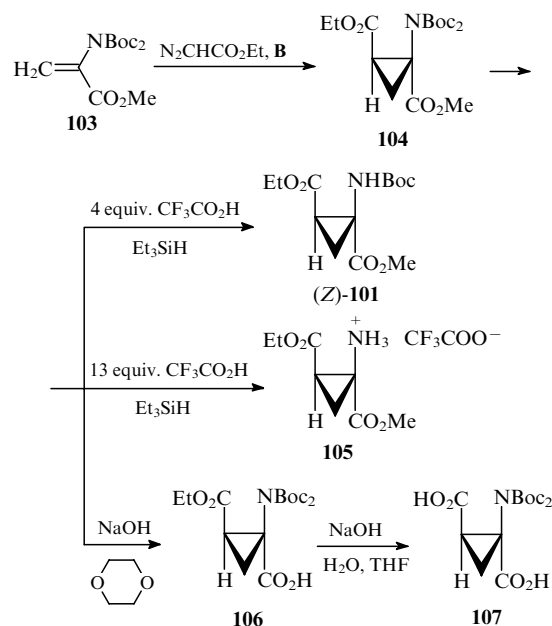
Chiral metal complexes are widely used for the preparation of enantiomerically pure substituted cyclopropanes⁷⁷ including amino cyclopropanecarboxylic acids. This approach was used, in particular, for the synthesis of stereoisomers of cycloaspartic acid derivatives.

Reaction of methyl *N*-protected 2-aminoacrylate (**100**) prepared by dehydration of serine methyl ester with ethyl diazoacetate yields a mixture of four cyclopropanes which represent addition products of ethoxycarbonylcarbene at the double bond [(*E*)- and (*Z*)-**101**] and incorporation products into the *N*–*H* bond of the amino group [(*E*)- and (*Z*)-**102**] (Scheme 5).⁷⁸

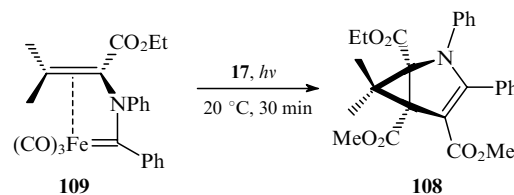
An achiral complex, copper acetylacetonate (**A**), and a chiral copper complex of hemicorrine (the Pfalz complex, **B**) were used as catalysts. *Z* Isomers of the reaction products were predominant; the use of the Pfalz complex made it possible to increase their content. The yields of substituted cyclopropanes **101** and **102** depend on both the amount of ethyl diazoacetate and the nature of the catalyst. Thus reaction of compound **100** with 1.3 equiv. of ethyl diazoacetate in the presence of catalyst **A** afforded a mixture of *E* and *Z* isomers of compounds **101** (**101a** : **101b** = 45 : 55, total yield 15%) and **102** (**102a** : **102b** = 41 : 59, total yield 8%). The reaction performed in the presence of 2.5 equiv. of ethyl diazoacetate and the Pfalz catalyst gave a mixture of *E* and *Z* isomers of compounds **101** and **102** in a 1 : 4 ratio (total yields 40% and 20%, respectively).

The methyl ester of dehydroalanine **103** with two *tert*-butoxycarbonyl groups at the nitrogen atom was synthesised in order to prevent the formation of products **102**; its treatment with an eightfold excess of ethyl diazoacetate in the presence of the Pfalz catalyst gave only the *Z* isomer of 1-[bis(*tert*-butoxycarbonyl)-amino]-2-ethoxycarbonyl-1-methoxycarbonylcyclopropane (**104**)

(yield 85%). Removal of one Boc-group from compound **104** was performed by treatment with trimethylsilyl chloride in methanol–dichloromethane or with a fourfold excess of trifluoroacetic acid in the presence of triethylsilane, which gave the *Z* isomer of the derivative **101**. The same conditions were used for the cleavage of two Boc-groups from compound **104** in the presence of 13 equiv. of trifluoroacetic acid to give trifluoroacetate **105**. Saponification of the diester **104** with an alkali gave consecutively compound **106** with a free α -carboxy group and a dicarboxylic acid **107**.



1-Ethoxycarbonyl-4,5-bis(methoxycarbonyl)-6,6-dimethyl-2,3-diphenyl-2-azabicyclo[3.1.0]hex-3-ene (**108**), a chiral derivative of the acid (*E*)-**2**, was prepared in 62% yield using a photo-induced reaction of the *N*-vinylaminocarbene iron complex **109** with acetylenedicarboxylate **17**.⁷⁹

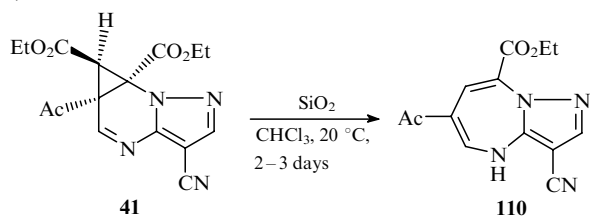


IV. Properties of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives

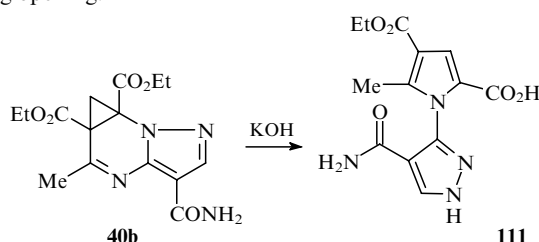
Rearrangements of compounds **40** and **41**, which yield diazepines with potential biological activities, have been studied.^{80,81}

Thus compound **41** is converted into diazepine **110** in the presence of silica gel in chloroform; this reaction is accompanied

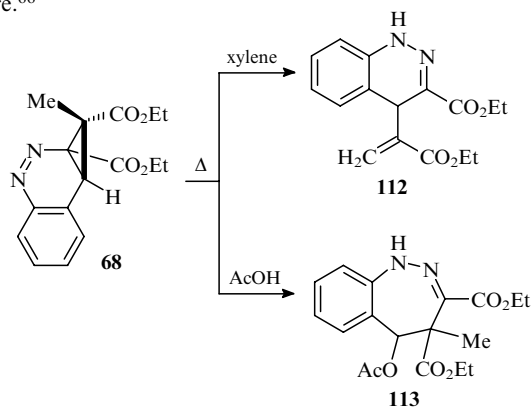
by the cleavage of one ethoxycarbonyl group (^1H and ^{13}C NMR data).⁸⁰



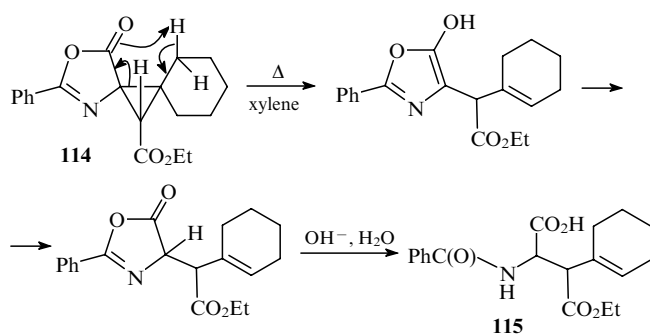
Treatment of diethyl ester **40b** ($\text{R}^1 = \text{CO}_2\text{Et}$) with ethanolic KOH leads to profound rearrangement of the molecule and the formation of substituted pyrazolopyrrole **111** by cyclopropane ring opening.⁸¹



Boiling of 1,1a-bis(ethoxycarbonyl)-1-methyl-1a,7b-dihydro-cyclopropa[c]cinnoline (**68**, $\text{R} = \text{Me}$) in xylene affords a 1,4-dihydrocinnoline derivative **112** in 60% yield,⁶⁵ while boiling in acetic acid gives an individual isomer of an acetoxydiazepine derivative **113** (yield 60%) with a non-established spatial structure.⁶⁶



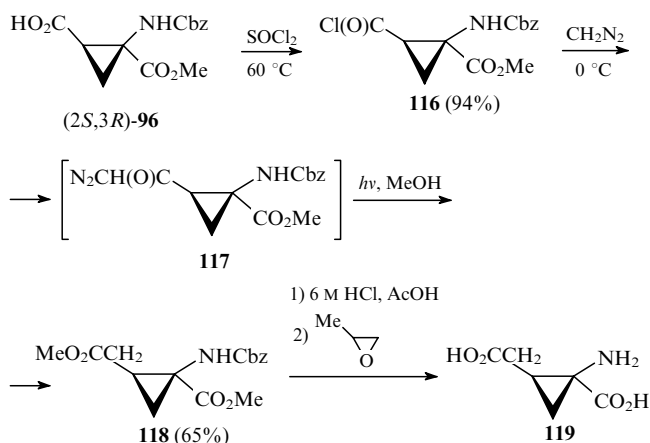
Thermolysis of spirocyclopropane **114** in boiling xylene and subsequent alkaline hydrolysis yield a mixture of stereoisomers of amino acid **115** of unknown configuration.⁶³



Protected (*Z*)-cycloaspartic acid (*2S,3R*)-**96** was used as an optically pure starting compound in enantioselective synthesis of (–)-(*Z*)-2,3-methano-L-glutamic acid.⁸²

The reaction of acid **96** with thionyl chloride in toluene gives acid chloride **116**; treatment of the latter with diazomethane in

ether afforded the corresponding diazo ketone **117**. Photolysis of compound **117** in methanol was accompanied by the Wolff rearrangement resulting in methyl ester **118**. Subsequent hydrolysis of the ester **118** with 6 M HCl in the presence of several drops of glacial acetic acid (90 °C, 6 h) and treatment with propylene oxide at 35 °C gave a free amino acid **119** in quantitative yield.



V. Peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid

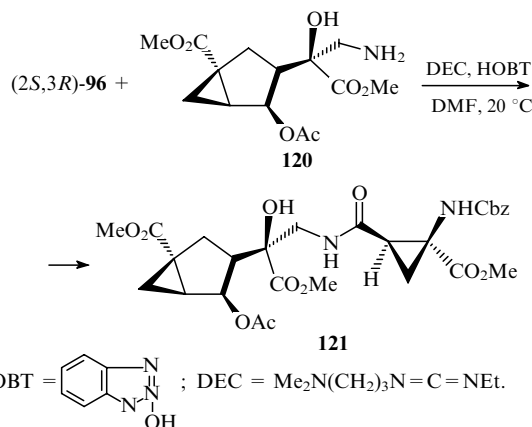
The synthesis of peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid having a sweet taste has been described.⁸³

The yields of di- and tripeptides containing a residue of acid **2** prepared by oxidation of peptides containing (±)-(*Z*)-2,3-methanohomoserine with sodium periodate in the presence of RuCl_3 are given below.⁸⁴

Peptide	Yield (%)
Boc-Val-Asp-L-Phe-OMe	8
Bz-Val-Asp-L-Phe-OMe	59
$\text{CF}_3\text{CO-Val-Asp-L-Phe-OMe}$	82
Ac-Val-Asp-L-Phe-OMe	36
Boc-Gly-Val-Asp-OMe	45
Bz-Gly-Val-Asp	51
Bz-Gly-Val-Asp-Gly-OMe	42
Bz-Gly-Val-Asp-L-Phe-OMe	62

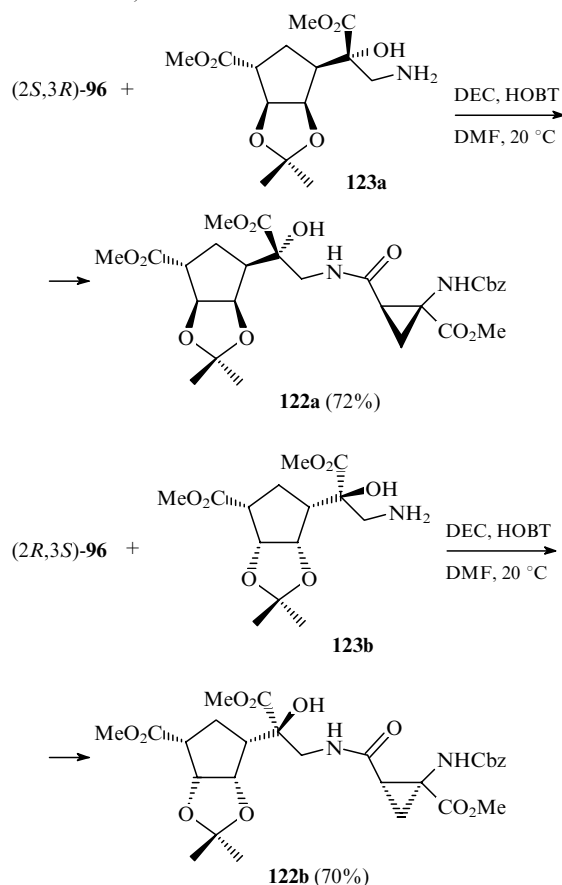
The possibility of removal of *N*-protective groups from peptides where cycloaspartic acid is not terminal and the presence of free carboxy groups in the side chain allow incorporation of these short fragments into more complex peptides.

Condensation of the (*2S,3R*)-isomer of acid **96** with amine **120** in the presence of 1-(3-dimethylaminopropyl)-3-ethylcarbodi-

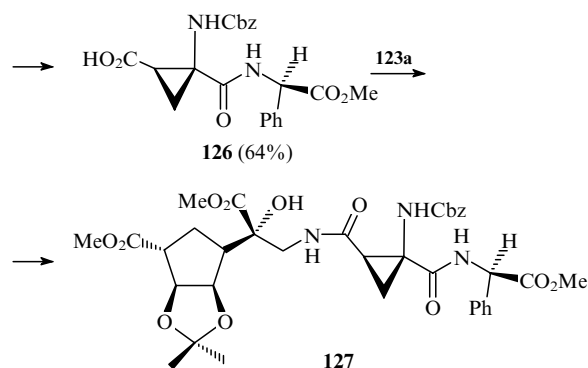
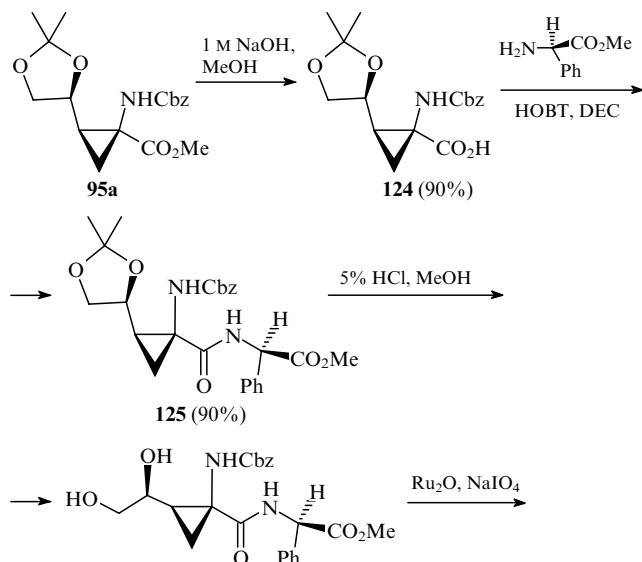


imide (DEC) as an activating reagent and 1-hydroxybenzotriazole (HOBT) as a catalyst affords a conformationally rigid dipeptide **121** (yield 64%).⁸⁵

Dipeptide analogues **122a,b** were synthesised⁸⁶ by a reaction of enantiomers of acid **96** with chiral α -substituted isoserine derivatives **123a,b**.



Reaction of (1*S*,2*R*,4'*S*)-1-[*N*-(benzyloxycarbonyl)amino]-2-(2,2-dimethyl-1,3-dioxolan-4-yl)cyclopropanecarboxylic acid (**124**), obtained by saponification of the ester **95a** with 1 M methanolic NaOH, with the methyl ester of (*R*)-phenylglycine yields the dipeptide **125**. Removal of isopropylidene protection in the peptide **125** with 5% HCl in methanol and subsequent oxidation of the diol affords product **126**. Condensation of compound **126** with α -substituted isoserine derivative **123a** afforded the tripeptide **127**.⁸⁶



In addition to conformational rigidity, incorporation of a cycloaspartic fragment into a peptide chain results in the introduction of an additional lateral carboxy group, which may affect the binding of the peptide to the active site of an enzyme or a receptor. Some peptides containing cycloaspartic acid act as analgesics and renin inhibitors and manifest antiviral activities against the hepatitis C virus.⁸⁷ They can also be used as sweeteners.⁴⁵

* * *

1-Aminocyclopropane-1,2-dicarboxylic acid occupies a special place in the series of 2,3-methano amino acids, firstly because it represents a structural analogue of glutamic and aspartic acids which play a crucial role in various metabolic processes occurring in living organisms. Despite the instability of this amino acid, original approaches to the synthesis of its numerous derivatives some of which possess physiological activity have been developed. The use of modern synthetic approaches has made it possible to develop elegant procedures for the synthesis of individual stereoisomers of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives based on diastereoselective reactions and the use of readily available enantiomeric starting compounds. Conformationally rigid peptides containing 1-aminocyclopropane-1,2-dicarboxylic acid play the role of molecular 'probes' in the study of biochemical processes. At the same time, the potentialities of 1-aminocyclopropane-1,2-dicarboxylic acid derivatives in the study of mechanisms of biochemical reactions and the synthesis of physiologically active compounds have not been completely exhausted. Further progress in this branch of amino acid chemistry is expected in the near future.

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Fluorine-containing alkyl(aryl) vinyl sulfides

A Yu Sizov, A N Kovregin, A F Ermolov

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Abstract. Approaches to the synthesis of fluorine-containing alkyl(aryl) vinyl sulfides, their reactions with electrophilic and nucleophilic reagents and the behaviour in cycloaddition and oxidation reactions are considered systematically. The bibliography includes 136 references.

I. Introduction

The first data concerning fluorine-containing vinyl sulfides appeared in the early 1950s;^{1,2} however, no reviews considering the chemistry of these compounds have been published so far. The interest in this type of compound is due to their high reactivity and the possibility of converting them into biologically active preparations and materials for engineering. In addition, researchers keep an eye on the theoretical aspects of the chemistry of fluorine-containing vinyl sulfides. The presence of the sulfur atom, possessing p electrons and vacant d orbitals, together with a multiple bond within the same molecule stipulates the occurrence of intramolecular p π -interactions, which have a substantial influence on the properties of vinyl sulfides. Recent studies discuss fundamental problems such as the ability of the sulfur atom to stabilise carbocations, carbanions and radicals and the possibility of migration of substituents in the carbon–carbon–sulfur triad. The influence of the fluorine atoms rich in 2p electrons and the electron-withdrawing polyfluoroalkyl groups on the properties of α,β -unsaturated sulfides are under investigation.

This review covers the most important data on methods of synthesis and chemical properties of alkyl(aryl) vinyl sulfides containing fluorine atoms and/or fluorinated substituents both at the double bond and at the sulfur atom. The scope of consideration includes compounds with several heteroatoms at the double bond having a high preparative value, for example, ketene thioacetals and their O- and N-analogues, whose chemical properties are similar to those of vinyl sulfides.

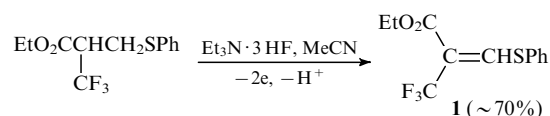
II. Methods of synthesis

Fluorinated α,β -unsaturated sulfides are synthesised by means of electrophilic and nucleophilic substitution, addition, elimination and condensation reactions usual for organic chemistry.

1. α,β -Elimination in fluorine-containing sulfides

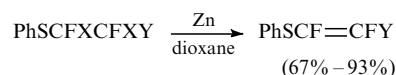
Elimination reactions, first of all, dehydrohalogenation, are employed most widely to prepare fluorine-substituted vinyl sulfides, because sulfides are readily produced upon the addition of thiols to fluoroalkenes. Various organic and inorganic bases are used as dehydrohalogenating agents. Examples of such reactions are listed in Table 1.

Anodic oxidation of ethyl 3,3,3-trifluoro-2-phenylthiomethylpropionate in the presence of $\text{Et}_3\text{N} \cdot 3 \text{ HF}$ in acetonitrile results in β -phenylthio- α -(trifluoromethyl)acrylate **1**.³⁰



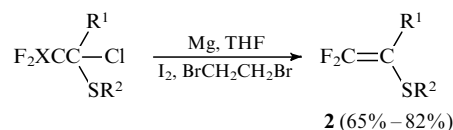
Presumably, this reaction proceeds *via* a radical cation, which reacts with the fluoride ion. The β -fluorinated sulfide formed in the first step is unstable under the reaction conditions and is readily dehydrofluorinated to give sulfide **1**.

Vinyl sulfides can be efficiently purified from saturated sulfides by halogenation of the reaction mixture, separation of the resulting high-boiling dihalides and the subsequent dehalogenation with zinc in dioxane.^{5,6}



X = Cl, Br; Y = F, Cl, CF_3 .

Vinyl sulfides **2** with a terminal difluoromethylidene group were prepared by dehalogenation of the corresponding sulfides on treatment with magnesium in the presence of catalytic amounts of iodine and 1,2-dibromoethane.³¹



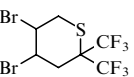
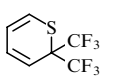
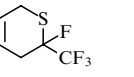
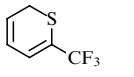
$\text{R}^1 = \text{H, F, Cl, EtS}$; $\text{R}^2 = \text{Ph, Et}$; X = F, Cl.

A Yu Sizov, A N Kovregin, A F Ermolov Military University of Radiational, Chemical and Biological Defence, Brigadirskiy per. 13, 107005 Moscow, Russian Federation.
Fax (7-095) 267 51 07. Tel. (7-095) 265 92 23

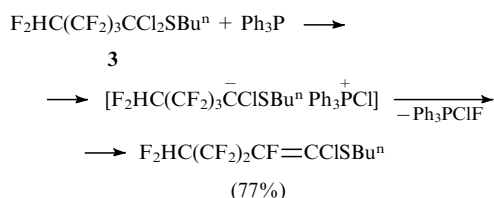
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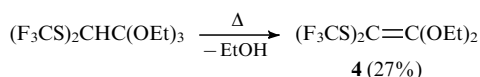
Table 1. Synthesis of vinyl sulfides by dehydrohalogenation of halogen sulfides.

Starting sulfide	Vinyl sulfide	Reagents and conditions	Yield (%)	Ref.
RSCF ₂ CHXY (X = F, Y = Cl, R = Me, Et, Bn, Ph; X = Y = Cl, R = Ph; X = F, Y = CF ₃ , R = Bn, Ph)	RSCF=CHY	KOH (solid)	~ 75	1, 3–8
MeSCF ₂ CHX ₂ (X = F, Cl)	MeSCF=CHX ₂	KOH, DMSO	80–90	9
RSCH(CF ₃)CH ₂ Cl	$\begin{array}{c} \text{RSC}=\text{CH}_2 \\ \\ \text{CF}_3 \end{array}$	KOH, MeOH	~ 90	10, 11
F ₃ CSCH ₂ CH ₂ Cl	F ₃ CSCH=CH ₂	KOH, EtOH	97	12
Cl ₂ FCCF ₂ SCH ₂ CH ₂ Cl	Cl ₂ FCF ₂ CSCH=CH ₂	KOH, (EtOCH ₂ CH ₂) ₂ O	71	13
(F ₃ C) ₂ CHSEt	F ₂ C=C(CF ₃)SEt	KOH, Et ₂ O	58	14
F ₃ CSCH ₂ CHBrSCF ₃	F ₃ CSCH=CHSCF ₃	KOH, EtOH	38	12, 15
PhSCH ₂ CHBrCF ₃	PhSCH=CHCF ₃	KOH, EtOH	—	16
PhSCHBrCHBrCF ₃	PhSCH=CBrCF ₃	KOH, EtOH	85	16
F ₃ CCH(SPh) ₂	F ₂ C=C(SPh) ₂	KOH, THF	62	17
F ₂ HC(CF ₂) ₃ CH(SR) ₂ (R = Bn, Pr ⁿ , 4-MeC ₆ H ₄)	F ₂ HC(CF ₂) ₂ FC=C(SR) ₂	NaOH, C ₄ H ₈ O ₂	~ 77	18
R _f F ₂ CCH(SR) ₂ (R _f = F, CF ₃ , C ₂ F ₅ ; SR = SEt, S(CH ₂) ₃ S)	R _f FC=C(SR) ₂	KOH, H ₂ O, CH ₂ Cl ₂ , Bu ₄ NBr	80–97	19
F ₃ CCH(SPh) ₂	MeOFC=C(SPh) ₂	KF, MeOH	71	17
F ₃ CSCH(CH ₂ Cl)CO ₂ Me	$\begin{array}{c} \text{F}_3\text{CSC}=\text{CH}_2 \\ \\ \text{CO}_2\text{Me} \end{array}$	NEt ₃	60	20
F ₃ CCH(SR)CH ₂ Cl (R = Alk, Ar)	$\begin{array}{c} \text{F}_3\text{CC}=\text{CH}_2 \\ \\ \text{SR} \end{array}$	NEt ₃	~ 90	21–23
(F ₃ C) ₂ CHSMe	F ₂ C=C(CF ₃)SMe	BF ₃ ·NEt ₃	73	24
F ₃ CCH(X)CF ₂ SR (X = CF ₃ , CO ₂ Me; R = Bn, Bu ^t)	$\begin{array}{c} \text{F}_3\text{CC}=\text{CFSR} \\ \\ \text{X} \end{array}$	BF ₃ ·NEt ₃	57–70	3, 25
F ₃ CCH(SR ¹)XR ² (R ¹ , R ² = Me, Et, Ph; X = O, S)	$\begin{array}{c} \text{F}_2\text{C}=\text{CXR}^2 \\ \\ \text{SR}^1 \end{array}$	AlkLi	62–70	26, 27
F ₃ CCH ₂ SPh	F ₂ C=CHSPh	LiNPr ₂ ⁱ	15	28
		KOH	60	29
		in a glass vessel	—	29

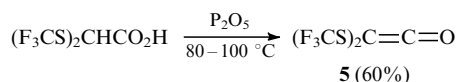
Dehalogenation takes place also in the reaction of n-butyl 2,2,3,3,4,4,5,5-octafluoro-1,1-dichloropentyl sulfide (**3**) with triphenylphosphine.³²



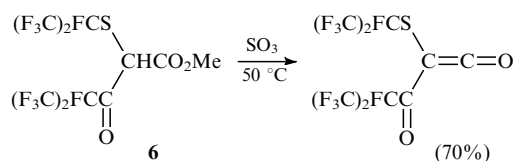
Distillation of 1,1,1-triethoxy-2,2-bis(trifluoromethylthio)ethane, prepared by the reaction of trifluoromethanesulfonyl chloride with ethyl orthoacetate, is accompanied by elimination of an ethanol molecule to give 1,1-diethoxy-2,2-bis(trifluoromethylthio)ethylene (**4**).³³



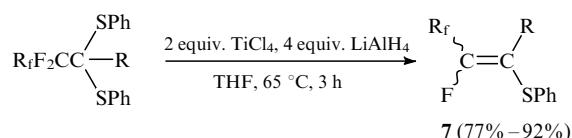
Dehydration of bis(trifluoromethylthio)acetic acid on heating with P_2O_5 gives bis(trifluoromethylthio)ketene (**5**).³⁴



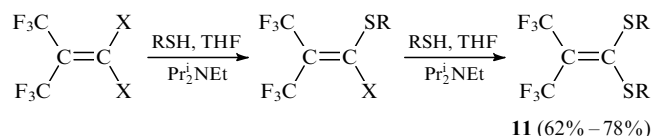
Perfluorinated isobutyryl(isopropylthio)ketene is formed on heating of the methyl ester **6** in SO₃ at 50 °C.³⁵



An efficient method which allows one to prepare tetrasubstituted phenylthioalkenes **7** in high yields has been developed.³⁶



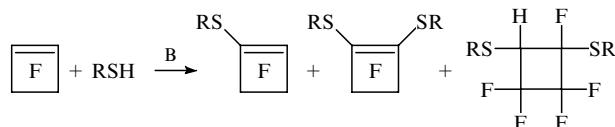
R = Me, Prⁿ, cyclo-C₆H₁₁, Ph; R_f = F, F₃C, F₅C₂.

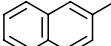


R = Ph, 2-MeOC₆H₄, 4-MeOC₆H₄; X = F, Cl.

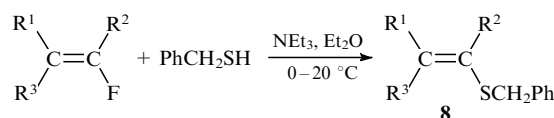
2. The introduction of alkyl(aryl)thio groups into unsaturated compounds using nucleophilic substitution reactions

Fluorinated vinyl sulfides were first prepared¹ by the reaction of perfluorocyclobutene with thiols in the presence of organic bases (NEt₃, Triton B). This gave a mixture of products resulting from replacement of one or two vinylic fluorine atoms.



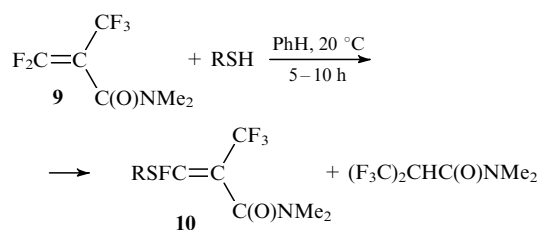
R = Buⁿ, HO₂CCH₂, .

Subsequently, this reaction was extended to various fluoroalkenes of both aliphatic and alicyclic series with an internal double bond.^{37–39} For example, the reaction of fluoroalkenes with α -toluenethiol in the presence of triethylamine gives vinyl sulfides **8** in 40%–65% yields.³⁷



R¹ = R² = CF₃, R³ = Cl; R¹–R² = (CF₂)₃, R³ = CF₃;
R¹–R² = (CF₂)₂, R³ = F; R¹–R² = (CF₂)₄, R³ = Cl;
R¹ = R² = CF₃, R³ = C₂F₅.

Unlike internal alkenes, fluoroalkenes with a terminal double bond are usually converted into addition products at the C=C bond when they react with thiols in the presence of organic bases; in some cases, the reaction mixtures contain vinylic substitution products as impurities (up to 20%).^{3,4,40,41} An exception to this rule is the dimethylamide of perfluoromethacrylic acid (**9**), which reacts with PhSH and PhCH₂SH to give products of replacement of the fluorine atom **10** (as a mixture of *cis*- and *trans*-isomers according to ¹⁹F NMR data) apart from hexafluoroisobutyric dimethylamide.⁴²

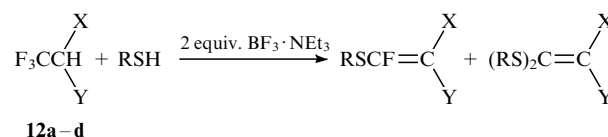


R = Ph, Bn.

This outcome was explained in the study cited by the noticeable basicity of the dimethylamide group, which can trap the eliminated proton thus preventing its addition to the carbanion centre. As a consequence, the intermediate carbanions are stabilised by giving off a fluoride ion to afford vinyl sulfides.

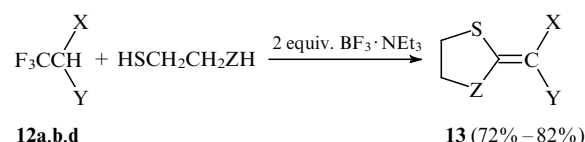
It has been shown recently that perfluoroisobutylene and its chlorinated analogue, *viz.*, 1,1-dichloro-2-trifluoromethyl-3,3,3-trifluoropropene, react with aromatic thiols in THF in the presence of equimolar amounts of diisopropylethylamine giving rise to bis(trifluoromethyl)ketene dithioacetals **11**.⁴³ When the stoichiometry is strictly maintained, monosubstitution products can also be isolated in these reactions.

The reactions of thiols with α -trifluoromethyl-substituted CH-acids such as compounds **12a–d** in the presence of BF₃·NEt₃ represent a convenient method for the synthesis of β -functionally substituted vinyl sulfides and ketene dithioacetals.⁴⁴



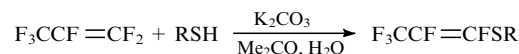
R = Me, Bu^t, Bn, CH₂CO₂Me; X = CF₃; Y = CO₂Me (**a**), CN (**b**);
X = Y = CO₂Me (**c**); X = F, Y = CN (**d**).

Undoubtedly, the first step of this reaction involves dehydrofluorination of the CH-acid to give fluoroalkene, which is attacked *in situ* by the anion generated upon the action of BF₃·NEt₃ on the thiol. The intermediate thus formed is stabilised through β -elimination of the fluoride ion, which is bound irreversibly by the BF₃·NEt₃ complex. This is why the reaction mixture contains no addition products. The ratio of mono- to di-substituted products depends on the CH-acidity of the substrate, on the reactant ratio, and on the structure of the starting thiol. When sterically hindered 2-methylpropane-2-thiol was used, no even traces of the corresponding ketene dithioacetals were detected in the reaction mixture. By using three equivalents of BF₃·NEt₃ and two equivalents of the thiol, one can deliberately obtain disubstituted products. In particular, bifunctional thiols such as ethane-1,2-dithiol and mercaptoethanol are converted into cyclic thioacetals **13** in high yields.⁴⁴



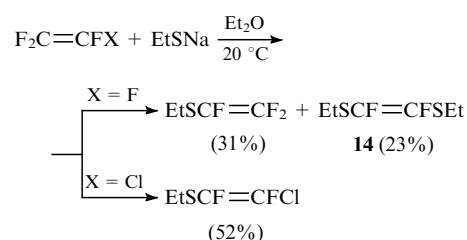
X = F, CF₃; Y = CO₂Me, CN; Z = O, S.

A method for the synthesis of vinyl sulfides by the reaction of perfluoropropylene with thiols in the presence of a solution of potassium carbonate in aqueous acetone has been patented.⁴⁵

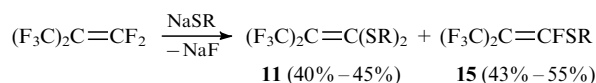


R = Alk, Ar.

When fluoroalkenes are made to react with sodium or lithium thiolates, fluorinated vinyl sulfides mixed with the addition products are formed.^{5,6,46,47} In some cases, these reactions do not give saturated thioethers.^{48,49} In the case of tetrafluoroethylene, further reaction takes place resulting in symmetrical bis(ethylthio)alkene **14**.⁴⁸

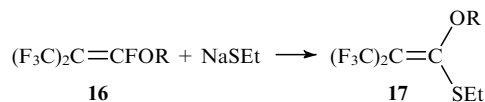


The order of mixing of the reactants is significant in the reactions of fluoroalkenes with thiolates. Indeed, the addition of perfluoroisobutylene to a suspension of RNa in ether gives rise to double substitution products, namely, ketene dithioacetals **11**, whereas the reverse order of reactant mixing results in the predominant formation of monosubstituted compounds **15**.^{50, 51}



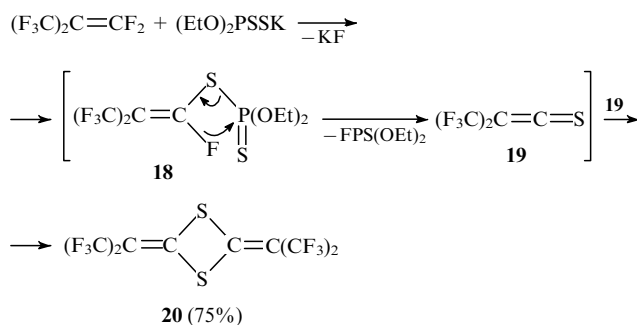
R = Et, Buⁿ, Ph.

A similar nucleophilic displacement of fluorine on treatment with sodium ethanethiolate takes place for perfluoroalkenyl ethers **16**. The reaction affords mixed ketene acetals **17**.⁵⁰



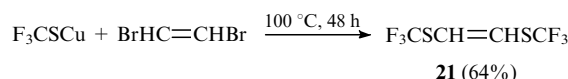
R = Me, Et.

When perfluoroisobutylene reacts with potassium diethyl phosphorodithioate, one fluorine atom is replaced in the first stage to give compound **18**, which cannot be isolated because it spontaneously decomposes. The resulting thioketene **19** dimerises to give dithiacyclobutane derivative **20**.⁵²

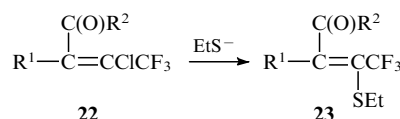


The dimer **20** is also formed in the reaction of perfluoroisobutylene with salts of other thiol acids.^{52–55}

Heating of copper trifluoromethanethiolate with 1,2-dibromoethylene in *N*-methylpyrrolidone furnishes 1,2-bis(trifluoromethylthio)ethylene (**21**).⁵⁶

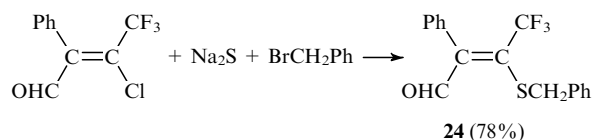


On treatment with the ethanethiolate anion, the chlorine atom in β-functionally substituted α-trifluoromethyl-α-chloroethylenes **22** is substituted. The reaction affords a mixture of *Z* and *E* isomers of vinyl sulfides **23** where the *Z* isomer markedly predominates.⁵⁷ Unfortunately, the method of generation of the thiolate anion is not indicated in the study cited.

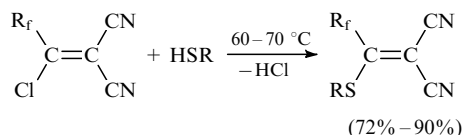


R¹ = H, R² = Ph; R¹ = Ph, 4-ClC₆H₄, ; R² = H.

Successive treatment of 3-chloro-2-phenyl-3-trifluoromethylacrolein with sodium sulfide and benzyl bromide yields vinyl sulfide **24** resulting from substitution of the benzylthio group for the chlorine atom.⁵⁸



1-Chloro-2,2-dicyano-1-polyfluoroalkylethylenes react with thiols on heating in the absence of bases. The reaction can be followed by monitoring the evolution of hydrogen chloride.⁵⁹



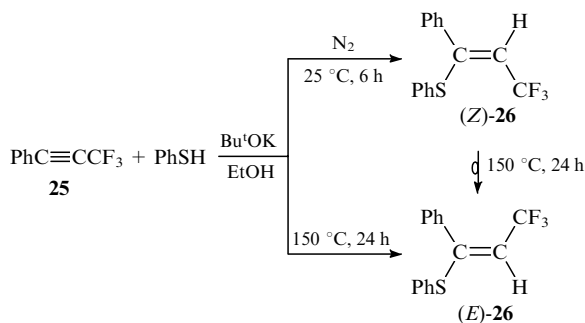
R = Bn, CH₂CO₂Me; R_f = CF₃, C₂F₅.

When bases, for example, triethylamine, are added as HCl acceptors, resinification of the reaction mixture takes place.

3. The addition of sulfur-containing reagents to alkynes and allenes

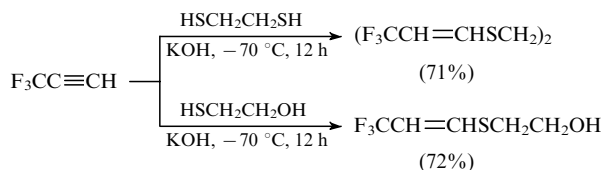
Nucleophilic and radical addition of sulfur-containing reagents to alkynes, which allows one-step synthesis of vinyl sulfides, has been thoroughly studied.⁶⁰ Both fluorine-containing alkynes and fluorinated thiols can be used to prepare fluorine-containing vinyl sulfides.

The addition of PhSH to trifluoromethyl(phenyl)acetylene (**25**) proceeds in the presence of potassium *tert*-butoxide in ethanol; the product yield is nearly quantitative.⁶¹

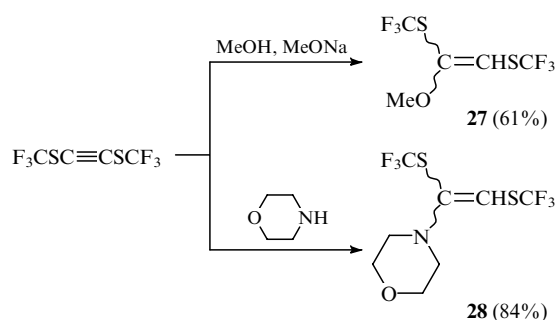


Under kinetically controlled conditions, this reaction gives only *Z* isomer of vinyl sulfide **26**, while under conditions of thermodynamic control, a mixture of products is formed with substantial predominance of the *E* isomer (*Z*:*E* = 23:64). At 150 °C, vinyl sulfide (*Z*)-**26** isomerises to give the *E* isomer. It is noteworthy that the oxygen analogue of sulfide **26** does not tend to undergo such *Z,E* isomerisation. The easy isomerisation of vinyl sulfide (*Z*)-**26** was explained by orbital interaction between the sulfur atom and the trifluoromethyl group. A similar situation is observed for the addition of thiols to trifluoromethyl-containing alkynes activated by an aldehyde or a keto group.⁶²

The reaction of 1,1,1-trifluoropropyne with bifunctional thiols proceeds in good yields under mild conditions; in the case, of 2-mercaptoethanol, the reaction proceeds selectively involving the sulfur atom.⁶³

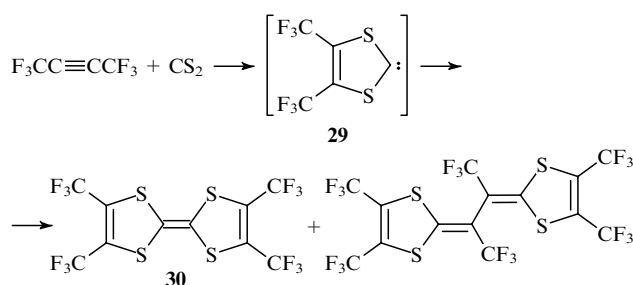


Nucleophilic addition of methanol (in the presence of sodium methoxide) or morpholine to bis(trifluoromethylthio)acetylene gives rise to mixtures of *cis*- and *trans*-isomers of the corresponding vinyl sulfides **27**, **28**.¹²

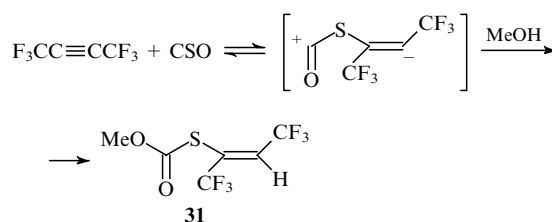


The addition of morpholine to benzylthiopolyfluoroalkylacetylenes also gives products in high yields.⁶⁴

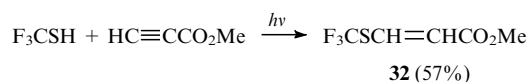
Carbon disulfide reacts with activated alkynes at $\sim 100^\circ\text{C}$ in methanol to give mixtures of products.⁶⁵ The initial stage of the reaction is cycloaddition of the alkyne to carbon disulfide to give intermediate carbene **29**; it can either dimerise to give adduct **30** or participate in other reactions.



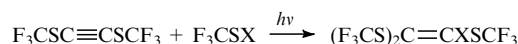
Carbonyl sulfide reacts with hexafluorobutyne in methanol to give *O*-methyl *S*-vinyl thiocarbonate **31**.⁶⁵



Radical addition of trifluoromethanethiol to methyl propiolate affords a mixture of *cis*- and *trans*-isomers of methyl β -trifluoromethylthioacrylate **32** in good yield.²⁰ Ester **32** was converted by standard procedures into the corresponding acid, acyl chloride, amide and nitrile.

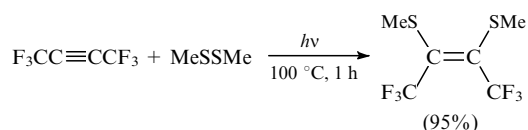


Under free radical reaction conditions, trifluoromethanethiol or trifluoromethanesulfonyl chloride add to bis(trifluoromethylthio)acetylene.¹²



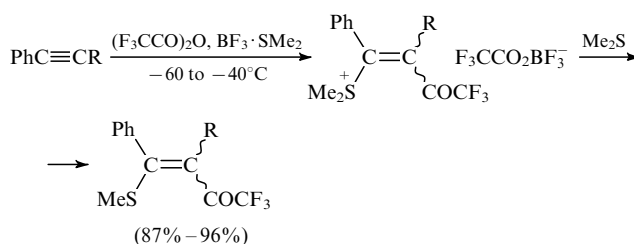
X = H (39%), Cl (47%).

The reaction of dimethyl disulfide with hexafluorobutyne occurs on irradiation and heating.⁶⁶



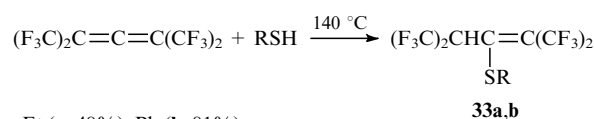
When trifluoroacetic anhydride and the dimethyl sulfide–BF₃ complex react with alkynes, conjugate addition of the CF₃CO group and dimethyl sulfide takes place to give sulfonium salts. In

the reaction with excess dimethyl sulfide, they are demethylated yielding β -methylthio-substituted α,β -unsaturated trifluoromethyl ketones.⁶⁷



R = H, Me, Et.

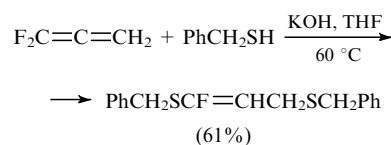
Tetrakis(trifluoromethyl)allene reacts with thiols on heating with the formation of α,β -unsaturated sulfides **33a,b**.⁶⁸



R = Et (**a**, 48%), Ph (**b**, 81%).

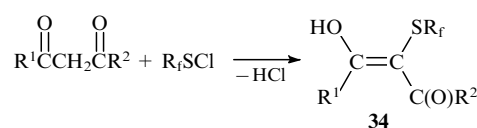
The substantially lower yield of compound **33a** is due to the fact that ethanethiol is able to efficiently reduce the multiple bond in the allene, which gives (F₃C)₂CHCH=C(CF₃)₂ and Et₂S₂.

The reaction of 1,1-difluoroallene with α -toluenethiol in the presence of KOH gives initially the addition product; this is followed by vinylic replacement of the fluorine atom in this product.⁶⁹



4. C-Sulfonylation involving fluorine-containing sulfonyl chlorides

The reactions of β -diketones, β -ketoesters and their anilides with polyfluoroalkanesulfonyl chlorides afford compounds that exist almost completely, according to ¹H NMR spectra of CDCl₃ solutions, as enols, *i.e.*, β -hydroxyvinyl sulfides **34**.^{21, 70–72}



R¹ = Me, Ph; R² = Me, Ph, OEt, NH₂, NHPh; R_f = CF₃, ClCH₂CH(CF₃), MeO₂CCF₂, MeO₂CCF(CF₃), MeO₂CC(CF₃)₂.

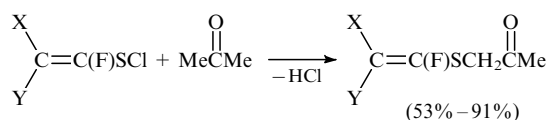
These reactions usually proceed under mild conditions without a solvent and give products in high yields.

Similarly to enolisable ketones, enamines react with polyfluoroalkanesulfonyl chlorides to give monosubstituted products.^{73, 74}



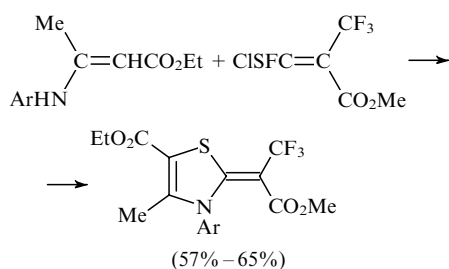
R = C(O)NH₂, CN.

α -Fluoro- α,β -unsaturated sulfonyl chlorides easily form C-sulfonylated products with π -donor aromatic and hetero-aromatic compounds, various enolisable carbonyl compounds, and some enamines.^{25, 75–77} For example, the reaction with acetone affords monosulfonylation product.

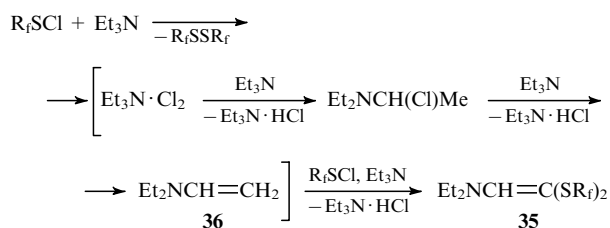


X = CF₃, Y = CF₃, CO₂Me, CN; X = Y = CO₂Me.

The reaction of 1,3,3,3-tetrafluoro-2-methoxycarbonylpropenesulfenyl chloride with esters of 3-(arylamino)crotonic acid takes place under mild conditions. The reaction is accompanied by intramolecular dehydrofluorination and cyclisation giving rise to substituted *N*-aryl-2-(1-methoxycarbonyltrifluoroethylidene)-2,3-dihydrothiazoles.⁷⁶



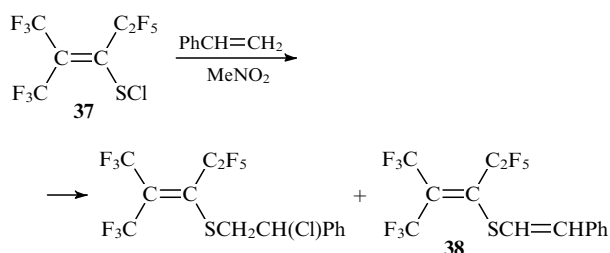
The reactions of chlorofluoromethanesulfenyl chlorides with triethylamine furnish vinyl sulfides **35**. This can be a result of electrophilic replacement of hydrogen in enamine **36**.⁷⁸



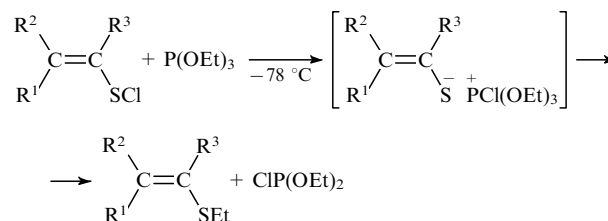
R_f = CF₃, CF₂Cl, CFCl₂.

In the first step, sulfenyl chloride acts as a chlorinating agent, as indicated by the presence of disulfide in the reaction mixture. Consecutive chlorination–dehydrochlorination of triethylamine results in enamine **36**, which reacts with two sulfenyl chloride molecules. The reaction with dicyclohexylethylamine proceeds in a similar way.⁷⁹

Aliphatic and alicyclic α,β-unsaturated perfluorosulfenyl chlorides readily enter into electrophilic addition to a double bond; this is a way of introducing fluorine- and sulfur-containing unsaturated fragments into diverse alkenes. When activated alkenes, polar solvents and salt additives are used, replacement of vinylic hydrogen atoms and skeletal rearrangement of alkenes become possible apart from the addition reactions. For example, the reaction of perfluoro-3-chloro-2-methylsulfenylphenylpent-2-ene (**37**) with styrene gives vinylic substitution product **38** in a yield of up to 20%.⁸⁰



The reactions of fluorine-containing α,β-unsaturated sulfenyl chlorides with triethyl phosphite give the corresponding alkenyl-ethyl sulfides.³



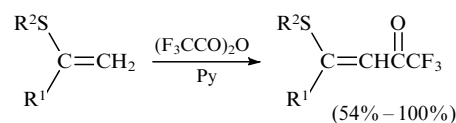
R¹ = R² = CF₃, R³ = F; R¹ = CF₃, R²–R³ = (F₂C)₃.

Presumably, the attack is directed at the chlorine atom rather than at sulfur (in saturated nonfluorinated sulfenyl chlorides, nucleophiles attack the sulfur atom). As a consequence, the formally positively charged halogen is transferred to the phosphorus atom.

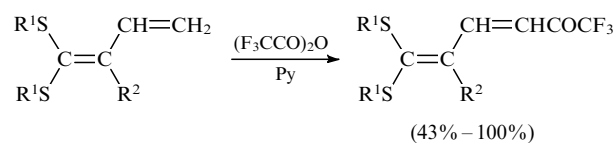
5. Trifluoroacylation of α,β-unsaturated sulfides

Trifluoroacetylation of alkyl(aryl)thioalkenes with trifluoroacetic anhydride at 20 °C or with cooling affords α,β-unsaturated β-alkyl(aryl)thio trifluoromethyl ketones.^{81–83} In the presence of pyridine, the yields of reaction products increase. As the sulfur-containing alkenes, one can use vinyl sulfides, ketene dithioacetals and activated dienes such as 1,1-di(alkylthio)alka-1,3-dienes. In the last-mentioned case, the reaction proceeds stereoselectively to give the *E* isomers of enones.

Using ¹H NMR spectra and kinetic measurements, it was found that the reaction follows an addition–elimination mechanism.⁸⁴ Vinyl sulfides are trifluoroacylated non-stereoselectively.

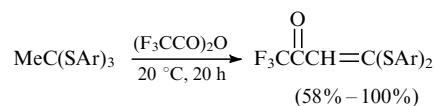


R¹ = H, Alk, Ar, SAlk, SAR; R² = Alk, Ar.

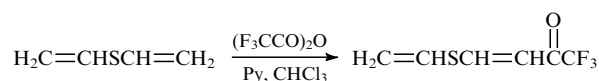


R¹ = Alk; R² = H, Et.

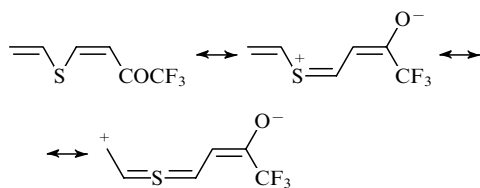
Aryl orthothioacetates react with excess trifluoroacetic anhydride with elimination of aryltrifluorothioacetate to give trifluoromethyl-α,β-enones, which are precursors of the corresponding ketene dithioacetals.⁸⁵



In the case of divinyl sulfide, one vinyl group is trifluoroacylated.⁸⁶

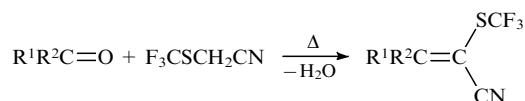


The unexpected reaction selectivity was explained⁸⁶ by assuming that the lone electron pair of sulfur occurs in strong p,π-conjugation with the trifluoroacetyl group, which substantially decreases the nucleophilicity of the second vinylthio group.



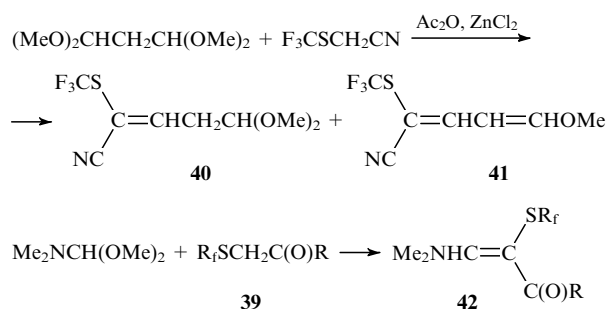
6. Condensation

α -Trifluoromethylthio-substituted acrylonitriles are produced according to the Knoevenagel reaction from trifluoromethylthioacetonitrile and carbonyl compounds.²⁰ This reaction can be carried out for aliphatic, alicyclic and aromatic aldehydes and ketones.



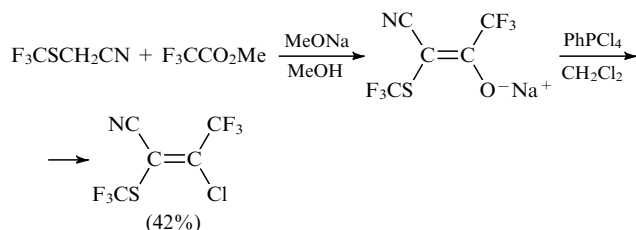
Ethyl(2-trifluoromethylthio)acetate, which has a lower CH-acidity, reacts with aldehydes under similar conditions but does not react with ketones.⁸⁷

In some cases, aldehydes are replaced by their dimethyl acetals in condensations with CH-acids. For example, reactions of malondialdehyde bis(dimethyl acetal) with trifluoromethylthioacetonitrile⁸⁸ and *N,N*-dimethylformamide dimethylacetal with ketones^{39,89} have resulted in the formation of functionally substituted vinyl sulfides **40–42**, which are used in the syntheses of heterocyclic compounds.



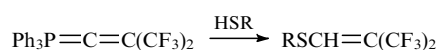
$\text{R}_f = \text{CF}_3, \text{CF}_2\text{Cl}$; $\text{R} = \text{Me}, \text{Pr}^n$.

Due to the high CH acidity caused by the presence of two electron-withdrawing groups, the nitrile and trifluoromethylthio ones, trifluoromethylthioacetonitrile enters into ester condensation with methyl trifluoroacetate. Chlorination of the resulting enol sodium salt leads to 3-chloro-3-trifluoromethyl-2-trifluoromethylthioacrylonitrile.⁹⁰



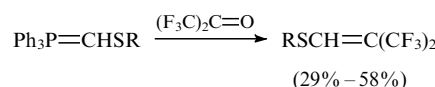
7. Syntheses based on phosphonium ylides

Bis(trifluoromethyl)vinyl sulfides were prepared by heating triphenyl-2,2-bis(trifluoromethyl)vinylidenephosphorane with thiols.⁹¹

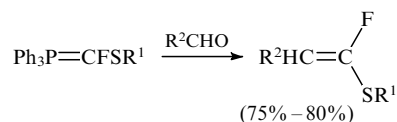


$\text{R} = \text{Et}, \text{C}_6\text{Cl}_5$.

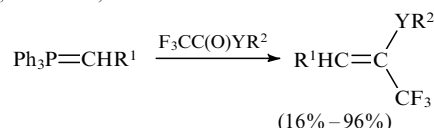
Methods for the synthesis of diverse trisubstituted alkenes containing the alkyl(aryl)sulfonyl group have been developed on the basis of the Wittig reaction. The reaction involves various carbonyl compounds: ketones,⁹² aldehydes,⁹³ esters,⁹⁴ and thioesters.^{94–96}



$\text{R} = \text{Me}, \text{Bn}, \text{Ph}$.



$\text{R}^1, \text{R}^2 = \text{Alk}, \text{Ph}$.

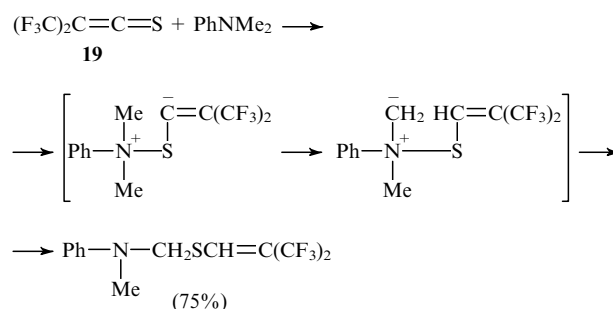


$\text{R}^1 = \text{Alk}, \text{Ph}, \text{SMe}, \text{SPh}, \text{CO}_2\text{Et}, \text{CN}$; $\text{R}^2 = \text{Et}, \text{C}_6\text{H}_{13}$; $\text{Y} = \text{S}, \text{O}$.

Butyllithium or sodium hydride is used as the base to generate ylides from the corresponding phosphonium salts.

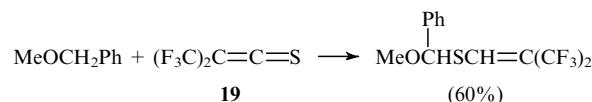
8. Syntheses based on fluoro-containing thioketenes

Bis(trifluoromethyl)thioketene (**19**) adds to *N,N*-dimethylaniline at 10 °C by attacking one of the methyl groups.⁹² The process is interpreted as the electrophilic attack of the nitrogen atom by the sulfur atom followed by proton migration.



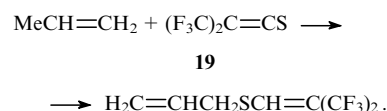
N,N-Dimethyl-*p*-toluidine and *N,N,N',N'*-tetramethylbenzidine also enter into this reaction (in the latter case, the bisadduct is formed). *N*-Ethyl-*N*-methylaniline and *N,N*-dimethyl-1-naphthylamine function as bases catalysing dimerisation of thioketene **19**.

Diethyl ether and methyl benzyl ether react with bis(trifluoromethyl)thioketene (**19**) by a similar mechanism. In the latter case, 3,3,3-trifluoro-2-trifluoromethylpropenyl sulfide is produced.⁹²

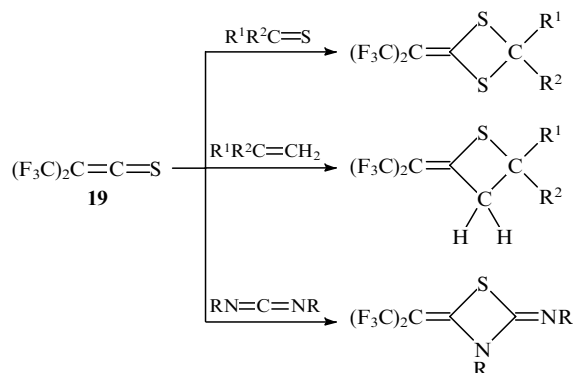


The ability of bis(trifluoromethyl)thioketene (**19**) to enter into ene reactions with some alkenes giving the corresponding propenyl sulfides and with allene and dialkylketenes was demonstrated using a large number of examples.⁹²

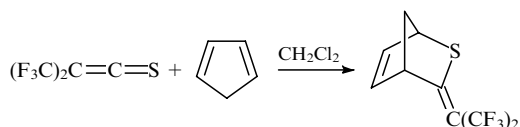
For example, ketene **19** reacts with propylene to afford compound **43** in 61% yield.



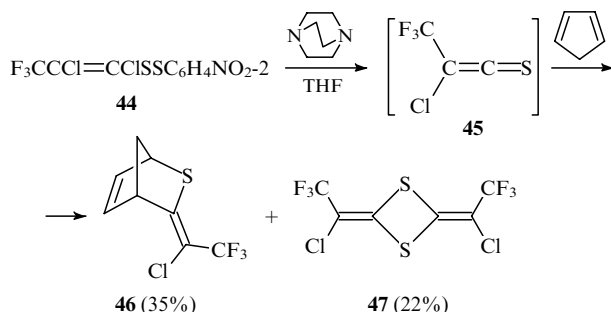
The reactions of bis(trifluoromethyl)thioketene **19** with unsaturated substrates such as thiocarbonyl compounds, alkenes unable to form the products of ene reactions, carbodiimides, *etc.* follow the [2 + 2]-cycloaddition pattern.⁹⁷



When made to react with dienes such as 2,3-dimethylbuta-1,3-diene,⁹⁷ cyclopentadiene and its derivatives, bis(trifluoromethyl)thioketene (**19**) is converted into [4 + 2]-cycloaddition products.⁹⁸ The adduct with cyclopentadiene was obtained in 96% yield.

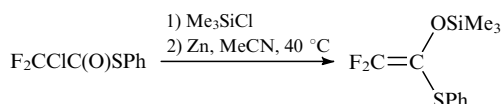


Disulfide **44** reacts with 1,4-diazabicyclo[2.2.2]octane with intermediate formation of chloro(trifluoromethyl)thioketene **45**, which was isolated as the adduct with cyclopentadiene. Along with bicyclic compound **46**, this reaction produces chloro(trifluoromethyl)thioketene **47**.⁹⁹

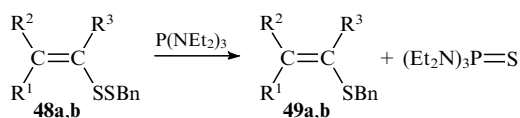


9. Other methods of synthesis

The addition of chlorotrimethylsilane to *S*-phenyl chlorodifluorothioacetate followed by dehydrochlorination on treatment with zinc was used to prepare a mixed acetal of difluoroketene.¹⁰⁰

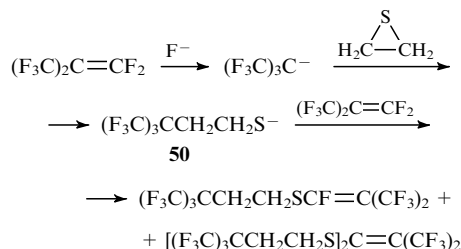


The reaction of benzyl polyfluoroalkenyl disulfides **48a,b** with phosphorous hexaethyltriimide is accompanied by desulfurisation and gives vinyl sulfides **49a,b**.^{101, 102}

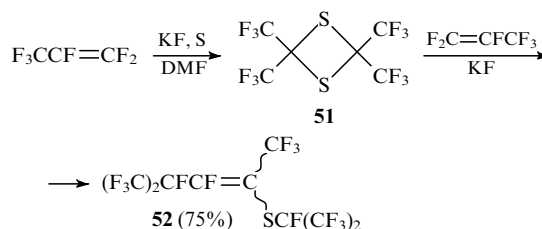


$\text{R}^1 = \text{R}^2 = \text{CF}_3$, $\text{R}^3 = \text{C}_2\text{F}_5$ (**a**, 72%);
 $\text{R}^1 = \text{R}^2 = \text{H}$, $\text{R}^3 = \text{CF}_3$ (**b**, 81%).

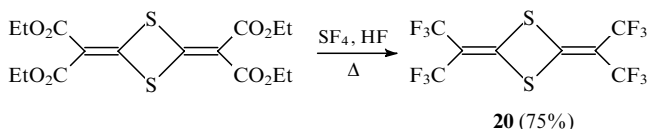
An interesting example of ring opening in ethylene sulfide on treatment with the perfluoro-*tert*-butyl carbanion, which is formed from perfluoroisobutylene in the presence of KF or CsF, has been reported.¹⁰³ Nucleophilic substitution of the resulting thiolate anion **50** for one or two fluorine atoms in perfluoroisobutylene results in a mixture of vinyl sulfides.



The reaction of hexafluoropropylene with potassium fluoride and sulfur in dimethylformamide leads to hexafluorothioacetone dimer **51**. The subsequent reaction of compound **51** with hexafluoropropylene leads to a mixture of *E* and *Z* isomers of perfluoro-2,4,6-tris(trifluoromethyl)-5-thiahept-3-ene (**52**).³⁵



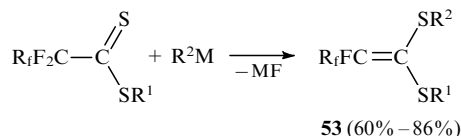
Heating of tetraethyl 1,3-dithiethanediylienedimalonate with SF_4 in the presence of HF results in the formation of 2,4-bis[2,2,2-trifluoro-1-(trifluoromethyl)ethylidene]-1,3-dithiethane (**20**), which is the dimer of bis(trifluoromethyl)thioketene **19**.⁹⁷



Depending on the amount of hydrogen fluoride used, it is possible to isolate also the products of transformation of two or three ester groups into trifluoromethyl groups.

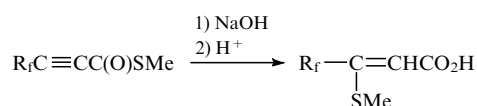
Dimer **20** is also obtained by the reaction of bis(trifluoromethyl)ketene (**19**) with triphenylphosphine sulfide at 200 °C.^{104–106}

When reacting with organometallic reagents, esters of perfluoroalkanedithiocarboxylic acids are subjected to a thiophilic attack. The intermediate carbanion is stabilised by elimination of the α -fluorine atom. This reaction yields dithioacetals **53**.¹⁰⁷

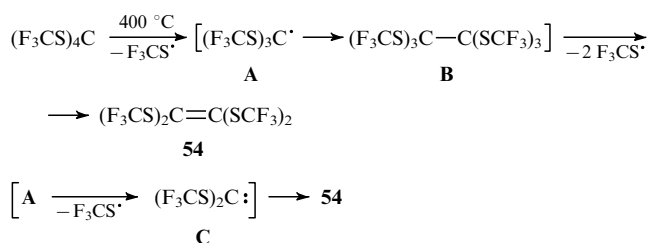


$\text{R}_f = \text{F}, \text{CF}_3, \text{H}(\text{CF}_2)_3$; $\text{R}^1 = \text{Et, Pr, Bn}$; $\text{R}^2 = \text{Et, Pr, Bu}$;
 $\text{M} = \text{MgBr, Li}$.

The electron-withdrawing properties of the polyfluoroalkyl substituent are favourable for the 1,3-shift of the methylthio group in *S*-methyl β -polyfluoroalkylthiopropiolates on treatment with the hydroxide anion.¹⁰⁸ β -Polyfluoroalkyl- β -methylthioacrylic acids containing more than 90% *Z* isomer are formed in these reactions in high yields.



Pyrolysis of tetrakis(trifluoromethylthio)methane at 400 °C and at atmospheric pressure affords tetrakis(trifluoromethylthio)ethylene **54**.¹²



Presumably,¹² this reaction follows a radical mechanism. Two pathways to the reaction product **54** are possible. The radical **A** formed initially can dimerise to give adduct **B**, which loses two trifluoromethylthiyl radicals being transformed into compound **54**. Radical **A** can be converted into bis(trifluoromethylthio)carbene **C**, which dimerises to give product **54**.

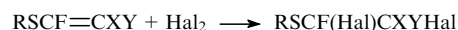
III. Chemical properties

Fluorine-containing vinyl sulfides behave both as alkenes and as sulfides. The reactivity of these compounds depends on the nature and position of substituents. If the fluorinated substituent occurs at the sulfur atom, the double bond differs little in properties from the usual double bond if one takes into account the electron-withdrawing influence of the substituent. Meanwhile, vinyl sulfides with fluorine-containing substituents at the double bond resemble to a larger extent electron-deficient fluoroalkenes, which exhibit a low reactivity toward electrophilic reagents. The behaviour of fluorine-containing vinyl sulfides depends appreciably on a number of factors including the presence of other electron-donating or electron-withdrawing substituents, the positive mesomeric effect of fluorine atoms at the multiple bond, the presence of a good leaving group in the molecule, and the degree of p, π -interaction between the sulfur atom and the double bond, which also depends on the electronic effects of the substituents. The diversity of factors influencing the reactivity of fluorine-containing vinyl sulfides markedly extends the synthetic potential of these compounds. In view of these considerations, the description of chemical properties of fluorinated vinyl sulfides is classified in this review in terms of the nature of the active reagent, irrespective of the reaction route.

1. Reactions with electrophilic reagents

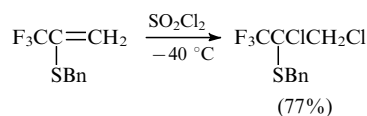
a. Halogenation

Alkyl(aryl)thiochloropolyfluoroethylenes are readily halogenated on treatment with equimolar amounts of chlorine or bromine.^{3, 5, 6, 9}



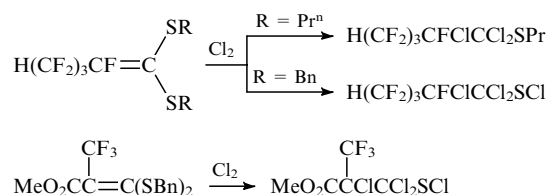
R = Me, Bn, Ph; X, Y = F, Cl, F₃C; Hal = Cl, Br.

The use of sulfuryl chloride in this reaction gave a mixture of products, although SO₂Cl₂ chlorinates the double bond in benzyltrifluoroisopropenyl sulfide under very mild conditions.¹⁰¹

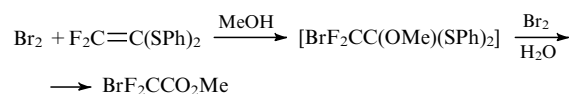


On treatment with excess chlorine, dithioacetals of fluorine-containing ketenes are chlorinated at the double bond with

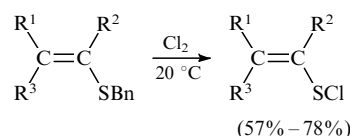
simultaneous replacement of one alkylthio group.¹⁸ In the case where the sulfur atom carries a good leaving group, for example, a benzyl group, chlorolysis proceeds further to give sulfenyl chlorides.^{18, 77}



Bromination of 2,2-difluoro-1,1-diphenylthioethylene in methanol is accompanied by conjugate electrophilic addition, as indicated by the formation of methyl bromodifluoroacetate after hydrolysis of the intermediate compound formed.¹⁰⁹

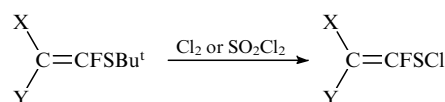


Some perfluoroalkenyl and perfluorocycloalkenyl benzyl sulfides having an electron-deficient multiple bond undergo chlorolysis at the S–Bn bond with retention of the vinyl fragment.³



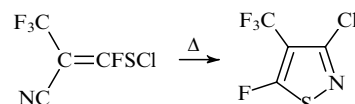
R¹–R² = (CF₂)₄, R³ = Cl; R¹–R² = (CF₂)₃, R³ = CF₃;
R¹ = R³ = CF₃, R² = F.

A number of β -functionally substituted polyfluoroalkenesulfenyl chlorides have been prepared by chlorolysis of *tert*-butyl sulfides by chlorine⁷⁷ or sulfuryl chloride.²⁵

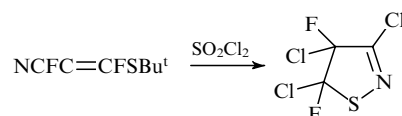


X = CF₃, Y = CO₂Me, CN; X = Y = CO₂Me.

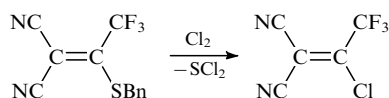
2-Cyano-1,3,3,3-tetrafluoropropenesulfenyl chloride synthesised in this reaction is a labile compound; on heating, it undergoes intramolecular cyclisation involving the nitrile group to give isothiazole.⁷⁷



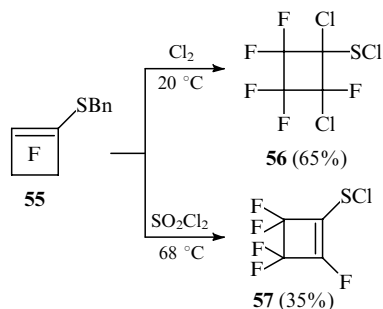
A similar intramolecular cyclisation of the intermediate sulfenyl chloride involving the nitrile group is observed in the chlorolysis of *tert*-butyl (2-cyano-1,2-difluorovinyl) sulfide.⁷⁷ Simultaneously, the double bond is chlorinated.



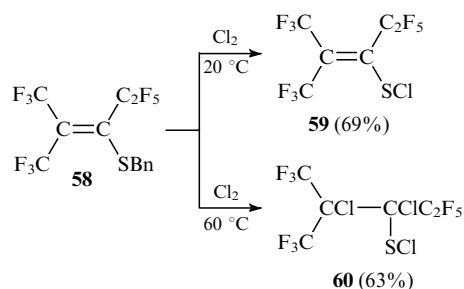
Chlorination of 1-benzylthio-2,2-dicyano-1-trifluoromethylethylene does not yield the expected sulfenyl chloride because both C–S bonds are immediately cleaved to give sulfur disulfide and 1-chloro-2,2-dicyano-1-trifluoromethylethylene.⁷⁷



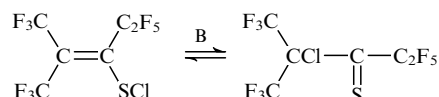
When 1-benzylthioperfluorocyclobutene (**55**) reacts with molecular chlorine, the replacement of the benzyl group is accompanied by chlorination of the double bond; as a result, saturated sulfenyl chloride **56** is formed as the final reaction product. Perfluorocyclobut-1-enesulfenyl chloride (**57**) was prepared by the reaction of benzyl sulfide **55** with SO_2Cl_2 .³



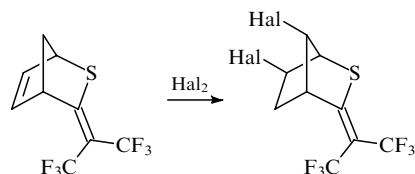
Vinyl sulfide **58** reacts with chlorine at 20 °C to give the corresponding unsaturated sulfenyl chloride **59**,¹⁰² while at higher temperature, the product of further chlorination **60** was obtained together with sulfenyl chloride.



The formation of compound **60** was interpreted¹⁰² as being due to chlorotropy in the carbon–carbon–sulfur triad.



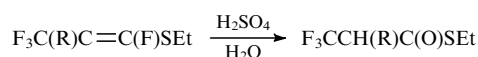
3-(Hexafluoroisopropylidene)-2-thiabicyclo[2.2.1]hept-5-ene and its derivatives are halogenated at the endocyclic double bond giving rise to the Wagner–Meerwein rearrangement products. The exocyclic double bond is not halogenated in this reaction.⁹⁸



Hal = Cl, Br.

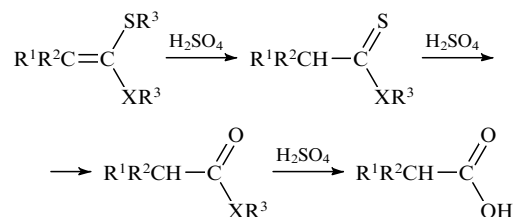
b. Acid hydrolysis

Acid hydrolysis of alkyl perfluorovinyl sulfide carried out under mild conditions affords *S*-esters of α -*H*-thiocarboxylic acids.¹¹⁰



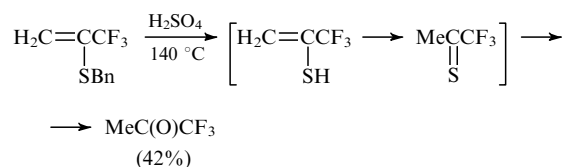
R = F, CF_3 .

On treatment of *S,S*- or *S,O*-acetals of fluorine-containing ketenes with sulfuric acid, esters of dithiocarboxylic acids or thiocarboxylic *O*-acids, and esters of thiocarboxylic *O*-acids or carboxylic acids are formed successively, depending on temperature. Fluorine-containing carboxylic acids are the final reaction products.^{18, 26, 27, 110, 111}



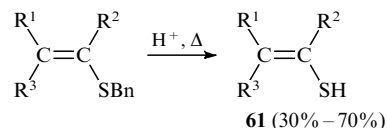
$\text{R}^1 = \text{CF}_3, \text{F}, \text{CHF}_2$; $\text{R}^2 = \text{F}, \text{CF}_3, \text{H}, \text{Alk}, \text{OMe}$;
 $\text{R}^3 = \text{Alk}, \text{Ar}$; X = O, S.

1,1,1-Trifluoroacetone was obtained by acid hydrolysis of benzyl 1,1,1-trifluoroisopropenyl sulfide.¹⁰¹



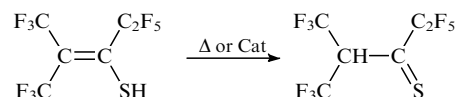
This reaction is assumed to give first enethiol, which isomerises to give a thioketone and is subsequently oxidised to a ketone.

A general method for the synthesis of polyfluorinated enethiols **61** of the aliphatic and alicyclic series has been described.³⁷ Polyfluoroalkenyl(cycloalkenyl) benzyl sulfides are heated under conditions of kinetic control in the presence of fluorosulfonic acid or concentrated sulfuric acid with simultaneous removal of volatile products by evaporation.

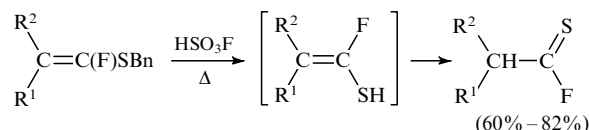


$\text{R}^1 = \text{R}^2 = \text{CF}_3, \text{R}^3 = \text{Cl}$; $\text{R}^1 = \text{R}^3 = \text{CF}_3, \text{R}^2 = \text{C}_2\text{F}_5$;
 $\text{R}^1 = \text{R}^3 = (\text{F}_3\text{C})_2\text{CF}, \text{R}^2 = \text{CF}_3$; $\text{R}^1-\text{R}^2 = (\text{CF}_2)_2, \text{R}^3 = \text{F}$;
 $\text{R}^1-\text{R}^2 = (\text{CF}_2)_3, \text{R}^3 = \text{CF}_3$; $\text{R}^1-\text{R}^2 = (\text{CF}_2)_4, \text{R}^3 = \text{Cl}$.

Enethiols **61** are colourless liquids stable on storage; they do not isomerise spontaneously into the corresponding thioketones. The enethiol to thioketone isomerisation was accomplished only for perfluoro-2-methylpent-2-ene-3-thiol on heating (150 °C, 20 h) or in the presence of catalysts (HSO_3F , Et_2O , $\text{BF}_3 \cdot \text{NEt}_3$). The back transformation of the thioketone into enethiol does not take place.



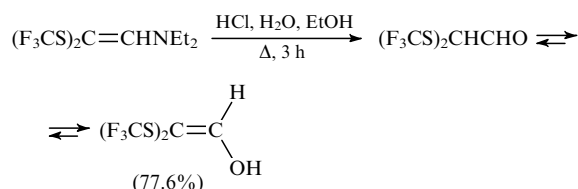
In the case where the α -position with respect to the sulfur atom is occupied by a fluorine atom instead of the perfluoroalkyl group, the acid-induced cleavage of the corresponding perhaloalkenyl benzyl sulfides gives fluorides of fluorine-containing α -hydrothionic acids rather than enethiols as the final products.⁴



$\text{R}^1 = \text{R}^2 = \text{CF}_3$; $\text{R}^1 = \text{CF}_3, \text{R}^2 = \text{F}$; $\text{R}^1 = \text{F}, \text{R}^2 = \text{Cl}$.

It is reasonable to assume that this transformation involves the intermediate formation of enethiols, which are unstable under the reaction conditions (due to the substantial positive mesomeric effect of the vinylic fluorine atom) and isomerise to thermodynamically more stable forms.

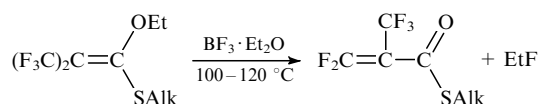
Hydrolysis of the enamine, prepared from trifluoromethanesulfonyl chloride and triethylamine, furnishes bis(trifluoromethylthio)acetaldehyde, which mainly exists as the enol form.¹¹²



A similar reaction carried out for β -alkyl(aryl)thio- α -polyfluoroalkyl-containing enamines readily gives the corresponding ketones.^{64, 74}

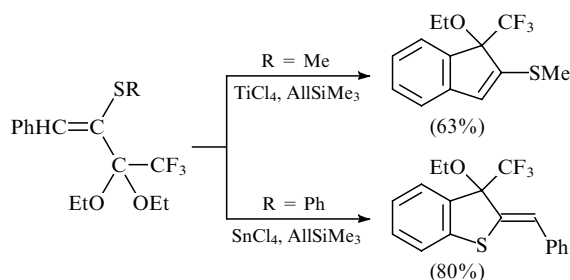
c. Other reactions

Electrophilic elimination of ethyl fluoride from bis(trifluoromethyl)ketene *O*-ethyl-*S*-alkyl acetals takes place on heating with boron trifluoride etherate.¹¹³

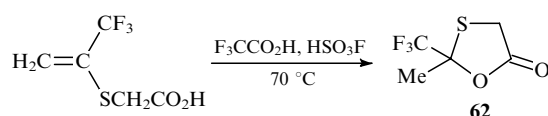


The reaction mechanism is similar to the mechanism of elimination of alkyl fluorides from bis(trifluoromethyl)ketene *O,O*-di- and *O,N,N*-trialkyl acetals in the presence of Lewis acids. On treatment with the Lewis acid, the allylic fluorine atom is eliminated from alkoxyalkene to give the mesomeric carbenium ion.¹¹⁴ A similar reaction for *S,S*-dialkyl dithioacetals of bis(trifluoromethyl)ketene could not be performed.¹¹³

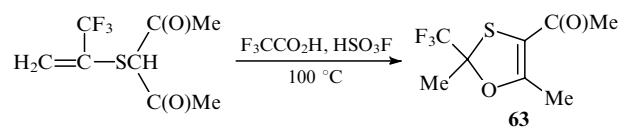
Acetals of α,β -unsaturated trifluoromethyl ketones containing an α -methylthio or α -phenylthio group do not undergo Lewis acid-catalysed intermolecular allylation. The products of intramolecular cyclisation are formed instead.¹¹⁵



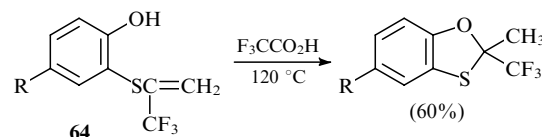
Some trifluoroisopropenyl sulfides enter into acid-catalysed intramolecular cyclisation. Thus heating of 2-(1-trifluoromethylvinylthio)acetic acid in F_3CCO_2H in the presence of fluorosulfonic acid as the catalyst is accompanied by lactonisation giving thialactone **62** in a preparative yield.²¹



The intramolecular cyclisation of 3-(1-trifluoromethylvinylthio)pentane-2,4-dione occurs under more rigorous conditions.²¹ The reaction is accompanied by resinification, the yield of compound **63** being not higher than 30%.

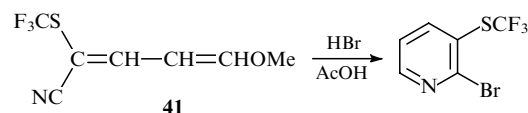


Cyclisation of *o*-(1-trifluoromethylvinylthio)phenols **64** occurs when this compound is heated to 120 °C in trifluoroacetic acid in a sealed tube.¹¹⁶

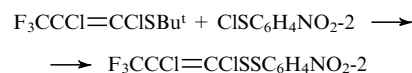


R = H, Me, Et.

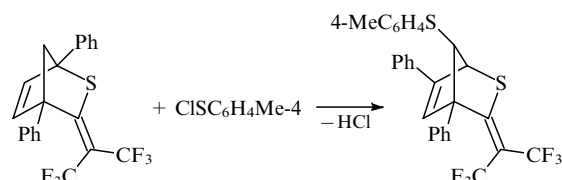
The intramolecular cyclisation of 5-methoxy-2-trifluoromethylthiopenta-2,4-dienonitrile (**41**) induced by HBr and AcOH involves the nitrile group. This reaction was patented as a method of synthesis of 3-trifluoromethylthio-substituted pyridines.¹¹⁷



In the reaction of *tert*-butyl 2-trifluoromethyl-1,2-dichlorovinyl sulfide with *o*-nitrophenylsulfenyl chloride, the *tert*-butyl group at the sulfur atom is replaced, which results in an asymmetric disulfide.⁹⁹

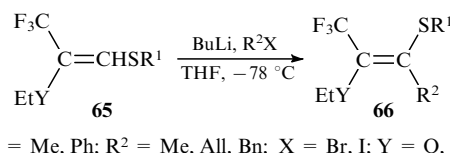


The reaction of 3-(hexafluoroisopropylidene)-1,4-diphenyl-2-thiabicyclo[2.2.1]hept-5-ene with *p*-methylbenzenesulfonyl chloride yields the Wagner–Meerwein rearrangement product, which is spontaneously dehydrochlorinated.⁹⁸

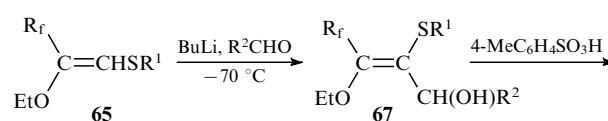


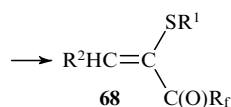
An important feature of sulfur compounds is the ability to stabilise both carbanionic and carbocationic centres.

The ability of sulfur atoms to stabilise α -carbanions has been used in the alkylation of β -polyfluoroalkyl- α -hydrovinyl sulfides **65**. Successive treatment of compounds **65** with butyllithium and alkyl halides⁹⁴ or with non-ionisable aldehydes leads to alkylation products **66** and **67**.¹¹⁵



R¹ = Me, Ph; R² = Me, All, Bn; X = Br, I; Y = O, S.



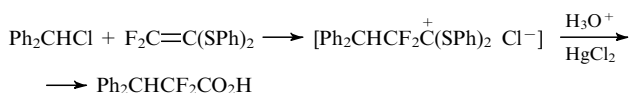


$\text{R}_f = \text{CF}_3, \text{C}_2\text{F}_5$; $\text{R}^1 = \text{Me}, \text{Ph}$;

$\text{R}^2 = \text{Ph}, \text{Bu}^t, \text{PhCH}=\text{CH}, \text{PhC}\equiv\text{C}, \text{Bu}^t\text{C}\equiv\text{C}, 2\text{-furyl}$.

The adducts **67**, formed in the reactions with aldehydes, are converted into α,β -unsaturated perfluoroalkylvinyl ketones **68** on treatment with *p*-toluenesulfonic acid. This reaction is stereoselective, giving rise to *Z* isomers of alkenes **68**.

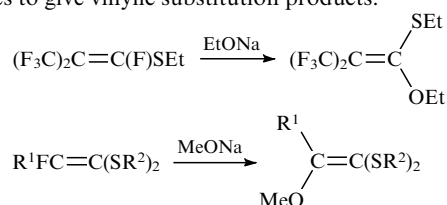
The electrophilic addition of chlorodiphenylmethane to 1,1-difluoro-2,2-di(phenylthio)ethylene involves the difluoromethylene fragment; thus, the sulfur atom stabilises a positive charge more efficiently than a fluorine atom.¹⁰⁹



2. Reactions with nucleophilic reagents

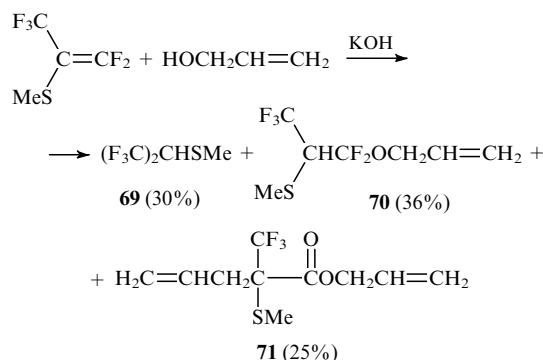
a. Reactions with O-nucleophiles

Vinyl sulfides^{32,52} and ketene *S,S*-acetals^{18,26} with a fluorine atom at a multiple bond are prone to react with aliphatic alcohols to give vinylic substitution products.

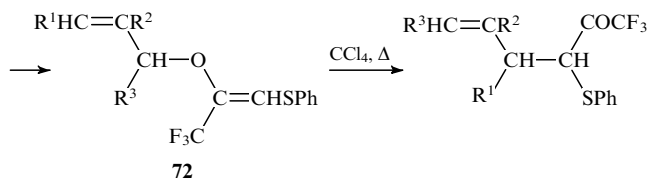
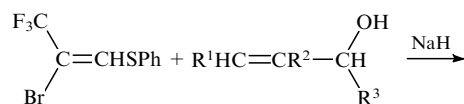


$\text{R}^1 = \text{F}, \text{H}(\text{F}_2\text{C})_3$; $\text{R}^2 = \text{Alk}$.

The exothermic reaction of 2-(methylthio)pentafluoropropene with allyl alcohol in the presence of a catalytic amount of KOH produces a mixture of three products, namely, sulfide **69**, allyl ether **70**, and allyl 2-methylthio-2-trifluoromethylpent-4-enoate (**71**), the last compound being the product of a [3,3]-sigmatropic rearrangement.²⁴



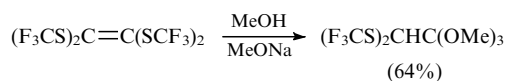
The reaction of 2-bromo-1,1,1-trifluoro-3-phenylthiopropene with substituted allylic alcohols in the presence of sodium hydride leads to the products of bromine replacement.¹¹⁸ The intermediate formation of 1,1,1-trifluoro-3-phenylthiopropyne was assumed for these reactions.



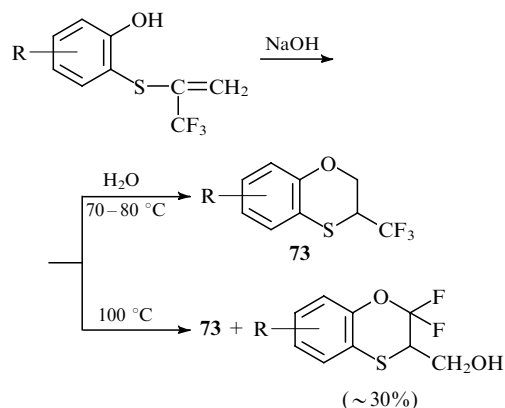
$\text{R}^1, \text{R}^2, \text{R}^3 = \text{H}, \text{Alk}, \text{Ph}$.

Unsaturated ethers **72** have been used in the Claisen rearrangement for stereocontrolled synthesis of trifluoromethyl ketones.

The final product formed in the reaction of tetrakis(trifluoromethylthio)ethylene with methanol in the presence of sodium methoxide is trimethyl bis(trifluoromethylthio)orthoacetate. This reaction is assumed to occur in several steps that include successive addition of the methoxy anion and elimination of the trifluoromethoxy anion.¹²



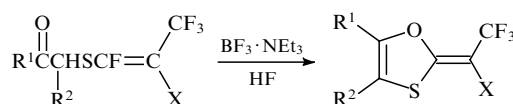
On heating to 70–80 °C with an aqueous solution of sodium hydroxide, *o*-(1-trifluoromethylvinylthio)phenols are converted into 3-trifluoromethylbenzo-1,4-oxathianes **73** upon an intramolecular cyclisation.¹¹⁶ When this reaction is carried out under more rigorous conditions with excess NaOH, 2,2-difluoro-3-hydroxymethylbenzo-1,4-oxathianes are formed along with 1,4-oxathianes.¹¹⁹



$\text{R} = \text{Alk}, \text{OMe}, \text{F}$.

Apparently, the reaction mechanism includes the attack of the hydroxide anion on the $\text{C}=\text{C}$ bond of the initial compound, stabilisation of the resulting carbanion due to elimination of the fluoride ion and cyclisation of the intermediate difluoromethylene compound.

The products of sulfenylation of enolising carbonyl compounds with α -fluoro- α,β -unsaturated sulfonyl chlorides in the presence of the $\text{BF}_3 \cdot \text{NEt}_3$ complex are prone to undergo intramolecular cyclisation with elimination of HF and the formation of alkyliden-1,3-oxathioles.¹²⁰

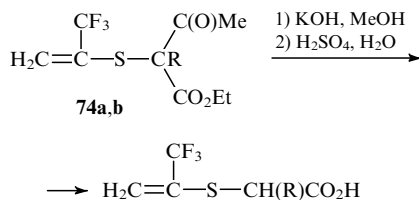


$\text{R}^1 = \text{Alk}, \text{Ar}$; $\text{R}^2 = \text{H}, \text{CO}_2\text{Et}, \text{C}(\text{O})\text{Me}, \text{C}(\text{O})\text{CF}_3$;
 $\text{X} = \text{CF}_3, \text{CO}_2\text{Me}, \text{CN}$.

The reaction conditions are determined by the ability of the carbonyl compound to undergo enolisation. In the case of β -dicarbonyl compounds, cyclisation takes place even in the

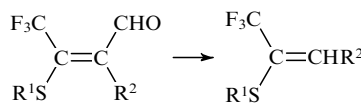
absence of $\text{BF}_3 \cdot \text{NEt}_3$ on moderate heating. A similar reaction is also typical of *o*-sulfenylated phenols.⁷⁵

When reacting with potassium hydroxide, ethyl 2-(1-trifluoromethylvinylthio)acetoacetates **74a,b** are deacetylated to give the corresponding acids.²¹ The vinylthio group does not participate in the reaction.



$\text{R} = \text{H}$ (**a**, 57%), Me (**b**, 52%).

The decarbonylation of vinyl sulfides containing an aldehyde group at the multiple bond takes place on treatment with KOH in dichloromethane⁵⁷ or potassium *tert*-butoxide in toluene.⁹⁶

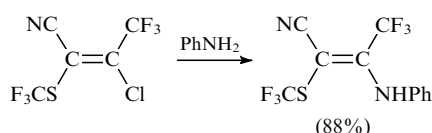


$\text{R}^1 = \text{Et, Ph; R}^2 = \text{Ph, 4-ClC}_6\text{H}_4, \text{furan-2-yl}$.

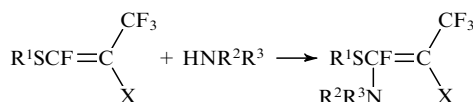
The *Z* isomer markedly predominates in the reaction products, the *Z* to *E* isomer ratio being changed with respect to the initial compounds in favour of the *Z* isomer.

b. Reactions with N-nucleophiles

In reactions with N-nucleophiles, the replacement of various good leaving groups at the multiple bond is most typical of fluorinated vinyl sulfides containing strong electron-withdrawing substituents (including functional ones). For instance, the chlorine atom in 2-chloro-1-cyano-2-trifluoromethyl-1-trifluoromethylthioethylene can be easily replaced by a phenylamino group.⁹⁰



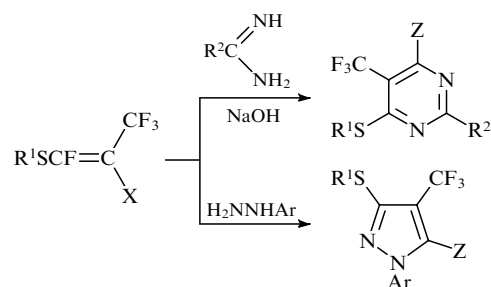
The replacement of the vinylic fluorine atom in β -alkylthio derivatives of perfluoromethacrylic acid on treatment with ammonia and primary or secondary amines proceeds equally smoothly.¹²¹



$\text{R}^1 = \text{Bu}^t, \text{Bn; R}^2, \text{R}^3 = \text{H, Alk, Ar; X} = \text{CO}_2\text{Me, CN.}$

Meanwhile, 3-benzylthio-2,3-difluoroacrylonitrile not activated by the trifluoromethyl group does not react with primary arylamines even on heating.

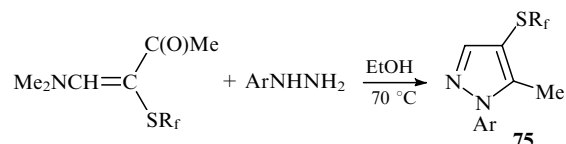
β -Functionalised alkyl(aryl)polyfluoroalkenyl sulfides react with acid amidines and arylhydrazines to form substituted pyrimidines and pyrazoles. Intramolecular cyclisation involves the functional group in the products of replacement of the fluorine atom formed initially.¹²¹



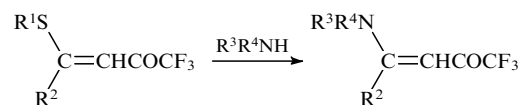
$\text{R}^1 = \text{Bu}^t, \text{Bn, Ar, Het; R}^2 = \text{Me, Ph; X} = \text{CO}_2\text{Me, Z} = \text{OH; X} = \text{CN, Z} = \text{NH}_2.$

2-Chloro-1-cyano-2-trifluoromethyl-1-trifluoromethylthioethylene¹²² and 3-benzylthio-2,3-difluoroacrylonitrile¹²¹ enter into analogous reactions with acid amidines to give aminopyrimidines.

The reaction of 1-polyfluoroalkylthio-2-dimethylaminovinyl methyl ketones with arylhydrazines is also accompanied by heterocyclisation. 4-Polyfluoroalkylthiopyrazoles **75** thus formed have been patented as pesticides.⁸⁹

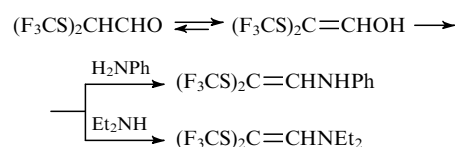


The alkylthio group in β -alkylthio- α,β -unsaturated trifluoromethyl ketones is easily substituted by amines. This affords enamines in yields of 56% to 100%.¹²³

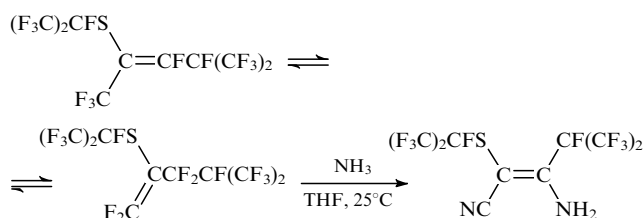


$\text{R}^1 = \text{Me, Et; R}^2 = \text{H, Me, Ph; R}^3, \text{R}^4 = \text{H, Me, Et, Bn.}$

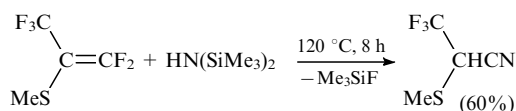
Bis(trifluoromethylthio)acetaldehyde, which mainly exists as the corresponding enol, reacts with amines to give the products of replacement of the hydroxy group.¹¹²



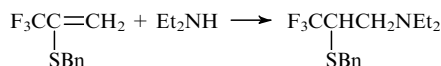
The reaction of perfluoro-2-isopropylthio-4-methylpent-2-ene, which isomerises to the terminal fluoroalkene, with anhydrous ammonia affords cyano-containing enamine.¹²⁴



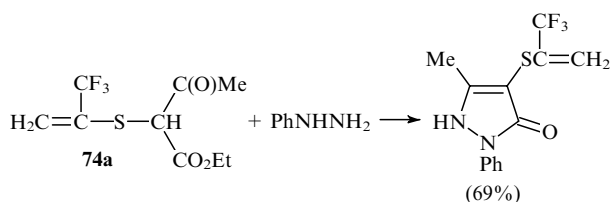
Hexamethyldisilazane adds to 2-methylthiopentafluoropropene under rigorous conditions. The reaction is accompanied by elimination of trimethylfluorosilane to give 2-methylthio-3,3,3-trifluoropropionitrile.²⁴



The double bond in 2-benzylthio-1,1,1-trifluoropropene exhibits diphilic properties being able to add both electrophilic (for example, Cl_2) and nucleophilic reagents. The reaction with diethylamine proceeds with a yield of 66%.¹⁰¹



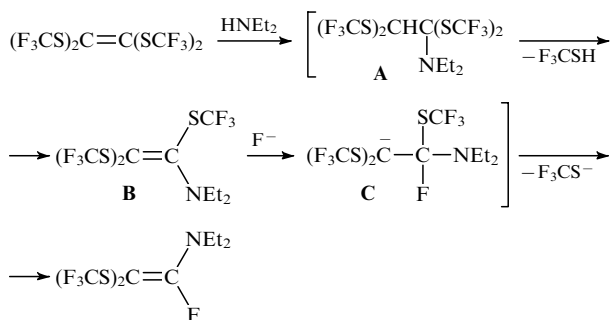
However, the reaction of ethyl 2-(1-trifluoromethylvinylthio)acetoacetate **74a** with phenylhydrazine leads to substituted pyrazoline, the vinylthio group remaining intact.²¹



The reaction of 2,2,2-trifluoroethyl phenyl sulfide with lithium diisopropylamide (LDA) affords (phenylthio)ynamine.²⁶ The first step involves dehydrofluorination to give 2,2-difluorovinyl phenyl sulfide.



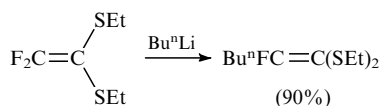
Unexpectedly, 2-diethylamino-2-fluoro-1,1-bis(trifluoromethylthio)ethylene was found to be the major product in the reaction of tetrakis(trifluoromethylthio)ethylene with excess diethylamine.¹²



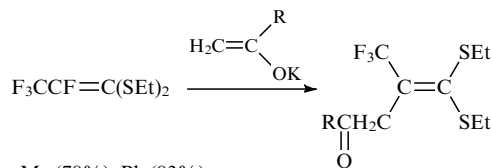
The reaction mechanism proposed in the study¹² includes the addition of diethylamine to the double bond and elimination of trifluoromethanethiol from adduct **A** yielding the product of replacement of one trifluoromethylthio group **B**. Compound **B** reacts with the fluoride ion, which is produced in the reaction mixture upon decomposition of the trifluoromethylthio anion, and is stabilised due to elimination of the second trifluoromethylthio group from intermediate **C**.

c. Reactions with C-nucleophiles

Difluoroketene *S,S*- and *S,O*-acetals react with C-nucleophiles such as organolithium compounds or Grignard reagents to give products of replacement of the fluorine atom.^{17, 26, 27}

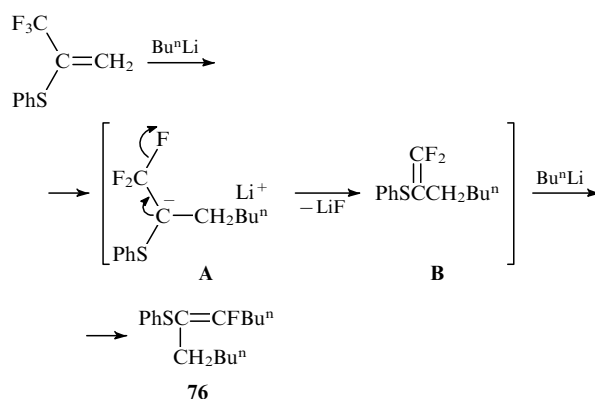


In reactions with enolates, generated by treatment of methyl ketones with potassium hydride, fluoro(trifluoromethyl)ketene diethyl dithioacetal also forms the products of replacement of the vinylic fluorine atom.¹²⁵

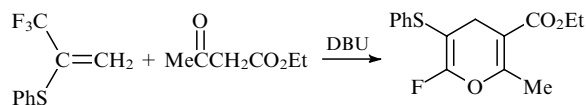


R = Me (78%), Ph (83%).

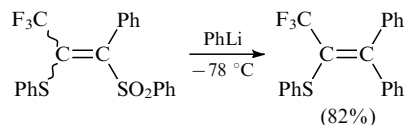
1,1,1-Trifluoroisopropenyl phenyl sulfide adds butyllithium at the double bond.¹⁰ The carbanion **A** thus produced is stabilised by elimination of a fluoride ion being converted into difluoromethylidene compound **B**. This reacts subsequently with BuLi leading to monofluorine-containing vinyl sulfide **76**.



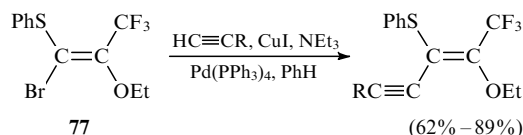
The reaction of the same 1,1,1-trifluoroisopropenyl phenyl sulfide with the anion generated from ethylacetoacetate on treatment with diazabicycloundecene (DBU) proceeds by a similar mechanism. Heterocyclisation takes place to give substituted 4*H*-pyran.¹⁰



The replacement of the phenylsulfo group in phenyl vinyl sulfone takes place in the presence of phenyllithium.⁴⁹

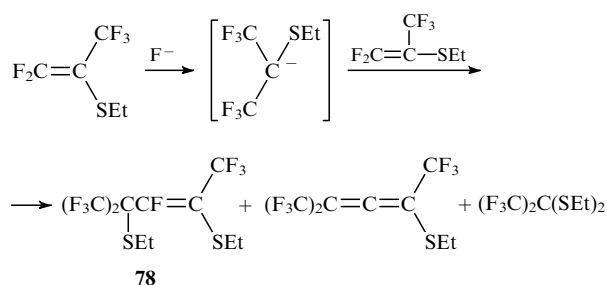


Sulfides containing conjugated double and triple bonds have been prepared by reactions of α -bromovinyl sulfide **77** with alkynes catalysed by palladium complexes.¹²⁶

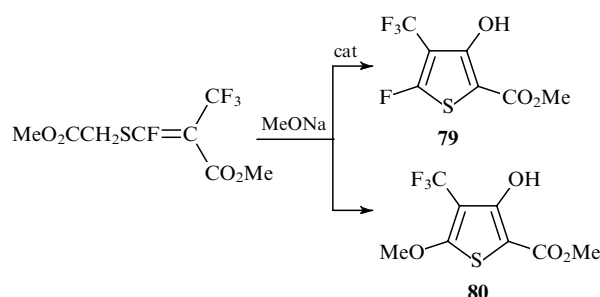


R = Bu, Bu^t, Ph, SiMe₃, CH₂OH.

Treatment of 2-ethylthiopentafluoropropene with caesium fluoride results in a carbanion, which reacts with a second molecule of the initial vinyl sulfide to give dimer **78** and other products.¹⁴



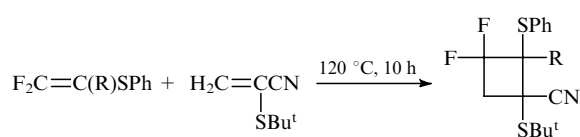
Alkoxy carbonylmethyl polyfluoroalkenyl sulfides containing a functional group in the β -position readily cyclise to thiophenes under the action of bases.^{59, 127, 128} Thus on treatment with sodium methoxide, methoxycarbonylmethyl 1,3,3,3-tetrafluoro-2-methoxycarbonylpropenyl sulfide generates a carbanion with participation of the methylene group and undergoes intramolecular cyclisation, which affords 5-fluoro-3-hydroxythiophene **79**. The vinylic fluorine atom remains intact. When an excess of sodium methoxide is used, the vinylic fluorine atom in the cyclic structure **79** is substituted by the methoxy group, which yields 3-hydroxy-5-methoxythiophene **80**.⁵⁹



3-(Methoxycarbonylmethylthio)acrylates with different structures readily enter into a similar reaction. In this case, substituted acrylonitriles are converted into 3-aminothiophenes. The reaction is catalysed more efficiently by triethylamine. With this catalyst, the yields of the reaction products are nearly quantitative.⁵⁹

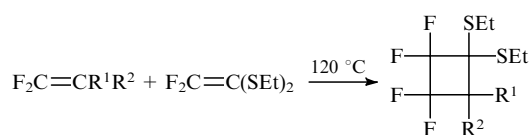
3. Cycloaddition

Published data on cycloaddition involving fluorine-containing vinyl sulfides are scarce. For example, [2 + 2]-cycloaddition of 2,2-difluorovinyl phenyl sulfide and its 1-halogenated analogues to α -*tert*-butylthioacrylonitrile has been reported.¹²⁹



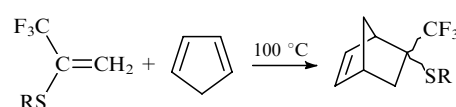
R = H (47%), F (57%), Cl (88%).

α -Substituted acrylic acid derivatives react with difluoroketene *S,S*-diethyl acetal to give cyclobutanes in up to 100% yields.¹²⁹



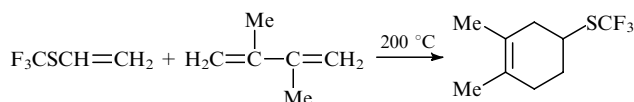
R¹ = CN, CO₂Me; R² = OMe, SePh, SBu^t, SPh, $-\text{N} \begin{array}{c} \diagup \quad \diagdown \\ \text{O} \end{array}$.

1,1,1-Trifluoroisopropenyl sulfides enter into the Diels–Alder reaction with cyclopentadiene on heating to 100 °C being thus converted into mixtures of *endo*- and *exo*-adducts.^{21, 130}



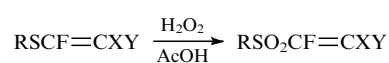
R = CH₂CH₂Cl, CH₂C(O)Me.

Cycloaddition of trifluoromethylthioethylene to 2,3-dimethylbuta-1,3-diene occurs under drastic conditions.⁶²



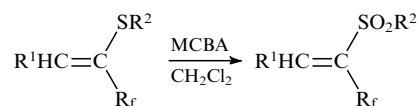
4. Oxidation

Hydrogen peroxide in acetic acid was the first reagent to be used to oxidise vinyl sulfides to α,β -unsaturated sulfoxes.^{5, 6, 8, 16, 67}



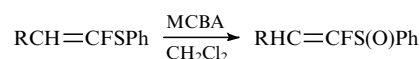
R = Et, Prⁱ, Ph; X, Y = F, Cl, F₃C, SPh.

However, lately, organic oxidants have been used most often. For example, 2 equivalents of *m*-chloroperbenzoic acid (MCBA) in dichloromethane ensure oxidation of fluorine-containing vinyl sulfides to sulfoxes at 20 °C.^{49, 93, 96, 126, 131, 132}



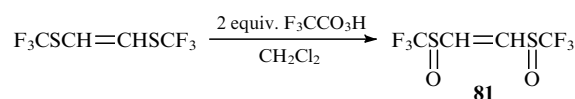
R¹ = Alk, Ar, CO₂Et, CN; R² = Et, C₆H₁₃, Ph; R_f = F, CF₃, C₂F₅

When 1 equivalent of MCBA is used, the reactions normally produce mixtures of oxidation products; however, in the case of α -fluorovinyl sulfides, selective preparation of sulfoxides in 79%–83% yields is possible.⁹³

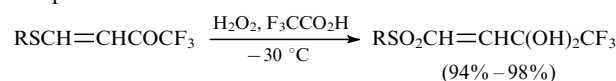


R = Alk, Ar.

By oxidation of *n*-butyl 1-chloro-2,3,3,4,4,5,5-heptafluoropent-1-enyl sulfide with excess trifluoroperacetic acid at 20 °C, the corresponding sulfoxide was obtained in 70% yield.³² On treatment of a mixture of *cis*- and *trans*-1,2-di(trifluoromethylthio)ethylenes with trifluoroperacetic acid in dichloromethane at 20 °C, a mixture of disulfoxide **81** isomers was obtained in a high yield. The racemic modification of the *trans*-isomer was isolated from this mixture in 8% yield.¹⁵

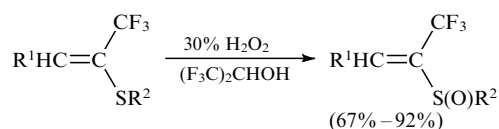


The reaction of β -trifluoroacetylated vinyl sulfides with H₂O₂ in CF₃CO₂H involves not only oxidation of the sulfur atom but also transformation of the carbonyl group, giving rise to diols stable up to 40 °C.¹³³



R = Me, Ph.

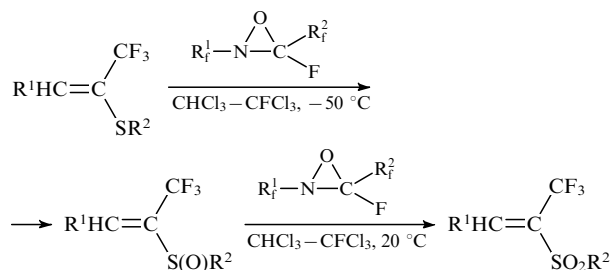
An efficient method for selective oxidation of 1-trifluoromethylvinyl sulfides to sulfoxides consists of treatment of the compounds with 30% hydrogen peroxide in hexafluoroisopropyl alcohol.¹³⁴



$\text{R}^1 = \text{Bu}^i, \text{Ph}, \text{CO}_2\text{Et}, \text{HC}=\text{CHPh}, \text{CH}_2\text{CH}_2\text{Ph}; \text{R}^2 = \text{Et}, \text{C}_7\text{H}_{15}.$

The selective formation of sulfoxides in this reaction is due to the effect of the solvent, *i.e.*, hexafluoroisopropyl alcohol ($\text{p}K_a = 9.3$), which activates H_2O_2 through the formation of a hydrogen bond. Simultaneously, hexafluoroisopropyl alcohol forms a hydrogen bond with the oxygen atom of the sulfoxide obtained in the reaction; this markedly changes the nucleophilicity of the sulfur atom and prevents oxidation to sulfone. With a more basic solvent, trifluoroethanol ($\text{p}K_a = 12.8$), the reaction is very slow.

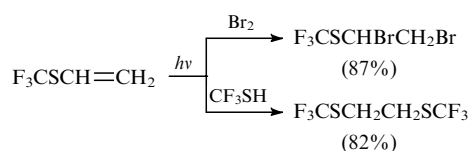
Vinyl sulfides can be oxidised using perfluoro-*cis*-2,3-dialkyl-oxaziridines. They oxidise α -trifluoromethylvinyl sulfides to the corresponding sulfoxides in the $\text{CHCl}_3\text{--CFCl}_3$ solvent system at -50°C .¹³¹ Further oxidation of sulfoxides at 20°C leads to sulfones.



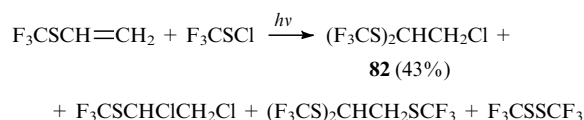
$\text{R}^1 = \text{Alk}, \text{Ar}, \text{CO}_2\text{Et}; \text{R}^2 = \text{Et}, \text{C}_6\text{H}_{13}; \text{R}_f^1, \text{R}_f^2 = \text{C}_4\text{F}_9, \text{C}_3\text{F}_7, \text{C}_6\text{F}_{13}, \text{C}_5\text{F}_{11}.$

5. Other reactions

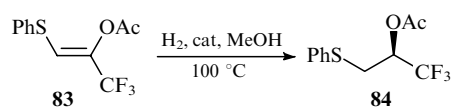
On exposure to UV radiation, trifluoromethylthioethylene reacts with bromine and trifluoromethanethiol by a free radical mechanism.¹²



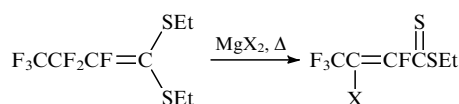
Meanwhile, the radical addition of trifluoromethanesulphenyl chloride to trifluoromethylthioethylene affords several products.¹² The major product is 2-chloro-1,1-bis(trifluoromethylthio)ethane (**82**).



Enantioselective hydrogenation of vinyl sulfide **83** in the presence of catalytic amounts of ruthenium complexes gives saturated sulfide **84** in 83% yield and with an enantiomeric purity of 89%.¹³⁵

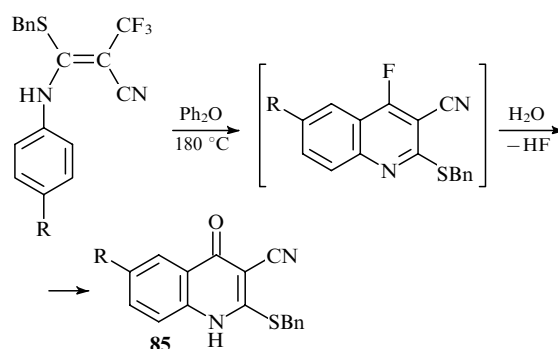


Esters of β -bromo- and β -chloro-perfluorodithiocrotonic acid have been prepared in high yields by heating fluoro(pentafluoroethyl)ketene with anhydrous magnesium halides.¹³⁶



$\text{X} = \text{Cl}, \text{Br}.$

Cyclisation involving the trifluoromethyl group occurs on heating of cyano(trifluoromethyl)ketene *N,S*-acetals in diphenyl oxide. At 180°C , the reaction was found to be accompanied by evolution of hydrogen fluoride and intramolecular cyclisation to form an aromatic nucleus.¹²¹



$\text{R} = \text{H}, \text{F}, \text{Me}, \text{PhO}.$

Evidently, the first step of the reaction is proton migration from the nitrogen atom to the α -carbon atom and thermal dehydrofluorination of the CH -acid thus formed. On alkaline hydrolysis of the reaction products, 3-cyanoquinolin-4-ones **85** were obtained and characterised.

* * *

To summarise the information covered in this review, one can state that fluorine-containing alkyl(aryl) vinyl sulfides are fairly reactive compounds with great synthetic potential. Numerous convenient methods for the synthesis of fluorinated vinyl sulfides based on readily available starting compounds have now been developed. Therefore, the problems of synthetic applications of these compounds come to the forefront, because until recently, they have been mainly used in reactions where the alkyl(aryl)thio group functioned as a leaving fragment. However, lately, the reactions with retention of the sulfur atom in the molecule as well as regio- and stereo-selective processes have attracted increasing attention.

The preparative accessibility of fluorine-containing alkyl(aryl) vinyl sulfides in combination with high reactivity creates prerequisites for the use of these compounds in the synthesis of diverse organic and heterocyclic products that present both theoretical and practical interest.

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^e — *Chem. Heterocycl. Compd. (Engl. Transl.)*

Nanochemistry: a direct route to high technologies of the new century

A L Buchachenko

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Abstract. This review deals with problems involved in creating and handling nanoparticles, as well as the integration of nanoparticles into various systems and the operation of such systems. The review analyses the chemical, electrical and magnetic properties of the three main elements of nanotechnologies, *viz.*, clusters, nanotubes and nanowires. The bibliography includes 77 references.

I. Nanochemistry: a science about the 'nanoworld'

Chemistry celebrated the end of the 20th century with a remarkable result of strategic importance: it has approached the threshold of being able to detect a single molecule and identify its physical and chemical behaviour. As a result, a new field of chemistry has appeared, *viz.*, the chemistry of single molecules. A molecule acquires identity and becomes a 'person'.^{1–3}

This new field defines precisely the upper boundary of yet another field of chemistry, called nanochemistry, which studies small ensembles of molecules (or atoms) comprising more than one species. However, there is no strict quantitative criterion for defining the lower boundary of this region; furthermore, setting any artificial limits (*e.g.*, size in nanometres or number of molecules or atoms in hundreds or thousands) is harmful.

The world of nanochemistry is a vast world from individual molecules to continual systems that constitute a phase. Nanoparticles are characterised by intermolecular interactions that deprive molecules of their personality; the properties and behaviour of molecules in ensembles differ from those of single molecules (social communities of people and animals show some similar features).

The main and fundamental problem of nanochemistry around which all interests of researchers are concentrated is the problem of dimensional effects. The intriguing questions are: how the properties of single molecules evolve into the properties of a phase when molecules are united; how bridges between the world of single molecules and the macroscopic world of substance are built; how the hierarchy of quantity is converted into the hierarchy

of properties. Dimensional effects are so diverse and unexpected that there is no general solution to the problem. The methods of quantum chemistry and molecular dynamics succeed in answering specific questions only. They can explain almost everything but cannot provide reliable predictions. However, science only then becomes real science when it can foresee. In this sense, nanochemistry altogether is still ahead of us; nanoparticles will long remain our 'employers'.

The lower boundary of nanochemistry (with the adjoining colloid chemistry and chemistry of highly dispersed systems) is rather vague and is determined by common sense, which appeals to two important considerations: first, the relationship between the concepts 'nanoparticle' and 'nanoreactor' (*vide infra*); second, the extent to which nanoparticles lose their individual properties when materials or colloid systems are formed from them, *i.e.*, how much they lose their identity as 'chemical persons'.⁴

1. The structural-chemical contours of nanochemistry

The simplest nanoreactors in which reagents are arranged spatially are van der Waals molecules, *i.e.*, weakly bound complexes of atoms, radicals, ions and molecules; the partners in such complexes are held by intermolecular non-valence interactions. The van der Waals molecules have been observed in supersonic molecular beams and studied by laser and microwave spectroscopy and by mass spectrometry. Very many molecules of this kind are known: He_2 , $(\text{H}_2)_2$, $\text{C}_6\text{H}_6 \cdot \text{CH}_4$, $\text{C}_2\text{H}_4 \cdot \text{Ar}$, $\text{HCl} \cdot \text{Xe}$, $\text{Ar} \cdot \text{I}_2$, CaMg , $(\text{C}_2\text{H}_2)_2$, $\text{He} \cdot \text{NH}_3$, *etc.* Various physical parameters have been determined for the majority of these molecules: symmetry and geometry (bond angles and lengths), dipole moments, rotation and oscillation frequencies, lifetimes and dissociation energies, magnetic susceptibilities and ionisation potentials, quadrupole and coupling constants and many others.

But why are van der Waals molecules so interesting to physicists and chemists and what are they good for? First, they are a reliable source of atom–atom potentials; it is due to them that interatomic potentials have acquired spectroscopic precision and are now widely used as the key parameters in calculations of chemical and molecular dynamics of liquids, glasses and macromolecules; they are used in calculations of intermolecular energy transfer and energy relaxation. Atomic potentials are responsible for the molecular organisation of crystals and macromolecules, polymorphism of crystals, self-organisation of molecular ensembles, self-replication of biomolecules, *etc.*

Second, van der Waals molecules are responsible for the macroscopic properties of gases (*PVT* diagrams, viscosity, second virial coefficient, *etc.*); they induce condensation, crystallisation

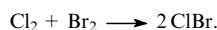
A L Buchachenko N N Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 119991 Moscow, Russian Federation. Fax: (7-095) 938 24 84. Tel. (7-095) 939 71 28

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and other phase transitions; they also define the critical points of substances and the density fluctuations and correlation radii in these points.

Do the van der Waals molecules play any role in chemical reactions? At first glance, the answer should be 'no', since the bond energy between the partners in these molecules is low, *viz.*, about kT or sometimes even lower. However, a partner in such a molecule may act as a 'rider', *i.e.*, as a third body that acts as a drain for the excess of energy evolved in the reaction, and eliminate reaction prohibition as regards the orbital symmetry or angular momentum. Here is a good example:



The cross-section of this reaction is negligibly small due to an orbital symmetry forbiddenness. However, the same reaction between $(\text{Cl}_2)_2$ (a van der Waals molecule) and Br_2 occurs in almost each collision, since orbital symmetry forbiddenness is eliminated by the third particle.

It is known that the angular distribution of products in reacting molecular beams suggests unambiguously that many reactions (even $\text{H} + \text{D}_2 \rightarrow \text{HD} + \text{D}$) are preceded by the formation of short-lived complexes between the reagents, *i.e.*, the van der Waals molecules, which can often be observed spectroscopically.

The interest in complexes between metal atoms and small molecules (H_2 , CO , CH_4 , C_2H_4 , N_2 , *etc.*) is increasing continuously; many complexes of this kind have already been studied to date: $\text{Al} \cdot \text{N}_2$, $\text{Ca}^+ \cdot \text{N}_2$, $\text{Hg} \cdot \text{N}_2$, $\text{Cr}^+ \cdot \text{N}_2$, *etc.* Pair non-valence interactions of atoms and molecules are at the upper boundary of nanochemistry.

In addition to the van der Waals molecules, there is an enormous number of other nano- and microreactors of diverse nature, scale and molecular ordering: complexes; crystal solvates; nanohydrates (*e.g.*, that of methane); clathrate compounds (*e.g.*, with cyclodextrins, semispherands and calixarenes as 'hosts' which interact with guest molecules); macromolecules (helices or rigid rods); cavities in zeolites and porous materials. Many characteristics are different in microreactors: molecular dynamics of reagents, mechanisms and rates of chemical transformations, pK values of acids and bases, local charges and their distribution, potentials and electron affinity, conformations and reactivity; new 'forced' reactions appear, and many other anomalies are found.

The area of nanochemistry which aims at the creation of closed or semiclosed nano- and microreactors is being developed rapidly. Methods to obtain polymers in which 75% of the volume is occupied with monodisperse empty spheres have been developed; the volumes of these spheres can be varied from 10 to 10^3 nm. Molecular 'vases' have been created, *i.e.*, calixarenes which can reversibly 'captive' guest molecules and release them (depending on the solvent, solution pH and calixarene structure);⁵ molecular traps have been synthesised, *i.e.*, carseplexes that can trap molecules like certain predacious insect-catching flowers. Unlike endofullerenes, they can release their molecular 'preys' after a change in the solvent, pH, *etc.* All these structures belong to the class of molecular containers or self-folding cavitands which can trap predefined molecules and release them as the conditions are changed.

'Empty' tubular silicon fibres, *viz.*, unidimensional nanoreactors, have been created. They are obtained by deposition of tetramethyl orthosilicate dissolved in supercritical CO_2 onto carbon fibres. Carbon is removed by thermal treatment in O_2 or by plasma etching to give nanotubular silicon fibres ready for various uses, *e.g.*, as nanoreactors or nanocontainers. The diameter of such fibres is determined by the diameter of the carbon fibre and is an order of magnitude larger than that of carbon nanotubes.

The interest in such well-known nanoreactors as micelles has not slackened, either. Dendrimeric megamolecules are also widely used as nanoreactors and nanocontainers.

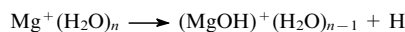
Novel unusual quasi-bidimensional nanoreactors have recently been synthesised, *viz.*, rigid graphite-like planes connected by flexible-chain bridges ('columns') consisting of carbon (polymethylene) chains. The distances between the graphite-like planes in such reactors can be varied by changing the number of atoms in a 'column' (*e.g.*, C_{10} , C_{16} , *etc.*); the lateral distances between the columns can be changed by varying the number of columns (the thickness of the column 'forest'). The reversible and continuous contraction–expansion of the interplanar distance is achieved by the stimulation of conformation transitions in polymethylene chains, *viz.*, from a coil conformation (the planes are spaced most closely) to a stretched chain (the most widely spaced planes).⁶ These transitions can be smoothly controlled by adjusting the nanoreactor to a given volume by filling it with solvents. Such a system is similar to a 'bellows' system; its reversible contraction–expansion mimics muscular contraction. It may be considered as an ideal reversible mechanochemical molecular machine. It can be used as a nanoreactor by loading with catalysts and carrying out catalytic reactions; it can also serve as a versatile and reversible molecular container, *etc.* The first system of this kind was based on a decane-1,10-diphosphonate derivative of γ -zirconium phosphate.

A 'contour' analysis of nanochemistry reveals two facets: on the one hand, nanochemistry produces its own objects, *viz.*, nanoparticles, nanoreactors, nanocontainers; on the other hand, it employs the numerous advantages of nanoparticles and their unusual and flexibly adjustable properties for its own needs, such as the development of new materials, reagents and elements for use in nanotechnologies.

2. A nanoparticle and a nanoreactor

Every year, nanochemistry becomes an increasingly structured science with strictly defined concepts and formulated terminology, the language as 'the dress of thought'. In view of this, it is necessary to define two key concepts, *viz.*, the nanoparticle and the nanoreactor. The former concept characterises the dimensional parameters, while the latter defines the nanoparticle function. For example, an iron cluster loses its specific functional properties (ionisation potential, magnetism) almost completely and approaches the properties of metallic iron when the number of atoms in the cluster (n) equals 15. At $n > 15$, it remains a cluster in terms of dimension, but it loses the properties of a 'nanoreactor' in which the properties become a function of the size. In those clusters where an α -naphthol molecule is surrounded by n water molecules, a cluster behaves as a nanoreactor at $n \leq 20$; its properties depend on its size. At $n > 20$, this dependence disappears and the cluster behaves as a macroscopic aqueous 'reactor' in which the reagent is localised; however, it does not display any chemical anomalies. For example, at $n > 20$, acid dissociation of α -naphthol and proton transfer to water molecules occur.

In clusters of monovalent magnesium (and calcium) with $(\text{H}_2\text{O})_n$ and $(\text{CH}_3\text{OH})_n$, the electron transfer and hydrogen reduction occur according to the reactions



only in the range $6 \leq n \leq 15$; no hydrogen evolution occurs for any other n values.⁷

Hence, the cluster demonstrates its dimensional effects and 'works' as a nanoreactor only at $n \leq 15$; at $n > 15$, the cluster behaves as a small reaction vessel without dimension-related anomalies in its reactivity.

Nanocavities in various porous materials may be considered as nanoreactors as long as the properties of the reagents which they incorporate (pK , ionisation potential), their structures (conformations) and properties of the reacting systems (rate constant, 'forced' reactions, molecular dynamics, *etc.*) depend on the cavity size. When these dependences do not exist any more, nanocavities

become just nanosized containers in which the trapped particles behave as if they were located in an infinite volume.

Of course, the nonequivalence of the concepts 'nanoparticle' and 'nanoreactor' is not always obvious; in many cases, it is impossible to distinguish them. However, it is important to perceive clearly the two aspects of the dimensional effect, both as a purely scale- and space-related effect and as a physicochemical phenomenon where the size affects the properties of trapped atoms and molecules. It is this second aspect that is the most attractive feature of nanochemistry.

3. Nanoclusters, nanowire and nanotubes: three key objects of nanotechnologies

The diversity of nanoobjects studied by nanochemistry is enormous (see the section about the contours of nanochemistry); the chemistry of these nanoobjects is equally diverse. However, we will consider only those nanoobjects which either already show real promise for the high technologies of the new century or which may ensure serious breakthroughs in the future, *viz.*, in the creation of nanolasers, nanocables, optical nanoconverters and nanosources, nanoelements of integrated circuits, nanocatalysts, nanomechanical devices, nanoresonators, nanowave guides, nanodiodes, *etc.* These objects include three-dimensional clusters, quasi-unidimensional clusters (nanowires) and nanopipes. It is these objects that may ensure extreme, almost on the molecular scale, miniaturisation of diodes, transistors and other elements of nanoelectronics, nanomechanics, nanophysics, nanoinformatics (nanocomputers, nanosensors), *etc.*

II. Nanoclusters

1. A cluster as a nanoreactor

The diversity of nanoclusters is infinite, and therefore they are inexhaustible. They can be neutral (atomic and molecular) or charged (ionic and molecular ionic). They are obtained and studied in gases (*e.g.*, in expanding supersonic molecular atomic beams), in zeolite channels (*e.g.*, the In_8 cluster), in liquids (including liquid helium), on solid surfaces, in solid matrices, *etc.* Clusters are extremely important in chemical materials science (cluster materials with unusual physics and mechanics), in chemical analysis and in diagnostics (detectors and sensors).

Clusters are relatively new objects in chemistry; they are studied by organoelement and organometallic chemistry and by chemical physics (atomic and molecular clusters). Many studies have dealt with the methods of their synthesis, their structures and properties. Their role in condensation, evaporation and crystallisation processes is also critical; they serve as precursors of new phases ('protophases'). However, it is the chemistry of these species, their reactivities, catalytic 'potential' and direct use in materials science that attracts the greatest interest. Cluster chemistry belongs to the future.

The rate of photoinduced isomerisation of a *trans*-stilbene molecule in a (hexane) $_n$ cluster was measured by picosecond spectroscopy in molecular beams.⁸ The isomerisation rate constant decreases with an increase in n in the order: 9.7×10^9 ($n = 0$, free molecule); 3×10^9 ($n = 1$); 1×10^9 ($n = 2$); 0.8×10^9 ($n = 3$); $0.5 \times 10^9 \text{ s}^{-1}$ ($n = 4$) to reach a limit at $n \geq 5$. Unexpectedly, all of these constants turned out to be smaller than the observed isomerisation constant of *trans*-stilbene in pure liquid hexane at the same temperatures and energies ($11.5 \times 10^9 \text{ s}^{-1}$). Thus, incorporation of a *trans*-stilbene molecule in a cluster decreases its reactivity. The cluster shell traps the molecule more strongly than the 'liquid-phase' shell: the former anomalously increases the kinetic (Kramers') friction, *i.e.*, the movement of a reacting molecule on the potential surface along the reaction coordinate.

The abundance and hence importance of clusters may turn out to be even greater than it seems now. It has recently been discovered experimentally (by cold neutron scattering and XRD) that liquid ammonia consists of $(\text{NH}_3)_7$ clusters where one molecule is located in the centre while the remaining molecules

are located at the periphery. The cluster structure of water is well known: water molecules are combined into hexa-, penta- and tetramers to give structures with similar energies resembling a prism, a cage, an 'open book', adamantane, as well as dodecahedra and other large clusters. Even liquid solutions of ethanol in water are inhomogeneous: they consist of coexisting water and alcohol clusters;⁹ the fractions of these clusters become equal when the alcohol content in water is about 40%. It is possible that the particular qualities of this water-alcohol solution originate from this fact. Liquid benzene was also found to have a cluster structure. It looks like this is a general phenomenon; in such cases, all liquid-phase reactions should be interpreted as reactions in nanoreactors.

What is more, a chemical reaction itself may favour the organisation of molecules into nanoreactors. For example, a colourless spiropyran with a long hydrocarbon 'tail' is converted photochemically into a coloured bipolar compound with separated charges; it is the molecules of this compound that are combined into micelles. Here, the photochemical reaction works as a trigger that switches micelling on.

A new trend in cluster chemistry is the study of the reactions of clusters with solids as a function of cluster energy. The elasticity of a cluster upon collision with a surface turns out to be very high. As is exemplified with $\text{H}^+(\text{H}_2\text{O})_n$, $\text{H}^+(\text{CH}_3\text{OH})_8$, $(\text{C}_6\text{H}_5\text{CH}_3)_5^+$ and $\text{H}^+(\text{NH}_3)_{10}$ ionic clusters and the diamond surface, clusters are reflected elastically from the surface and retain about 75% of their initial energy. The high elasticity of a cluster is explained by its high entropy (owing to the participation of different isomers in the molecular structure of the cluster).

However, when cluster ions acquire a high energy above a certain threshold, they disintegrate (mainly into monomeric fragments). In particular, $\text{H}^+(\text{NH}_3)_{10}$ disintegrates into NH_3 molecules faster than 80 ps. This suggests that fast energy redistribution occurs in such a 'superheated' cluster. Yet another remarkable phenomenon is the impact-induced chemical reactions in clusters [*e.g.*, the formation of I_2^- from the cluster ions $(\text{CH}_3\text{I})_n^+$ and F_2^- from $(\text{CH}_3\text{F})_8^+$]. This new direction is called the femtosecond cluster mechanochemistry.¹⁰

2. Clusters in catalysis

The importance of cluster materials in catalysis was recognized long ago, and intense development in this field is continuing.¹¹ However, the technological capabilities of cluster catalysis are much greater than the achievements: this is an iceberg the major part of which has not yet been explored.

There are two main circumstances that are promising for the technological application of cluster catalysis: the high surface area of catalysts (which is related to productivity) and dimensional effects, which manifest themselves in the properties of clusters as nanoreactors (this is related to the selectivity and possibility of 'tuning' a cluster for a specific reaction). As indicated above, a general solution to the 'dimensional' problem is unknown; because of that, clusters continue to remain mysterious objects. Their route to catalysis starts from testing their reactivities in model experiments. In particular, any cluster of any size can be prepared in molecular beams, and reactions of these clusters with added molecules can then be studied by mass spectrometry.

It was shown using this method that the Re atom does not react with CH_4 , whereas the Re_3 cluster is reactive. Linear three-atom Cu_3 and Ni_3 molecules do not react with H_2 and CH_4 , whereas triangular molecules are highly reactive (the Ni_{13} cluster is also very reactive). The Co_n clusters react with H_2 in a dissociative way upon virtually each collision if $n = 3, 4, 5$ or $10-18$, whereas clusters with $n = 6-9$ are completely inert.¹²

Figure 1 shows the dependence of rate constants on the cluster size n for the reactions $\text{Nb}_n + \text{D}_2$ and $\text{Nd}_n + \text{N}_2$. One can see a distinct stepwise dependence of reaction rates (dissociative adsorption of N_2 and D_2 molecules on an Nd_n cluster is the rate-determining step) on the size of the cluster; it is almost the same for both reactions and is insensitive to temperature. On the other

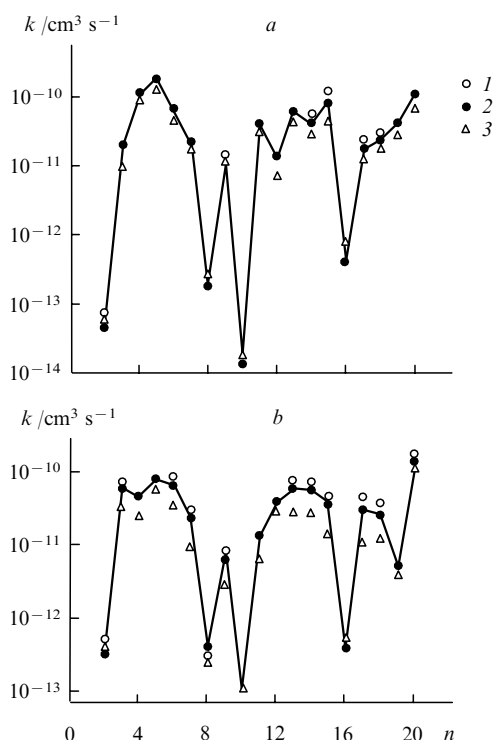


Figure 1. Dependence of the rate constants of dissociative adsorption of D_2 (a) and N_2 (b) on the size of a niobium cluster (n is the number of atoms in the cluster).

Temperature /K: (1) 280, (2) 300, (3) 370.

hand, the rate constant for the reaction of Nb_n with O_2 [$(3-7) \times 10^{-10} \text{ cm}^3 \text{s}^{-1}$] is similar to the constant of bimolecular collisions and does not depend on n (the dimer Nb_2 is an exception).¹³

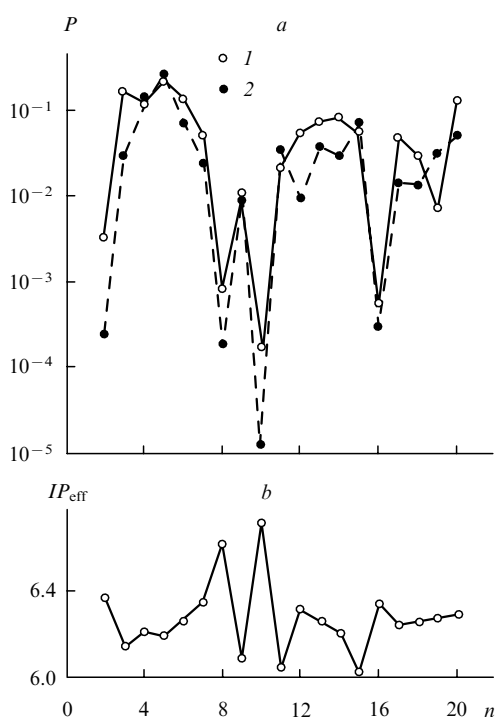
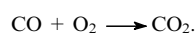


Figure 2. Dependence of the probability of the reactions $\text{Nb}_n + \text{D}_2$ (1) and $\text{Nb}_n + \text{N}_2$ (2) at 300 K (a) and of the ionisation potential of the Nb_n cluster (b) on the size of the cluster.

Figure 2 displays two relationships: the probability of the reactions $\text{Nb}_n + \text{D}_2$ and $\text{Nb}_n + \text{N}_2$ and the ionisation potential of the Nb_n cluster as functions of n . A pronounced and unambiguous ‘antiphase’ relationship between the reactivity of clusters and their ionisation potentials is observed: the lower the ionisation potential IP_{eff} of a cluster the higher its reactivity. It was concluded on this basis that charge transfer between a cluster and an adsorbed molecule is the main factor that governs the cluster reactivity; it is this factor that is responsible for the dimensional effects in Nb_n clusters.¹³ It is noteworthy that only the clusters with $n = 5, 6$ and 11 are reactive in the dehydrogenation of benzene.

The Mo_n clusters are highly reactive in the reaction with N_2 (dissociative adsorption). At $n = 16$ and 23, the reaction constant is close to the gas-kinetic threshold; at any other n values, the rate constants are two orders of magnitude lower.¹⁴ The W_n clusters react similarly: the maximum reactivity is observed for clusters with $n = 16$ and 23.¹⁵

Even gold loses its chemical ‘nobleness’ in clusters. Figure 3 demonstrates the catalytic activity of Au_n clusters in the reaction



One can see that clusters with $n = 8, 11, 15$ and 18 are the most active.¹⁶

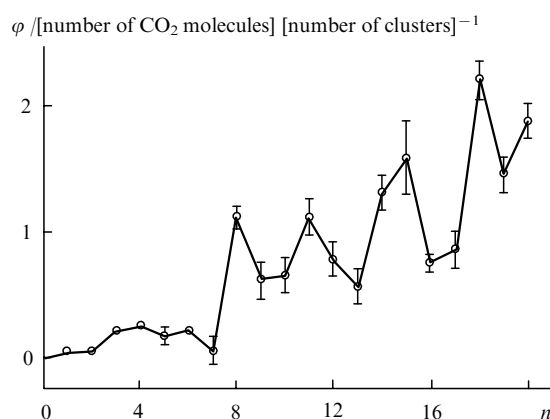


Figure 3. Yield of CO_2 molecules per cluster in the catalytic reaction $\text{CO} + \text{O}_2 \rightarrow \text{CO}_2$ as a function of the size of the Au_n cluster.

The MoO^+ ion does not react with NH_3 ; however, the ionic clusters Mo_3O_8^+ and Mo_3O_9^+ vigorously dehydrogenate ammonia to give a complex with the dehydrogenation product, *viz.*, nitrogen; they also oxidise CO into CO_2 .¹⁷ The V_3O_7^+ cluster is very efficient in the dehydrogenation and cracking of butane, butene and butadiene; the $\text{V}_3\text{O}_{12}^+$ cluster has low activity, whereas $\text{V}_3\text{O}_{17}^+$ is totally inert. The V_3O_6^+ and $\text{V}_3\text{O}_{11}^+$ clusters are inefficient in these reactions but are actively involved in oxidative condensation and cyclisation, *i.e.*, removal of only one oxygen atom from the cluster completely changes the type of the reaction involving the cluster.¹⁸

Studies on the use of titanium dioxide (TiO_2) as a photocatalyst for water and air purification from organic pollutants are under way. The drawback of TiO_2 is that its optical absorption band lies in the UV region (shorter than 390 nm), which decreases considerably its potential as a photocatalyst. Doping of TiO_2 with nitrogen (both in films and in clusters) shifts the $\text{TiO}_{2-x}\text{N}_x$ absorption band to the region of 520 nm, thus increasing considerably the efficiency of photocatalysis.

The dependence of the catalytic activity and reactivity of clusters on the dimensional effect follows, first, from the energetic parameters (the role of the ionisation potential in the reactivity of Nb_n clusters has already been noted above) and, second, from the structural changes in the atomic surfaces of clusters (exit of elements of different faces, edges and terraces on the surface). It

is the second reason that determines the difference in the reactivity of different faces of a single crystal in heterogeneous catalytic processes.

It has become clear now that the dimensional effects in catalysis are second in importance (the chemical nature of the catalyst is the most important). They can control both the rate (which can be changed by a few orders of magnitude) and the direction of a reaction.¹⁹

It should however be admitted that clusters as such are not catalysts yet. The use of high technologies in catalysis implies that clusters are tested for reactivity in specific reactions chosen with respect to reactivity and selectivity and finally combined in a macroscopic catalytic ensemble without losing the individuality of the clusters. The latter problem is not easy; many research groups are working towards its solution. Although it is unlikely that a general solution to this problem can be found, it can, in principle, be solved in each particular case.

A new strategy in heterogeneous catalysis involves a combination of catalysis with tunnelling scanning microscopy. The tip of a tunnelling microscope can deposit any number of atoms (including single atoms) onto any topological element of a surface (face, edge, terrace), thus creating catalytic nanoreactors and making it possible to test any reactions on them. The creation of an 'atomic pump', *i.e.*, prototype of a machine that deposits single atoms which drift through a nanotube, is a brilliant breakthrough that may occur in this nanotechnology. The drift of atoms is controlled by a laser (see Section IV.3). This is a new direction in the fundamental science of catalysis and a direct route to the use of high technologies in catalysis.

3. Optical converters

Particularly impressive are dimensional effects in semiconducting nanocrystals with sizes smaller than the Bohr exciton radius. In such nanoclusters (called quantum points), the quantum trapping of an electron-hole pair (photochemically or radiation-induced) in a restricted volume results in the expansion of the forbidden band as the cluster size decreases. This means that recombination luminescence shifts to the blue region (high energies) with a decrease in the cluster size. The CdSe nanocrystals 'dressed' in one or two ZnS monolayers represent a good example. If the diameter of the internal CdSe nucleus is changed stepwise from 23 to 55 Å, the bright blue luminescence changes to green, yellow, orange and finally bright red.²⁰ Upon coherent excitation of the electronic gas, gold clusters (nanorods) fluoresce with a quantum yield 10^6 times higher than metallic gold; furthermore, the quantum yield is proportional to l^2 (where l is the nanorod length), while the maximum of the luminescence band is proportional to l . It has been shown recently that a carbon nanotube is also a quantum point.²¹

Quantum points are mainly studied by physicists. The creation of quantum points doped by admixture ions is a subject of nanochemistry. In doped quantum points, the excitation energy 'mounts' the admixture site and is emitted by it. For instance, high-quality nanocrystals of ZnSe doped with Mn^{2+} ions were obtained by a reaction of a solution of selenium in trioctylphosphine with diethylzinc and dimethylmanganese.²² In this case, each nanocrystal contained one Mn^{2+} ion. Using the magnetic circular dichroism and electron spin resonance, it was proved that the Mn^{2+} ion is located inside the nanocrystal, replacing the Zn^{2+} ion in the cubic lattice of ZnSe. It should be noted that such perfect doped nanocrystals could not be obtained when diethylmagnesium was used instead of diethylmanganese; the Mg^{2+} ions were partially located on the surface and distorted the optical conversion.

The blue fluorescence characteristic of undoped crystals is suppressed almost totally in manganese-doped ZnSe nanocrystals and is changed for red fluorescence (2.12 eV, 585 nm); the quantum yield of luminescence at 293 K is 22% and reaches 75% below 50 K. Thus, the admixture Mn^{2+} ion in semiconduc-

tor crystals is a collector of the electron-hole recombination energy and its efficient monochromatic emitter.

Of light-converting organic nanoclusters, J-aggregates are very popular, *i.e.*, ensembles of molecules of organic dyes which efficiently collect the electron excitation energy (directly or through electron-hole recombination) and emit it with a high quantum yield (as a rule, in a narrow spectral region). In fact, they act like molecular antennae in photosynthetic centres.

4. Magnetism and spintronics

Because the ratio of the surface and bulk atoms in ferromagnetic metal clusters is infinitesimal, the mutual compensation of the atomic magnetic moments of clusters is incomplete. Furthermore, the crystal lattice of the cluster can differ from that of the metal. For this reason, the magnetization and magnetic atomic moment in clusters depend on the cluster size and differ from the macroscopic characteristics of the metal. Based on this, new nanocluster magnetic materials with new attractive properties are created. This field of research has been successfully developed for a long time; good books and reviews on the topic are available (see, *e.g.*, Refs 23 and 24), which allows us to refrain from discussing it here.

Over the past three years, a new field of electronics, *viz.*, spintronics (spin electronics), has developed rapidly. Spintronics opens up new horizons for developers of new-generation electronic devices and instruments using high technology.²⁵ Unlike classical electronics, which controls the movement of electrons and holes (negative and positive charges) by means of potentials (both biasing and stopping potentials), spin electronics controls both charges and spins (magnetic moments) of current carriers. Two controlling factors work in spintronics, *viz.*, electric potentials and magnetic fields.

The main material of spintronics is represented by either a film of a conducting metal (copper, ruthenium) enclosed between layers of ferromagnetic metals or a semiconductor nanometre-thick film separating ferromagnetic layers. Owing to the magnetic resistance effect, the electric current in a film of a non-magnetic metal or the tunneling current in a semiconductor film (tunnel barrier) depends not only on the controlling electric potentials but also on the magnetic field created by the ferromagnetic layers and the external field. Clearly, this circumstance increases considerably the number of methods to monitor and control electric currents by both selecting ferromagnetic films (with different hysteresis loops and different magnetisations) and by applying an external magnetic field. In combination with controlling potentials, this creates a flexible and multiparameter system for the control of electric currents.

Currently, there is a race to create new technologies and devices using spintronics; the tension of this race is only comparable to that of the 'cold cheminuclear synthesis' race at the end of the 1980s. However, unlike cold cheminuclear synthesis, spintronics is realistic. The development of many devices is underway, including spin-dependent field transistors, spin-dependent light-emitting diodes, spin tunnel diodes and optical switches in the terahertz frequency range, spin modulators, coders and decoders, spin-dependent sensors and elements of computer and communication memory, *etc.* Practical Americans estimate the new technology market to be worth multi-trillion dollars;²⁵ certainly, nanochemistry is the main paradigm of these new developments.

III. Nanotubes

The chemistry and physics of nanotubes are under rapid development. Many methods and technologies for the synthesis of these species have been developed, *viz.*, electric-arc discharge, laser-thermal ablation, flame synthesis and pyrolysis of hydrocarbons.²⁶ As of today, the best one is the pyrolytic method for the synthesis of nanotubes from CO, CH₄, C₂H₄ or C₂H₂ on a surface with a deposited catalyst or with a volatile catalyst precursor [like Fe(CO)₅]; in the latter case, the synthesis of the catalyst (*e.g.*, Fe

atoms and clusters) and the synthesis of the nanotubes are coupled. The combination of these diverse methods is the essence of the technology of chemical deposition from a gas (or vapour) phase on a solid surface (support), the technology which is considered the most efficient today. Methods for the continuous and large-scale production of nanotubes with controlled growth rate and adjustable diameters and lengths have already been developed.²⁶

1. Architecture of nanotubes

For nanotubes as technological objects, the architecture of their ensembles and the possibility of controlling it, adjusting it and combining objects into integrated circuits are important factors; the latter factor makes the problem of nanocontacts particularly important.

Considerable success has been achieved in the creation of controlled architecture. Multilayered tubes with preset architecture were obtained using a porous silicon support with submicron pores electrochemically pretreated (electrocutting) in an HF–MeOH solution. This treatment has made it possible to create a thin nanosized layer with nanopores (diameter about 3 nm) on silicon. Atop this nanolayer, a catalyst (iron film 5 nm thick) was sputtered through a shading mask. Subsequently, nanotubes were synthesised from ethylene at 700 °C by chemical deposition onto catalytic islands. The multilayered nanotubes formed on these islands looked like a thick forest of perfect ‘towers’ oriented strictly vertically. The length of the nanotubes (height of the ‘towers’) was controlled in the range 10–240 nm; the square of a ‘tower’ depended on the mask selected.²⁷

The reason for the architectural perfectness of the ‘nanopipe’ ensemble (and the advantage of the technology) is that the catalyst is strongly retained in the nanopores of the support, while the strong van der Waals interaction of the outer spheres of the growing nanotubes precludes their distortion and ensures the rigid fixation of the entire bunch of nanotubes growing on a single catalytic island. It was found that the growth of nanotubes on nanoporous silicon occurs much faster than on ‘non-cut’ planar silicon. The reason for the fast growth of nanotubes is that ethylene arrives at the catalytic islands not only from the gas phase but also through the nanopores of the support, ‘feeding’ the growing nanotubes with carbon from the inside. Finally, yet another remarkable result of this technology is the synthesis of nanotubes with monodisperse diameters.²⁸

Monolayer nanotubes are usually grown by arc discharge or laser ablation. In these cases, the evaporation of carbon atoms occurs at 3000 °C or higher, which restricts the growth of nanotubes; they bend and get entangled, and it is difficult to purify them and build ensembles from them. High-quality monolayer nanotubes are obtained by chemical deposition of carbon from methane. The advantage of methane is that its stability precludes the formation of amorphous carbon that contaminates the catalyst on which nanotubes grow.

A bimetallic Fe/Mo catalyst deposited on an aluminium–silicon material prepared by sol–gel technology was found to be the best catalyst for the synthesis of monolayer nanotubes. The diameters of the nanotubes grown on this catalyst range from 0.7 to 1.5 nm (this is their disadvantage); the tubes with a diameter of 1.4 nm are obtained in a maximum yield. Again, the main condition required to obtain high-quality nanotubes is a strong bond between the metal and the support. The high porosity of the support ensures a high density of catalytic sites on the surface and the easy access of methane to these sites. The latter circumstance is particularly important, since the growth rate of nanotubes is limited by gas diffusion.

It is important for nanotechnology that oriented nanotubes can be grown. The first steps in this direction have already been made. Lithographic methods are used to create islands (elevations with deposited catalyst ‘chips’) on supports. Nanotubes grow on such chips; many of them start from one chip and reach another one thus creating a network of suspended ‘bridges’ between the

islands. The architecture and density of the network is set by the initial architecture of the deposited chips. This may already be regarded as a prototype for integrated circuits.²⁸

The diameters of nanotubes obtained by chemical deposition are determined by the size of the catalytic cluster or the nanopore in which the catalyst is ‘sitting’, whereas those of the nanotubes obtained in an arc discharge are determined by the pressure of the inert gas (helium). It has recently been shown²⁹ that the mean diameter of nanotubes formed in an arc discharge increases proportionally to the logarithm of pressure. This result may prove to be useful.

2. Architecture of nanocontacts

Nanocontacts are the trouble spot of nanotechnologies. Based on current experience, two approaches to the formation of nanocontact architecture seem possible: by different growth mechanisms of nanotubes and by handling nanotubes (this will be explained below).

The growth mechanism may be judged from the state of the nanotube ends (they are usually visible under an electron microscope). When catalyst species are strongly fixed on a support, the ends of the growing nanotubes are free of catalyst species, hollow and covered with hemispheres (fullerene caps). In such cases, tubes grow from their bases: through adsorption and decomposition of methane (or some other carbon source) on the surface of the metal catalyst, dissolution of carbon and diffusion of carbon atoms to the metal surface layer, oversaturation of the solution with carbon and deposition of carbon on the lower part of a tube. A tube grows from its bottom (base); carbon arriving from the catalyst builds the ground floor of the tube and ‘pushes’ it upwards. In this case, a strong nanocontact of the tube with the prepared support, where the required architecture of nanotube chips has been preset, is formed at once.

It is possible to update this technology by feeding the catalyst from the gas phase; in such a case, catalyst nanoclusters ‘mount’ the top of the tube and growth continues on them.

A brilliant version of this technology has been implemented recently.³⁰ Nanotubes were grown on a quartz surface at 800 °C in a stream of an Ar/H₂ mixture to which drops of a solution of ferrocene in xylene were injected at regular intervals. Pyrolysis of ferrocene was accompanied by the formation of iron clusters which were deposited on quartz at the very beginning of the process. Xylene decomposed on these nanocontacts and carbon tubes started to grow there. New clusters formed on the tops of the nanotubes from subsequent portions of ferrocene and xylene, and the tubes continued to grow on these clusters. This process gives rise to a colony of nanotubes. It resembles a multistorey building: there are catalyst clusters in the base and between the storeys, whereas the distance between the storeys determined by the intervals between the injection of ferrocene + xylene portions is occupied by nanotubes.

Figure 4 demonstrates the architecture of the resulting nanotubes. The image on the left, obtained using a scanning electron

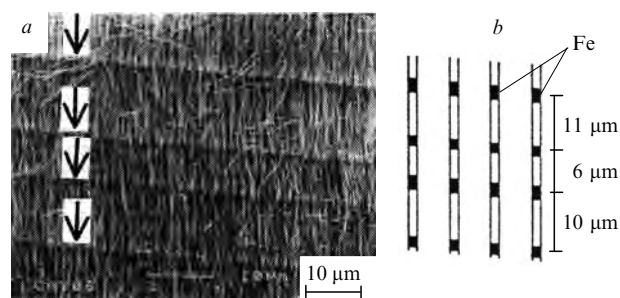


Figure 4. An electron-microscopic image of colonies of nanotubes grown on iron clusters (a) and a schematic drawing of tubes with incorporated iron clusters (b).

microscope, shows a colony of vertical nanotubes. The horizontal parallel lines (bridges between the storeys) correspond to the iron clusters which are formed at the moments when the solution of ferrocene in xylene is injected. If the intervals between the injections are constant, the 'storeys' grow strictly uniformly and have equal heights. Furthermore, the height of a storey depends on the ferrocene:xylene ratio in the solution which feeds the growth of the nanotubes. This ratio also affects the tube growth rate, because in fact it is the catalyst:carbon ratio.

This technology is remarkable because in this case iron clusters are included in the growing tube so that the catalyst is captured inside the tube and is in a strong contact with the tube wall from the inside (this is sketched in Fig. 4*b*). The growing tube shapes the cluster in such a way that it becomes oblong; the cross-section of the cluster exactly matches the inner diameter of the tube (this has been proven by transmission electron microscopy³⁰). What is more, the nanotube reliably protects the trapped iron clusters from oxidation. The nanotubes obtained by this method have ferromagnetic properties, which allows one to handle them using magnetic fields and magnetic manipulators. The architecture of such an ensemble of nanotubes resembles that of a macroscopic crystal in which the lattice points are occupied by iron clusters included in nanotubes with a preset space periodicity.

Clearly, this technology offers ways to create nanocontacts at both ends of nanotubes; it is flexible and controllable and may be combined with other technologies. It is also obvious that this technology can be used as a method to fill nanotubes with other metals.

3. Nanowires in nanotubes

A nanotube is a one-dimensional nanocontainer that can be filled with various compounds: metal oxides (PbO₂, CoO, PbO, V₂O₅, Bi₂O₃, MoO₃), salts and acids (KI, AgNO₃, HAuCl₄, H₂PtCl₆, ZrCl₄, CsCl, UCl₄, ThCl₄, HNO₃, PdCl₂, *etc.*), elements (S, Se, Sb, Ge, B) and metal carbides (Mg, Ni, Mn, Nd, Mo, Ta, Co, Cu, *etc.*). Filling can occur both during the synthesis of nanotubes and after the isolation and purification of the preformed nanotubes. The latter way is virtually always more reliable, controllable and target-oriented. Filling can be performed from a gas or vapour phase, from solutions and melts. In nanotubes, as in nanoreactors, chemical synthesis can be carried out (see the review by Rakov²⁶).

Of considerable interest is the filling of nanotubes with metals in order to obtain metallic conductors, *i.e.*, nanowires coated with a carbon 'cloth'. In this case, the nanotube not only shapes a nanowire but also protects it from oxidation and deteriorating effects of other corrosive media. It is clear that such nanoobjects are of particular importance from the viewpoint of high technologies.

In early studies on the synthesis of nanotubes containing Cu, Ni, Fe, Ag, Au, Pd and Pt, nanotubes were filled with metal oxides or chlorides which were subsequently reduced with hydrogen into the corresponding metals.³¹ Nanowires of β -Sn were obtained by electrolysis of a LiCl–SnCl₂ melt that filled a nanotube.³² Electrolysis was also used to obtain 40–90 nm-long nanowires of a Sn/Pb alloy.³³

The nanowires formed are usually polycrystalline; however, single-crystal wires were obtained in certain cases. For example, reduction with hydrogen of Bi(NO₃)₃ introduced into a single-layer nanotube from a solution in nitric acid gave single crystals of Bi hundreds of nanometers long and with a diameter of about 1 nm in high yield.³⁴ Unlike a macrocrystal, the nanocrystal obtained in a nanotube was slightly skewed (the planes are inclined). It is of interest that the diameter of a Bi-nanowire is considerably smaller than the diameter of a nanotube; on average, there are five Bi atoms in the tube cross-section. Filling nanotubes (~ 10 nm diameter) with gaseous Ni(C₅H₅)₂ results in a Ni wire with a diameter of 4 nm and a length up to 500 nm.³⁵ It has not yet

been understood why the diameter of the wire formed is so small, especially as the nanowire and nanotube diameters often coincide.

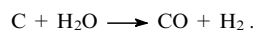
The incorporation of C₆₀ fullerene molecules in nanotubes is an exotic event.³⁶ Such structures resemble 'pods' filled with 'peas', *i.e.*, C₆₀ molecules from the gas phase. They are clearly visible under an electron microscope. If filling is incomplete, the fullerene molecules are grouped in twos, threes, *etc.*; they readily move along the tube jumpwise (the jump length ranges from 1 to 10 nm). A jump occurs almost instantaneously (in fractions of a second); the interval between the jumps is 10–20 s. The jumps are induced by electrons emitted by the electron microscope used for observation.

If a 'fullerene-in-a-nanotube' system (C₆₀@NT) is externally doped with metallic potassium, it acquires metallic conductivity owing to the chemical transfer of electrons from potassium to the nanotube and then to C₆₀. As a result, each C₆₀ molecule acquires the 6– charge, and a compact chain of such molecules inside the nanotube constitutes a nanowire of an organic metal.³⁷ It is hard to predict the place of such wires in nanotechnologies, but one of its advantages is obvious: it is possible to control charges and their mobilities by the Coulomb fields of external ions (outside the nanotube).

Even more interesting are nanotubes filled with endofullerenes. For example, the La@C₈₀@NT and Gd@C₈₂@NT systems have already been obtained.³⁸ In these structures, metal ions carry positive charges, whereas the surfaces of the nanotubes are most likely negatively charged.[†] These are new one-dimensional crystals, the properties and technological 'capabilities' of which are far from being studied completely and are therefore not yet recognized.

A new type of nanowire has recently been obtained. This is a nanocable in which the internal conductor is an iron rod about 10 nm thick and about a micron long 'dressed' with a boron nitride tube with a diameter of about 50 nm.³⁹ The BN ceramic is an excellent electric insulator, which reliably protects the inserted iron rod from oxygen and other corrosive media. A remarkable feature of these nanocables is that there is a carbon layer between the BN shell and the iron rod; this layer keeps iron in its reduced state and ensures a strong bond between the metal and the ceramic shell. The 'mediation' of carbon is particularly important, considering that BN ceramics are very poorly wetted with iron and their direct contact is very unstable.

The BN nanocables were obtained in an induction graphite furnace from B₄N₃O₂H and an aqueous solution of Fe(NO₃)₃ through which a stream of N₂ was passed. Upon heating, B₄N₃O₂H decomposed to give the boron oxides B₂O₃ and B₂O₂. Furthermore, synthesis of CO occurred in the graphite furnace according to the reaction



The resulting boron oxides entered the reaction zone at 1700 °C and reacted with the gas mixture N₂ + CO + H₂, whereas the Fe(NO₃)₃ that was present decomposed to give α -Fe. These reactions resulted in BNFe nanotubes. An electron-microscopic image of one of them is shown in Fig. 5.

It was shown by electron energy loss spectroscopy (EELS) that the outer shell of a nanocable contains only B and N atoms; carbon appears nearer to the centre and its concentration in the B–N–C system is higher nearer the α -Fe nanowire. Such high-conductivity ferromagnetic nanowires that are well protected by ceramics may find a well-deserved application in future nanotechnologies. It should be noted that this technology makes it possible to obtain nanocables containing not only Fe nanowire but also other metals.

[†] It should be noted that negative charges in C₆₀@HT structures are concentrated inside the tube (on C₆₀^{6–}).

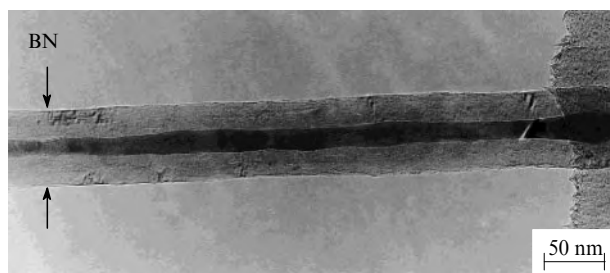


Figure 5. An electron-microscopic image of an iron nanowire (black band) inside a BN nanotube.

4. Nanotube as a field emitter

Perhaps the use of nanotubes as field emitters is their most widespread application. Field emission is emission of electrons from high-curvature surfaces (edges, blades, undulations) under applied voltage. The advantages of field emitters over thermal emission cathodes are well known: these are their small size, low energy consumption, high current density and a possibility of miniaturisation. No wonder that their small radius of curvature, high length/radius ratio, high conductivity and thermal stability make nanotubes a promising emitting material.

The first studies on emission from nanotubes were carried out by Chernozatonskii *et al.*⁴⁰ in 1995. Over the short time that has passed since then, working colour displays with diagonal axes of 10–20 cm, high luminosity (up to 800 cd cm⁻²) and long service life have been created. The working elements in such displays consist of nanotubes grown on porous silicon, mesoporous aluminosilicate or quartz using the technologies described above (in the section devoted to the architecture of nanotubes).⁴¹ Displays based on nanotubes will shortly become a market product; this will be the first breakthrough of nanotechnologies in the economy.

Using electron holography, the electric field of a nanotube was studied as a function of potential. This method is based on the interferometry of electrons that have passed through the electric field of a nanotube.[‡]

A scheme showing the instrumented set up is shown in Fig. 6. A nanotube was mounted on the holder in the electron microscope chamber using a conductive epoxy resin. A current-collecting gold

[‡] This brilliant technique is used to measure internal potentials, electrostatic and magnetostatic fields, contact potentials, *etc.*

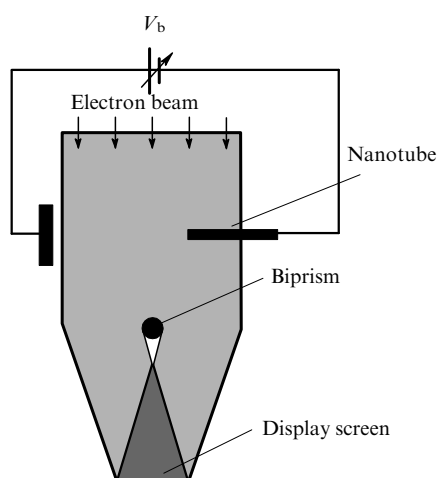


Figure 6. A scheme for the measurement of the electric potential of a nanotube using electron interference.

plate was placed opposite the nanotube at a distance of 6 μm from it. A piezoelectric handling device was designed specially for mounting nanotubes.⁴² The nanotube and the plate formed an electric circuit to which a voltage V_b was applied. The current in the chain was recorded continuously.

In the centre of the microscope electron beam, a biprism was placed, which divided the beam into two parts that were later brought together on a display screen at the bottom. The electron field emission of the nanotube manifested itself at a bias voltage of $V_b = 70$ V; the current between the nanotube and the plate was 40 pA. At $V_b = 120$ V, the current was already considerable, *viz.*, 0.54 μA , and a holographic picture of the nanotube electric field appeared on the display screen (Fig. 7). The holographic picture shows distinct interference bands along the nanotube (especially in the lower, increased image).

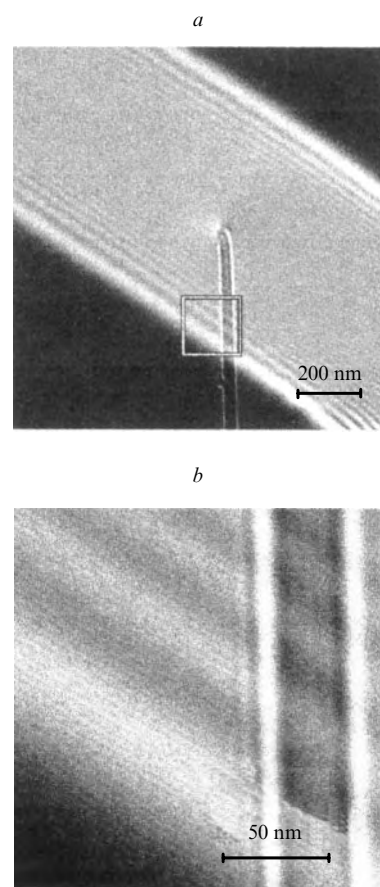


Figure 7. A holographic image of the nanotube potential (a) and an enlarged image of the portion marked by the square (b).

The observed interference bands appear because the phase of the coherent electron beam which passes near the tube is changed in the electric field of the tube. Superposition of this beam with the other beam which was not exposed to the field of the nanotube results in interference. By analysing the phase shift as a function of the voltage V_b , it is possible to reconstruct the electric field maps around the nanotube (see Fig. 8). Based on these maps, one can find the electric field strength at the tube end (H).⁴² The results of this experiment are shown below.

V_b / B	120	90	70
$H / \text{B nm}^{-1}$	1.22	0.82	0.64

It is remarkable that almost the entire electric field is concentrated at the tube end, whereas no other possible sources contribute to the field emission of the nanotube. Given a constant potential V_b , the local electric field at the top of a tube is inversely

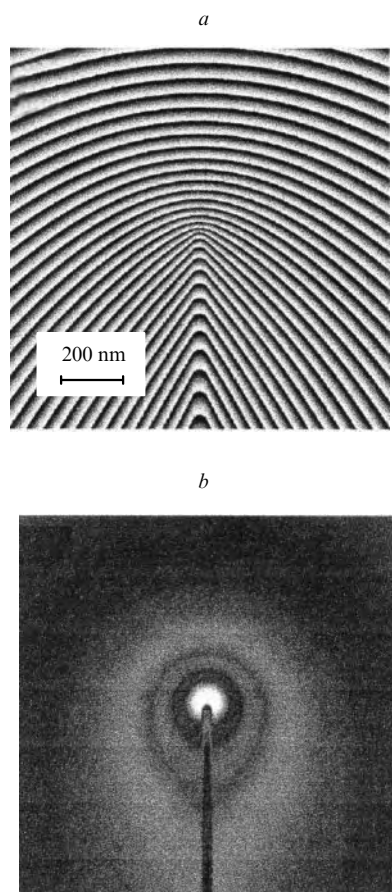


Figure 8. Images of the phase shifts (a) and phase gradients (b) of the electric potential at the end of a nanotube.

proportional to its radius and almost does not depend on the magnetic field. What is more, the holographic picture confirms that there is no potential drop along the tube even in a strong emission mode. Both of these circumstances, *viz.*, localisation of the electric field at the top of the tube and the absence of field gradient along the tube, make nanotubes a perfect material for field displays.

It should be noted that the advantages of the nanotechnological experiments involve not only the gathering of direct information about the properties and behaviour of nanoobjects but also acquiring experience in handling these objects and creating new, sometimes sophisticated, technologies for operating with such objects.

The emission properties of nanotubes can be tuned. For example, filling tubes with cesium decreases the work function by 2 eV; as a result, the emission current increases by an order of magnitude.⁴³

Recently, the thermal conductivity of carbon tubes was measured: it is $250 \text{ W m}^{-1} \text{ K}^{-1}$ at room temperature for one-layer tubes and about $3000 \text{ W m}^{-1} \text{ K}^{-1}$ for multilayer tubes. Since the dependence of thermal conductivity on temperature has the form $f(T^2)$, this means that 'two-dimensional' phonons are responsible for thermal conductivity; the free-pathlength of these phonons was estimated to be 500 nm.⁴⁴

The thermostimulated electromotive force (thermo-EMF) generated by a single multilayer nanotube linearly increases with temperature, with a constant gradient of $80 \mu\text{V K}^{-1}$; its sign is positive, *i.e.*, the thermo-EMF is created by 'holes'.⁴⁴

5. Nanotubes as molecular diodes

Electric conductivity is the key property of nanotubes as elements of nanoelectronics. It is measured by the four-probe method as

follows: four conductors [*e.g.*, consisting of tungsten obtained from $\text{W}(\text{CO})_6$ in a gas phase] are deposited on a nanotube lying on a support in such a way that the distances between the contacts are tens of nanometers. After that, the current–voltage characteristics of the nanotube are measured.

One-layer tubes with the indices (n,n) are metallic. Perfect tubes (without defects and admixture atoms) have ballistic conductivity: at low resistances of the metal–tube contacts, the resistance of the tube should approach half of the quantum limit of resistance h/e^2 (where h is the Planck constant and e is the electron charge), *i.e.*, reach 6500Ω . However, this limit could not be reached because of the high resistance of the contacts (several megaohms), which creates a Coulombic blockage. Of the metals tested, the best results were obtained for Ti: the Ti–tube nanocontacts have the lowest resistances.²⁸ At 2 K and nanotube length of $\geq 3 \mu\text{m}$, the resistance was about $12 \text{ k}\Omega$.

The resistance of such tubes is almost independent of temperature. Similarly, there is no explicit dependence on the bias voltage: when the blocking voltage changes from -100 to 100 V , the nanotube resistance changes only 2–4-fold and the tubes remain conductive. All of these are reliable indications of the 'metallic' behaviour of nanotubes.

Chiral nanotubes with indices (m,n) are semiconductors with the band gap $E \sim d^{-1}$, where d is the nanotube diameter. For nanotubes with diameters of 0.7 to 3 nm obtained by chemical deposition onto catalytic islands (see Sections III.1 and III.2), the band gap was from 1 to 0.25 eV, respectively. Dai *et al.*²⁸ thoroughly measured the electron transport properties of one-layer nanotubes obtained by this method. Their resistances at room temperature were 200–500 $\text{k}\Omega$ for tubes with $d > 2.0 \text{ nm}$; the resistances were higher (about megaohms) for tubes with smaller diameters ($d < 1.5 \text{ nm}$). Semiconductor tubes are hole-doped; their conductances decrease when a positive blocking voltage is applied. At 4 K, tubes with $d > 2.0 \text{ nm}$ become insulators in the range from ± 10 to $\pm 1000 \text{ mV}$. For tubes with smaller diameters, this range is broader.

A remarkable feature of all I – V -dependences for semiconductor tubes is that these characteristics are asymmetrical with respect to the bias voltage and its polarity: at a constant blocking voltage, the absolute current is higher at a positive bias than at a negative bias. The asymmetry increases abruptly as the blocking voltage increases, a feature that is known to characterise a semiconductor diode (rectifier).

Unambiguous evidence that a doped nanotube is a diode was obtained.⁴⁵ A one-layer nanotube contaminated with an admixture deposit on certain areas was provided with three Au electrodes (A, B and C, Fig. 9) in such a way that the tube segment between the electrodes B and C is clean, whereas the region between the electrodes A and B contains the impurity deposit (it is clearly visible near the electrode A). The entire device was arranged on a silicon substrate filled with an insulating SiO_2 layer 100 nm thick in such a way that the substrate worked as a capacitive blocking electrode. Resistances were measured in the range from 0.5 $\text{M}\Omega$ (for metallic tubes) to 10 $\text{M}\Omega$ (for semiconductor tubes). The contact resistances measured using the four-probe method were $\sim 0.5 \text{ M}\Omega$.

Figure 9b shows the I – V -characteristics of the electronic circuit shown in Fig. 9a. The inset shows the I – V -dependence for the 'non-contaminated' region of the tube (BC): it is symmetrical with respect to the bias potential, *i.e.*, the conductivity does not depend on the sign of the bias voltage, which is a feature of a homogeneous semiconductor with distributed *p*- and *n*-carriers. The I – V -dependence for the 'contaminated' region AB is strongly asymmetric and depends on the sign of the bias voltage, which is typical of diodes. Thus, the AB region of a nanotube is a molecular diode where the admixture acts as an *n*-type dopant and where an electron–hole junction with a junction potential appears. If the blocking voltage is positive, the current passing through the nanotube decreases. This suggests that holes dominate in the charge transport through the diode.

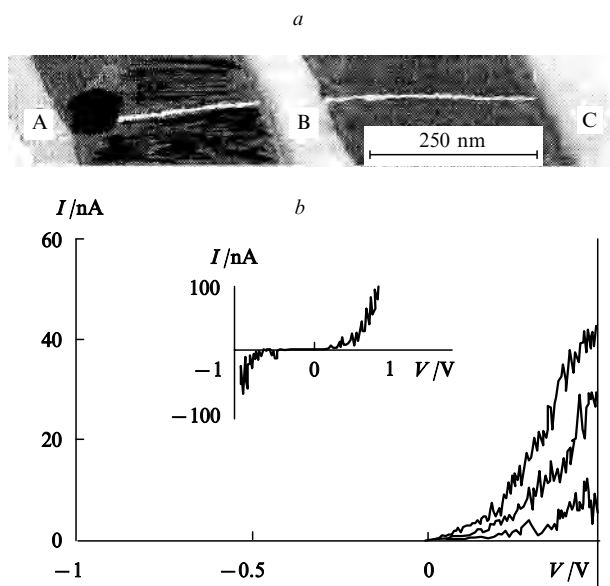


Figure 9. Image of a one-layer nanotube with attached electrodes A, B, C in an atomic force microscope (a) and dependence of current in the tube on the bias potential (b).

What is more, it turned out that current depends on the blocking voltage in a stepwise manner, *i.e.*, there are discrete zones in a doped nanotube. The following dopant types are possible: admixtures (like amorphous carbon or catalyst clusters), topologic defects (five- or seven-membered rings in the structure of a tube), incorporated atoms (N, B, *etc.*), contacts between tubes with different diameters, mechanical strain of a pipe where it is bent, *etc.*

Of great interest is the controlled doping of nanotubes using the tip of a tunnelling microscope or an atomic pump. It allows one to design flexible hetero-junctions (diodes, transistors) with controlled band structures. Diodes with a slope of $\partial I / \partial V \approx 200 \text{ nA V}^{-1}$ have already been obtained. The slope normalised with respect to the tube diameter (*i.e.*, to the channel width) is $\sim 0.1 \text{ mS } \mu\text{m}^{-1}$, which is comparable with the slope for a silicon diode.²⁸ Certainly, we do not speak of immediate replacement of the comprehensively developed silicon electronics by nanoelectronics; however, one can speak of a new direction, *viz.*, nanoelectronics (or molecular electronics) with its new advantages. The results of the studies described above allow ways to bring these potential capabilities into reality to be explored.

6. Superconductivity of nanotubes and cryoelectronics

Superconductivity of a bunch of one-layer nanotubes arranged in parallel (about 350 pipes with 1.4 nm diameter each) connected to an electric circuit by ordinary (non-superconducting) $\text{Al}_2\text{O}_3/\text{Pt}/\text{Au}$ contacts with layer thicknesses of 5, 3 and 200 nm, respectively, was first discovered by Kociak *et al.*⁴⁶ The resistance of such a bunch at 300 K was $\sim 10 \text{ k}\Omega$ and increased with a decrease in temperature from 300 K to 1 K; after that, an abrupt decrease in resistance occurred (by two orders of magnitude) to a limiting value of 74Ω at 100 mK. For an electric chain with normal (non-superconducting) contacts, the minimum resistance should not be smaller than half the quantum resistance limit h/e^2 ; it follows that about 25% of the total number of the tubes (350 tubes) participate in superconductivity. (As expected, a magnetic field of about 1 T destroys superconductivity.)

Taking into consideration the miniature size of electronic nanodevices and the moderate cost of cooling such devices, it can be considered that the superconductivity of nanotubes, nanocontacts and nanowires, even if it appears only at very low temperatures, can be introduced in practical nanoelectronics.

This is one of the advantages of cryoelectronics. Yet another advantage of cryoelectronics is the infinitely low noise level.

The discovered superconductivity is similar to that observed in graphite intercalated with alkali metals or in alkaline salts of fullerenes. However, the superconductivity temperature in nanotubes is much lower, which may be attributed to lower-frequency phonons in nanotubes (it is assumed that these phonons correspond to deformation oscillations of nanotubes).⁴⁷

Later,⁴⁸ the superconductivity of a single one-layer tube bridging two Au–Ti contacts was discovered. Figure 10 shows how the resistance of such a tube depends on temperature and how superconductivity is destroyed by magnetic fields.

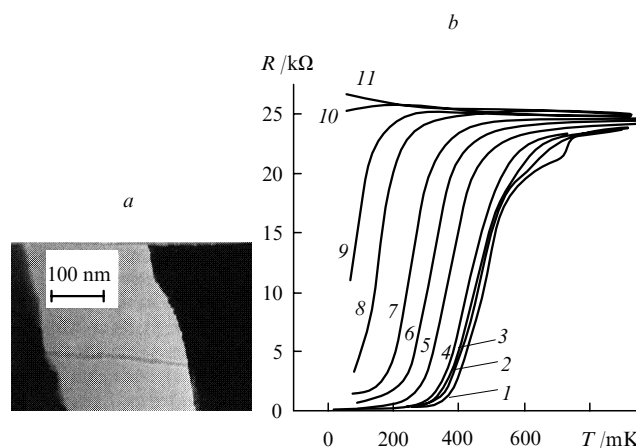


Figure 10. Arrangement of a single nanotube between Ti- and Au-contacts (a) and dependence of resistance on temperature in different magnetic fields at $I = 1 \text{ mA}$ (b).

Magnetic field strength /G: (1) 0, (2) 500, (3) 1000, (4) 2000, (5) 3000, (6) 5000, (7) 7000, (8) 10 000, (9) 12 000, (10) 15 000, (11) 20 000.

IV. Nanowires

Below, we consider ‘free’ (not enclosed in a carbon nanotube), conducting or light-emitting (metallic or semiconducting) nanowires.

1. Metallic wire

The most developed technique is drawing the wire from nanorods fastened between the cantilever and the tip of a tunnelling microscope.

Figure 11 a displays the scheme of a device for drawing nanowires. Gold nanorods (cylinders 0.125 μm in diameter and 2 μm long) were fastened between the gold tip of a tunnel scanning microscope and the tip of an auxiliary microscope. This arrangement enables the simultaneous detection of the electric conductivity and deformation force as a function of the stretch (length) of the nanowire.⁴⁹ The dependence of the conductivity and deformation force on the displacement (wire stretching) is shown in Figs 11 b,c, respectively.

It is interesting to note that electric conductivity and force change in a jump-wise manner: with an increase in length, the former decreases to a limiting value which corresponds to the quantum limit of conductivity.[§] The jump-wise behaviour of force means that the wire cross-section changes in a discontinuous manner; jumps occur when atoms rearrange and ‘jump into’ the final monoatomic chain. The molecular dynamics simulation of an atomic cluster during its stretching (Fig. 11 d) perfectly repro-

§ The quantum limit of conductivity is the conductivity of one (monoatomic) tunnelling channel.

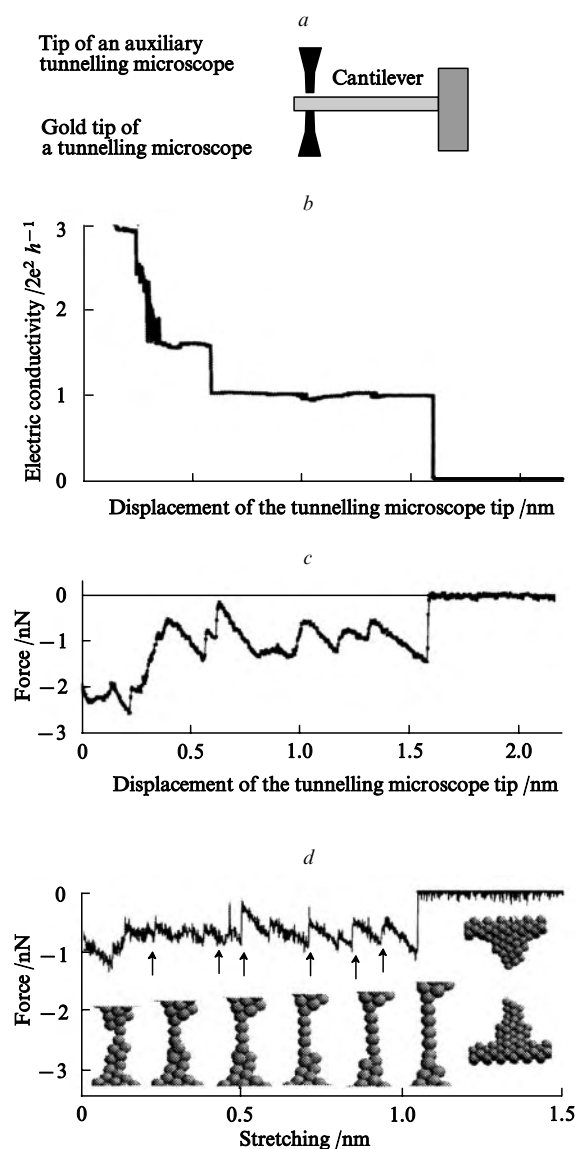


Figure 11. A scheme of a device for drawing nanowires (a) and dependence of electric conductivity (b) and deformation force (c) on displacement. The lower drawing (d) shows the results of a molecular dynamics simulation of force as a function of displacement and a scheme of the arrangement of atoms in a nanowire.

duces the experimental dependences. Quantum-chemical calculations within the framework of the density functional theory confirmed the stability of monoatomic chains.[¶] It follows from dynamic and quantum-chemical calculations that the degradation occurs in a five-atom linear chain⁵⁰ and requires a force of 1.5 ± 0.3 nN. It follows that the energy of an atom–atom bond in a monoatomic chain is twice as high as the atomic bond energy in the bulk metal. This is a reasonable result as a metal features multi-centred bonds and each of such bonds is weaker than a localised and isolated bond.

2. Semiconducting wires and nanolasers

Semiconducting nanowires are usually grown on clusters of metal catalysts. For example, GaP wires with controlled diameters (10,

20 and 30 nm) and > 10 μm long were obtained on gold clusters.⁵¹ Both types of clusters (GaP and Au) were obtained by laser ablation; a direct relationship between the Au cluster size and the diameter of GaP wires was observed, *i.e.*, the wire diameter ‘tuned’ to fit the size of the catalytic cluster.⁵²

Nanowires of GaN,⁵³ SiC,⁵⁴ Ga₂O₃,⁵⁵ *etc.* have been obtained to date. A simple technology has been developed to synthesise Ga₂O₃ by heating GaAs with sputter-deposited Au at 1240 °C in a stream of dry O₂; nanowires or nanostrips were obtained, depending on the technology used.⁵⁶ Nanowires are single-crystalline; they grow in a direction perpendicular to the (102) plane and display good photoluminescence characteristics. Wu *et al.*⁵⁷ synthesised GeO₂ nanowires with 50–120 nm diameters and hundreds of micrometres long. They luminesce upon photoexcitation; the quantum yield of their radiation is an order of magnitude higher than that for GeO₂ powders. A few other types of nanoobjects have recently been obtained, *viz.*, SnO₂ nanowires and nanotubes,⁵⁸ silicon nanowire ‘wrapped’ in a monolayer of gold atoms,⁵⁹ nanowires with the composition Mo_{1-x}W_xS₂ ($x < 0.1$) (one- and multilayer) with a bamboo trunk-type tubular architecture.⁶⁰

The high yield of optical radiation in semiconductor nanowires stimulated the search for strong nanoemitters that would work as coherent light sources (nanolasers and optical nanowaveguides). The first success was achieved with ZnO nanowires: excitation of densely packed nanowires resulted in laser emission (from the entire set of wires).⁶¹ A more detailed analysis of laser emission from individual nanowires was made by Johnson *et al.*⁶² ZnO nanowires were grown on the sapphire (110) surface. This plane is well compatible with the ZnO (0001) plane. ZnO nanowires grown vertically on sapphire were ultrasonically removed from the support and deposited on quartz from an ethanolic solution; their packing density on a horizontal surface was about 300 wires per 1 mm².

The wire diameters could be varied from 40 to 150 nm, and their lengths, from 4 to 10 μm . Each wire was detected separately. The laser emission was monitored using a near-field scanning optical microscope combined with fiberglass detection.

The majority of nanowires demonstrated intense light emission localised at their ends; however, they did not show the main sign of laser generation: the generation threshold was not reached even at very high excitation power (above 1 MW cm⁻²). However, certain nanowires behaved as ‘honest’ nanolasers: they gave high quantum yields and generation thresholds even at low pumping strength (Fig. 12).

To explain this laser-related ‘personality’ of nanowires, Johnson *et al.*⁶² devised a very plausible explanation: when the wires are ultrasonically detached from the sapphire, their end surfaces are formed in an arbitrary manner, hence light reflecting properties are poor (strong diffusion, phase detuning). This means that the Q value of such ‘maimed’ nanowires is low. Only part of the wires have well-reflecting ends (*e.g.*, if a nanowire is ‘torn out’ with

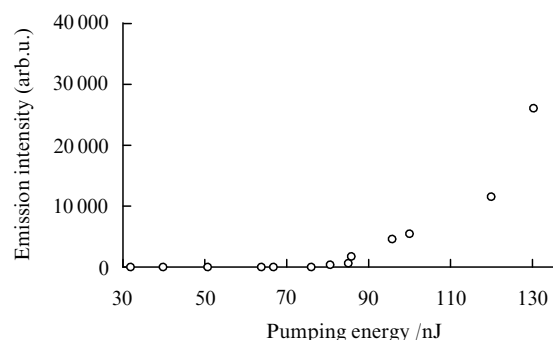


Figure 12. Generation intensity of ZnO nanolasers as a function of pumping energy.

¶ In this context, one has to remember G A Razuvaev who, as early as in the 1970s–80s, synthesised polyatomic metal chains using organometallic chemistry methods.

a nanopiece of sapphire) and hence behave as optical resonators. This is an important result that clearly shows the weaknesses in the technology and suggests ways to overcome them in order to make nanolasers with a low lasing threshold.

3. Ferromagnetic wires

It is considered that ferromagnetic nanowires may become the main elements of quantum magnetic disks, which are the subject of intense development by researchers in the field of nanochemistry. Discrete one-domain elements with high length/diameter ratios, arranged like columns and incorporated in a non-magnetic support, may serve as building blocks for a big information and operation system. Each such block carries one bit of information, and their density reaches hundreds of gigabytes per square centimetre.⁶³

The first steps in this direction have already been made:⁶⁴ cobalt was electrochemically deposited on anodised aluminium with high pore density (pore diameter 60 nm, density 10^{10} – 10^{11} cm⁻²); it filled all the pores to form a regular hexagonal surface 'lattice' of nanowires (columns ~ 60 nm in diameter and 1.6 µm high). This system is essentially a prototype of a quantum magnetic disk. Studies of this system by magnetic force spectroscopy confirmed that each nanowire incorporated in a pore is a one-domain magnet with strong magnetisation anisotropy (Fig. 13). The easy magnetisation axis is oriented along the nanowire. In this direction, the Co wire is a soft ferromagnet, while in the transverse direction, it is a hard ferromagnet as the hysteresis loops suggest.

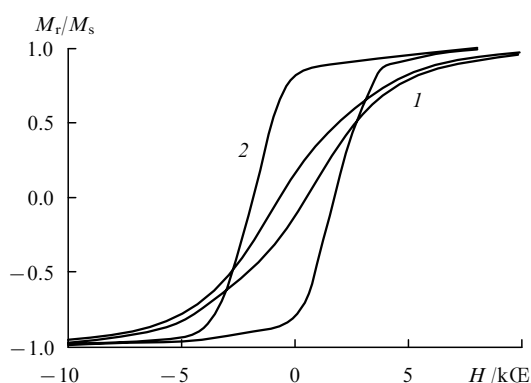


Figure 13. Hysteresis loops of magnetization of a Co nanowire parallel to the long axis (1) and perpendicular to it (2).

It was shown by magnetic force spectroscopy that the topography of the ferromagnetic columns matches exactly the topography of pores in the starting anodised aluminium, *i.e.*, one nanowire is trapped in each pore. The number of south magnetic poles exactly equals the number of north poles, and all the poles are arranged in a strictly regular manner: each south domain is surrounded by north domains, and vice versa. Magnetic field (1 T) causes complete magnetic orientation of all domains. Such a device is almost ready for recording and reading information (*e.g.*, using the tip of a magnetic force microscope).

It should be noted that the porous structure and hence the topology of ferromagnetic domains are sensitive to electrochemical anodisation and deposition modes, *i.e.*, the quality of nanomagnetic materials can be controlled technologically. There is no doubt that this area of nanochemistry has a great future.

V. Nanomechanics

Handling nanoobjects requires that their mechanical properties are known. The interest in nanomechanics stems from the possibility of creating nanopistons, nanosyringes, nanopumps

(*e.g.*, for cell biology), variable capacitance nanocapacitors, nanotweezers and other devices.

1. Internal friction in nanotubes

The first device in which the inner part of a multilayer carbon nanotube moved along an external part (as a piston in a cylinder) was created in 2000.⁶⁵ The authors opened the end of a multilayer nanotube and attached a nanomanipulator to the inner tubes. After that, they partially pulled the inner part out while observing this action under an electron microscope.

The first significant result of this work was the creation of a new nanomanipulator. Another result is the observation that, after the pulled-out part of the tube was released by the manipulator, it was instantly retracted back by the restoring force of the van der Waals interaction. It follows from this observation that nanotubes enclosed in each other move relative to each other with almost no friction and thus make an ideal wear-resistant molecular plain bearing.

Direct measurements of the force of cohesion between two coaxial nanotubes were carried out using an atomic force microscope.⁶⁶ An individual multilayer nanotube was fixed between the rigid cantilever of a spectrometer and the tip of the upper cantilever of an atomic force microscope (the latter served to measure the length and force). The distance between the cantilevers after stretching the nanotube and the stretching force were recorded.

The experiment was designed to consist of two stages. It was anticipated that disruption of the outer tubes would occur in the first stage due to stretching and that intact inner tubes would slide from under this 'wreckage' upon subsequent stretching.

However, of the 16 experiments that have been carried out, only the first stage, *i.e.*, total destruction of the outer tubes, was observed in 14 cases; it was only in two cases that 'sliding' of inner tubes from outer ones was observed after disruption of the outer tubes. The entire experiment (the measurement of the force F as a function of elongation L) was recorded on video. Analysis of the $F(L)$ relationship gave the cohesion force of sliding nanotubes.⁶⁶

The cohesion force per unit length of the contact was 0.45 and 0.67 N m⁻¹ for the two 'successful' experiments (the cohesion force expressed in N m⁻¹ corresponds to the cohesion energy expressed in J m⁻²). It is of note that the interplanar adhesion force in pure graphite is as small as 0.11–0.12 N m⁻¹. However, it should be taken into account that the values of 0.45 and 0.67 N m⁻¹ are overestimated, as they include not only surface cohesion but also cohesion due to boundary effects, *i.e.*, hindrance of the movement of the inner tube by the broken edges of the outer tube.

2. A nanotube as a high-frequency mechanical oscillator

The negligibly small friction between moving nanotubes opens up a route to nanomechanical oscillators. The mechanical scheme of such an oscillator is shown in Fig. 14.⁶⁷

A block of inner nanotubes that has been drawn out of outer tubes is then drawn back in due to the potential energy $U(x)$ of the van der Waals interaction between the atoms of two sliding tubes,

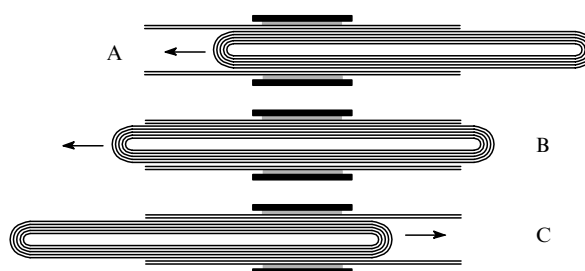


Figure 14. A scheme of movement of inner and outer nanotubes (see the text for comments relating to A–C).

viz., a cylinder and a piston (position A, Fig. 14). When the inner tubes return, the potential energy decreases, whereas the kinetic energy increases: in the equilibrium position B, the former equals zero, whereas the latter has a maximum value. Subsequently, the inner tube is drawn out on the other side because of momentum, until the kinetic energy decreases to zero. At this point (position C), the potential energy acquires a maximum value and draws the tube back in. In fact, this is a typical nanopendulum the oscillation frequency of which can be calculated if the van der Waals restoring force is known. The latter is a function of the displacement of the piston relative to the cylinder.

The van der Waals energy $U(x)$ of the cylinder–piston system was evaluated quantitatively using the Lennard–Jones potential and the structural parameters of the nanotubes (in particular, the gap between the tubes was considered to be 0.34 nm). The oscillation frequency was determined by solving the Newton equation

$$Mx(t) = F_{\text{vdW}} + F_{\text{fr}},$$

where M is the piston mass; $x(t)$ is the acceleration (the second derivative of the piston coordinate with respect to time); F_{vdW} is the force of the van der Waals cohesion between the piston and the cylinder, which equals $F_{\text{vdW}} = -dU(x)/dx$; F_{fr} is the friction force which was considered negligibly small, *i.e.*, $F_{\text{fr}} \ll F_{\text{vdW}}$.

Numerical estimates of the oscillation frequency for conditions similar to those used in the experiment by Yu *et al.*⁶⁶ gave values of $\sim 10^9$ Hz.

However, it is clear that an external impact is required to start such a gigahertz oscillator (mechanical pendulum). An alternating electric field can serve as the launching system; however, this requires that the piston be electrically charged (this can be achieved, *e.g.*, by chemical doping of the nanotubes). In any case, this appears to be a reasonable and promising direction of nanomechanics.

3. A nanopendulum as an electronic shuttle

There is a device known in classical physics, which consists of two big capacitor plates and a metal ball hung between the plates. By applying a DC voltage of several hundred volts to the plates, it is possible to make the ball rock between the plates and transfer charges. The charge carried by the ball in each oscillation is about 10^{10} electrons; the current in the circuit is 1–10 μA at an oscillation frequency of about 10 Hz.

In a nanoversion, such a device might work at frequencies of about 100 MHz and carry single electrons. It is quite obvious and realistic that such a device can serve as an element of a quantum computer or a current interrupter in nanocircuits. The first example of a nanopendulum (electronic shuttle) has been reported by Erbe *et al.*⁶⁸

The central part of the device (a) (it may be called a quantum bell) and its electrical scheme (b) are shown in Fig. 15. Its main part is the turning anchor C, which is (clamped and grounded) fastened in the upper part of a silicon plate. A metal island insulated from the rest of the turning anchor is deposited on its end. The control electrodes G_1 and G_2 carry a voltage (about 3 V) which controls the movement of the anchor-pendulum. The element S supplies electrons, whereas the element D is an electron receiver and plays the role of a FET drain. All the elements are deposited by nanolithography onto a silicon substrate.

The pendulum is brought into motion by an alternating voltage on the electrodes G_1 and G_2 with a frequency f . While moving, the metal island at the pendulum end regularly touches the S and D elements (the space between an element and an island is about 300 nm). The tunnelling of electrons from the element S to the island, and from the island to the element D, occurs during the short moments of contact. The electric capacitance of the contact under static conditions is 84 aF (attoFarads), which corresponds to ± 527 electrons at a voltage of ± 1 V.

At room temperature, the direct current between the elements S and D is about 20 nA; however, it increases or decreases

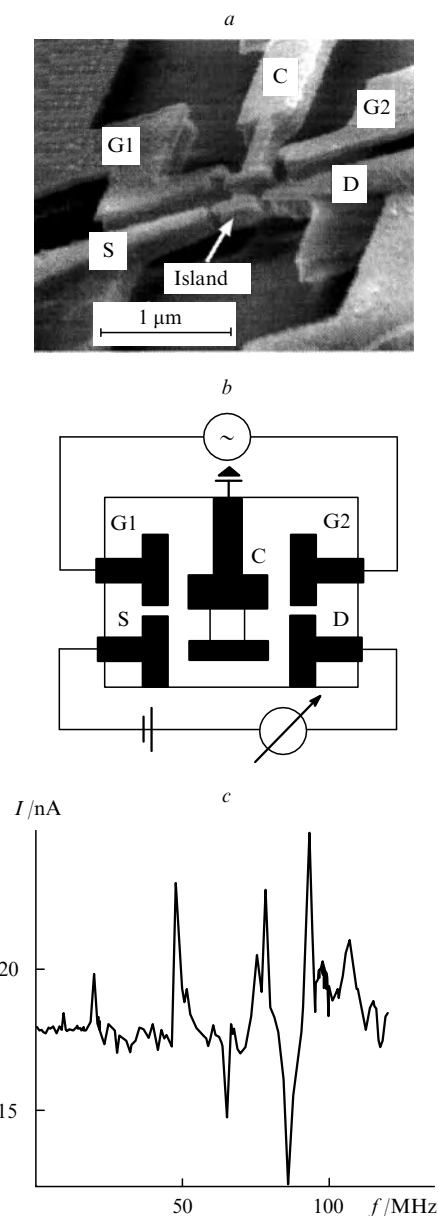


Figure 15. A scheme of a the nanopendulum (a, b) and the frequency dependence of current transferred by the pendulum at 300 K (c) (see text).

abruptly at certain resonance frequencies (see Fig. 15 c). Resonance appears at those instants when the frequency of the control current at the electrodes G_1 and G_2 coincides with the intrinsic mechanical frequency of the pendulum. One can see that the range 40–120 MHz contains several resonances of this kind, *i.e.*, there are several intrinsic frequencies of the pendulum, corresponding to different modes of high-frequency mechanical movement (bending, torsion, oscillation). The anti-resonances (current dips at certain frequencies) appear when the pendulum stops due to non-coincidence between the control frequency and the intrinsic frequency. In total, this mode may be called the ‘irregular movement’ of a pendulum.

However, as the temperature is decreased, the irregular mechanical modes start to ‘freeze out’, and only one intrinsic frequency of 120 MHz remains at 4.2 K; the current at this frequency corresponds to the transfer of 0.11 ± 0.001 electrons per pendulum oscillation. This is a pure mode in which the pendulum works as a discrete electron shuttle, transferring one electron on each ninth oscillation from S to D.

VI. Technologies for handling nanoobjects

Nanotechnology comprises two main constituents: (1) creating nanoobjects for nanodevices; (2) operations with these objects and mechanisms for handling them. And although studies along both directions are being carried out astonishingly quickly (similar development rates in the history of science have only been observed in relation to the discovery of superconducting ceramics and ‘cold thermonuclear fusion’), the second constituent still remains a weak, limiting point.

In the previous sections, we have already discussed some operating devices and nanomanipulators. Presently, the employment of the scanning tunnelling microscope (STM) and atomic force microscope (AFM) seem the most promising technologies. As Rakov has aptly noted in his paper,²⁶ ‘after the invention of STM and AFM molecular nanotechnology is no longer only a scientific concept’; it may be added that it has moved to the stage of acquiring practical experience.

1. Study of nanotubes and nanorods lying on a surface

The tip of an AFM reveals that nanotubes lying on a surface possess folds, bends, loops and even foldovers. The latter are changes in the lower tube occurring due to the compression force from the upper tube: it deforms markedly (by about 30%), its cross-section becomes elliptic, and the crossing point of the tubes is displaced downwards. By measuring this displacement and using the known Young modulus (about 1.5 TPa), one can evaluate the compression force and the energy of ‘adhesion’ of the pipe to the surface. For a multilayer nanotube with a diameter of 100 Å that lies on the surface of passivated silicon, the binding energy to the surface is 0.08 eV nm⁻¹ (per unit length of the tube). The compression force at the point of contact of two crossing tubes is about 35 nN; this corresponds to a pressure of about 10 GPa.⁶⁹ The compression of a one-layer tube with a diameter of 1.3 nm by 30% requires a force of ~10 nN.

The interaction between a nanotube and a surface determines both the normal force and the force of horizontal displacement (pinning), which is responsible for the friction of a tube moving along a support. The pinning force for a nanotube (10–30 nN) is comparable to the force with which the AFM tip affects an object. This possibility of moving nanotubes along the surface by means of an AFM tip has been implemented brilliantly.⁶⁹ It is possible to manipulate nanotubes in many ways: they can be moved, bent, twisted, oriented, turned around the normal line relative to the surface and shaped (in particular, Hertel *et al.*⁶⁹ shaped nanotubes as the contour of the Greek letter θ). Even an attempt to dissect a nanotube with an AFM tip succeeded, though after prolonged ‘dragging’ of the tube along the surface.

The mastering of the technology for manipulating nanotubes by means of an atomic force microscope is an important breakthrough in nanotechnology, as it removes barriers (including psychological ones) to the design of systems and ensembles from nanotubes with subsequent ‘welding’ of the ends with an electron or laser beam. An atomic force microscope was also used to move (rotate and displace) gold nanorods (10 nm in diameter, 70 nm long) on a SiO₂ surface;⁷⁰ it was shown that the ease of manipulation depends on the point of application of the force on a nanorod.

An interesting and seemingly promising technology for manipulating nanotubes has been proposed by Kim and Lieber.⁷¹ They ‘equipped’ a scanning probe microscope with nanotweezers, which are made of two gold leaflets with nanotubes and an insulating glass spacer. By applying a controlled electric field to the plates, it is possible to manipulate the nanotubes and grip nanoobjects with them. By varying the diameters of the nanotubes, it is possible to adapt the nanotweezers for gripping nanoobjects of various sizes.

2. Magnetic field as a manipulator

The spatial orientation and lining up of extended nanoparticles, as well as assembling them into ensembles can be performed by a magnetic field. For example, nanotubes are oriented in a magnetic field in such a way that their long axes are directed along the magnetic field (Fig. 16). The orientational probability (the fraction of nanotubes directed along the field) increases with an increase in the magnetic field.

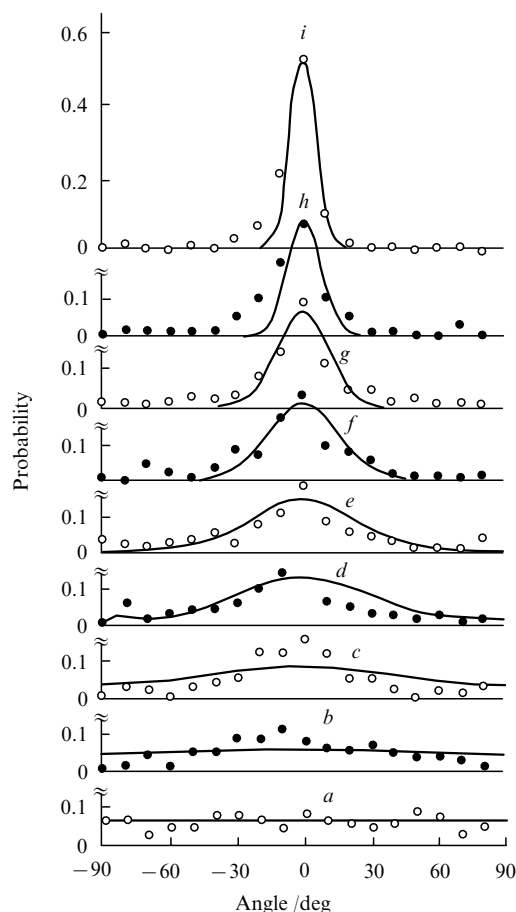


Figure 16. Dependence of the degree of nanotube orientation on the magnetic field strength (H).

(a) 0, (b) 5, (c) 10, (d) 16, (e) 20, (f) 30, (g) 40, (h) 60, (i) 80 kG.

For multilayer nanotubes (the number of layers is 23 ± 7 , the inner diameter is 2.8 nm, the outer diameter is 17.9 nm, the length is 1.5 μ m), the anisotropy of magnetic susceptibility measured from the dependence of orientation on the field (see Fig. 16) is $\chi_{\parallel} - \chi_{\perp} = (9 \pm 5) \times 10^{-6}$ cm³ K per mole of carbon atoms contained in a nanotube.⁷²

The anisotropy evaluated theoretically (under the assumption that the atomic magnetic susceptibility is the same as that in graphite) is 124×10^{-6} cm³ K mol⁻¹, which is much higher than that measured experimentally. This discrepancy is convincing proof that there are circular diamagnetic currents induced by the external magnetic field along the axis of the nanotube.

A remarkable (and unexpected) result is the dependence of the susceptibility anisotropy on temperature: at 231 and 314 K, it is 4×10^{-6} and 45×10^{-6} cm³ K mol⁻¹, respectively.⁷³ This dependence cannot be ascribed to kinetic effects in orientation mobility: the arrangement of nanoparticles in a magnetic field was always performed under the same conditions, *viz.*, in a CCl₄ solution, at prolonged exposure to the field and with the sub-

sequent fixation of the resulting orientation distribution by removal of the solvent. The origin of this effect remains unclear. It is possibly due to the internal coaxial rotation of tubes relative to each other. The high-frequency rotation of tubes (see the section on nanomechanics) may be the source of extra current and contributes to the anisotropy of magnetic susceptibility.

3. Atomic-molecular pump

A project has been proposed (and there are grounds to consider it highly realistic) involving a laser-controlled atomic-molecular pump in which a nanotube is used as a container for transporting atoms, ions or molecules (e.g., Li^+ or C_{60}^{6-}); these electrons will 'carry' atoms and ions along the tube. Usual direct excitation is not suitable for these purposes as a nanotube is a molecule with a centrally symmetric potential. In these molecules, the number of hot electrons that move in opposite directions (to the left and to the right) along the tube is the same, i.e., there is no electronic current. Asymmetry in the distribution of 'left' and 'right' electrons can be created by quantum interference of one- and two-photon excitation by coherent light at frequencies of $2\omega_0$ and ω_0 . Under such coherent two-frequency excitation, the electronic current appears in the tube, the direction of which is defined by the phase offset between the two laser sources and can be phase-controlled. Such laser-stimulated electronic current was called 'electronic wind' (Fig. 17).

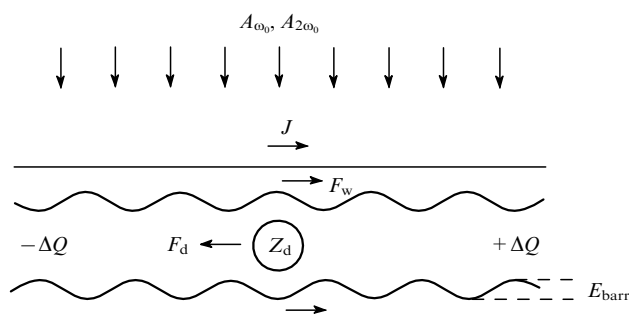


Figure 17. A scheme of a laser-controlled atomic-molecular pump (see text).

If the tube contains neutral (uncharged) atoms or molecules, the elastic scattering of hot electrons on these species will move the latter in the direction of the electronic wind. However, if the tube is filled with partially charged atoms or molecules, then the elastic scattering of hot electrons will create an electrostatic field the potential of which is directed against the electronic wind (see Fig. 17). This occurs because the number of electrons moving along the electronic wind (from the left to the right) is larger than that of electrons moving in the opposite direction. Hence, the number of electrons reflected to the left will be greater than the number of electrons reflected to the right. Thus, the electric charges $\pm\Delta Q$ created by reflection generate a field in which atoms move against the electronic wind.

Theoretical estimates of the operation of such a pump are very optimistic. In fact, for lithium with an effective charge of +0.6, the motive force F_d is $-0.8 \mu\text{eV}$; for a neutral Li atom carried by the electronic wind, the mean rate F_w is $25 \text{ nm } \mu\text{s}^{-1}$ (see Ref. 74).

An atomic-molecular pump can be easily controlled by light through phase ratios and intensities. There is no doubt that such a pump will be implemented in the near future. Following that, new breakthroughs in cluster chemistry and nanoelectronics should be expected.

4. Magnetic-resonance atomic-force spectroscopy as a new nanotechnology

The magnetic-resonance atomic-force spectroscopy combines the principles of atomic force microscopy and magnetic resonance. The areas of its application are obvious even now: these include the visualisation of magnetic nanostructures on the atomic scale, measurement of the density of electron magnetic moments and magnetic relaxation in nanostructures, use in spintronics devices (see Section II.4) and in reader elements of quantum computers, etc.

The typical elements of a magnetic-resonance atomic-force spectrometer are shown in Fig. 18. A micron-size ferromagnetic tip (made of an SmCo_5 or Pr-Fe-B alloy) is fastened at the end of an atomic-force cantilever. The sample to be studied is placed under the tip in a non-uniform field B_z with a vertical gradient dB_z/dz . The external field B_z and the magnetic field of the ferromagnetic tip create concentric surfaces with equal magnetic field strengths (isomagnetic surfaces) in the sample.[†] A microwave coil is placed aside of the sample; the purpose of the coil is to irradiate the sample at a frequency ω corresponding to the electron paramagnetic resonance.

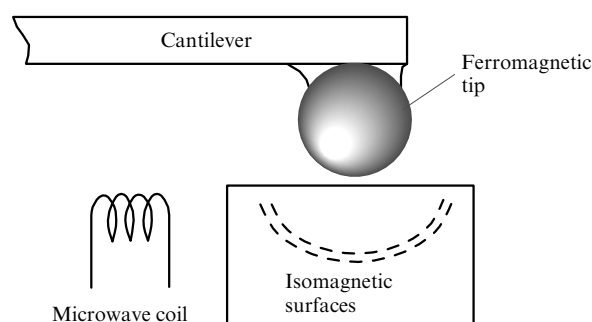


Figure 18. A scheme of a magnetic-resonance atomic-force spectrometer.

Because the magnetic field in the sample is non-uniform, only a small fraction of the spins (only those located on the isomagnetic surface with a field strength B_z) respond to the microwave frequency ω :

$$\omega = \gamma B_z,$$

where γ is the gyromagnetic ratio for the electron spin. On two neighbouring isomagnetic surfaces separated by a distance Δz , the resonance conditions have the form:

$$\omega_1 = \gamma (B_z)_1,$$

$$\omega_2 = \gamma (B_z)_2.$$

Then, the difference between the resonance frequencies $\Delta\omega = \omega_1 - \omega_2$ is expressed through the field gradient:

$$\Delta\omega = \gamma [(B_z)_1 - (B_z)_2] = \frac{dB_z}{dz} \Delta z.$$

If the resonance bandwidth for electron spins in the sample is $\Delta\omega$, then, at a given field gradient, all the electron spins in the Δz layer undergo microwave resonance.

In a few experiments using magnetic-resonance atomic-force spectroscopy, field gradients (dB_z/dz) of $300-2200 \text{ T m}^{-1}$ were used (see Refs 75 and 76); the largest gradient value was

[†]Note that isomagnetic surfaces are not necessarily spherical (more exactly, hemispherical). The surface shape is defined by the shape of the nanotip and the profile of its magnetic field. A ferromagnetic nanocrystal of any shape can serve as a nanotip.

250 000 T m⁻¹ (see Ref. 77). Given a resonance band width of $\Delta\omega = 1$ Hz (this band corresponds to an ESR line width of 1 Hz) and a field gradient of 2000 T m⁻¹ (i.e., 2×10^{-2} Hz nm⁻¹), we obtain $\Delta z = 50$ nm. This means that microwave irradiation with the band $\Delta\omega = 1$ Hz can affect the spins of the electrons located in a layer 50 nm thick. At the record gradient of 250 000 T m⁻¹ (this is 25 Hz nm⁻¹), the layer thickness is 0.4 nm. It is clear that the stronger the gradient of a non-uniform magnetic field the thinner the layer that is probed magnetically.

Unlike the electron spin resonance technology which detects and measures the microwave power absorbed by an electron spin system, magnetic-resonance atomic-force spectroscopy detects and measures the magnetic force on the cantilever. In this case, microwave irradiation results in reorientation of electron spins (transitions between Zeeman levels occur) and a change in the spin magnetisation of the probed layer in the sample being studied. As a result, the magnetic force on the cantilever changes.

As an elastic system, a cantilever has its own frequency of mechanical oscillations f (about 1–10 kHz, depending on its shape and mass) and elastic constant k (about 10^{-2} N m⁻¹). The oscillation frequency of the cantilever is maintained constant by a piezoelectric element which controls the cantilever movement. The electric field at the control piezoelectric element is created by a fibre-optic interferometer that monitors the position of the cantilever and generates a control signal, which maintains the cantilever's own frequency.

When an external gradient magnetic field B_z is applied, the spin system is polarised (the spins are oriented) and the magnetisation acquires a steady-state value. The magnitude of this magnetisation is determined by two factors: first, the external constant field B_z , and second, the magnetic field of the tip. The magnetic field of the cantilever with a ferromagnetic tip, which oscillates along the coordinate z , varies as a function of the tip's field; simultaneously, the sample layer with thickness Δz also undergoes height-oscillation along this coordinate.

At the instant when the cantilever is at its amplitude maximum, the microwave field is turned on (phase synchronisation). The spin system and spin magnetisation now change for two reasons: first, due to the microwave field that inverts the spins, and second, due to the movement of the cantilever, which changes the positions of the resonance layers in such a way that the spins are either affected by the resonance microwave field or come out of resonance.

In the new steady state (in the presence of a microwave field) a new value of magnetisation is established and the oscillating magnetic force F between the cantilever and the sample changes; as a result, the elastic constant of the cantilever changes and its new own frequency is established. The change in the elastic constant Δk is defined by the relationship

$$\Delta k = \frac{F}{\Delta a},$$

where Δa is the cantilever's oscillation amplitude (normally about 20 nm) and

$$\frac{\Delta f}{f} = 0.5 \frac{\Delta k}{k}.$$

This allows one to determine the oscillation part of the magnetic force F , which is a function of the number of spins being detected, the amplitude of the microwave excitation and the relaxation time of spin magnetisation. The sensitivity of this technology is as high as a hundred electron spins in a nanometre layer.⁷⁷

Thus, a magnetic-resonance atomic-force spectrometer is a superdynamic system that analyses the behaviour of two dynamic interacting subsystems: (i) a spin subsystem in a microwave field and in an oscillating field of a cantilever and (ii) a mechanical oscillating subsystem of the cantilever, which modulates the spin subsystem.

Of course, this new technology is still in its infancy; it operates under high vacuum conditions and at cryogenic temperatures and is still 'aristocratic'. However, its potential for studying the 'nanoworld' is huge.

* * *

Being the chemistry of nanoobjects, nanochemistry is inseparable from nanotechnologies as a combination of methods for handling nanoobjects. This field of chemistry has tempting prospects; some of these are already being implemented, while others are on the 'waiting list'. And, though making predictions is the same as writing memoirs for a person who has just been born and then making that person live according to those memoirs, it may be stated with certainty that nanochemistry and nanotechnologies will some day become as important as life chemistry.

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Ion transfer in ion-exchange and membrane materials

A B Yaroslavtsev, V V Nikonenko, V I Zabolotsky

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Abstract. Modern concepts of mass transport in solids are considered. Essential information on the structure of organic and inorganic ion-exchange materials and on defect formation processes is presented. The key methods of investigations of ion transfer are described. The results of studies on the transfer processes in membrane systems induced by various driving forces including the concentration, electric potential and electrochemical potential gradients are generalised. The bibliography includes 530 references.

I. Introduction

Mass transport in solids and across their surfaces is of importance for separation and purification of liquids (including water treatment),^{1–5} for fuel cell operation,⁶ catalytic reactions,⁴ as well as for numerous solid-phase,^{7–9} sorption^{4, 10} and many other processes. Therefore, the problem of description of the kinetics of ion and molecular transfer has attracted the attention of researchers. However, no general approach to the solution of this problem has been proposed as yet notwithstanding its obvious importance and topicality. For each particular case there are specific relations, methods and terminology. As a consequence, researchers who study the mass transport problem in a certain field often have almost no information on the studies carried out by their colleagues in allied sciences. Narrow specialisation is also determined by the extreme complexity of phenomena accompanying the ion and molecular transport, *e.g.*, sorption and desorption of substances, defect formation in the interior and on the surface of ion-exchange materials (ion exchangers) and occurrence of chemical reactions. Mass transport can also be affected by the dimension of the system under study and by the possibility for transfer to follow alternative routes.^{11, 12} Therefore, often the kinetic laws that are successfully used for description of ion transport in a

particular system can appear to be inapplicable to its close analogues. Nevertheless, the existence of some general regularities of the transfer processes occurring in solid systems of various nature seems not to be improbable. This requires the development of general approaches to the description of the chemical kinetics of ion transfer. Solving this problem has been the focus of considerable research involving a wide use of modern experimental equipment, theoretical concepts and various methods of numerical analysis.

The main goal of this review is to generalise approaches to the description of transfer processes in ion-exchange and membrane materials of various nature and to outline the main methods of investigations of ion transfer in such systems. In presenting the material the authors of this review tried to avoid the use of complicated mathematics. The emphasis is placed on consideration of relatively simple approaches and relations, on interpretation of the results obtained and on the description of regularities of transport processes in both organic high-molecular-mass and inorganic materials including systems possessing ion-exchange properties and ionic conduction.

II. Structure of ion-exchange and membrane materials

1. Structure of organic ion-exchange materials

Currently, organic ion-exchange and membrane materials are used much more widely than their inorganic analogues. Therefore, most of the modern models of transfer and structure of ion-exchangers have been developed for organic materials. In this connection it is appropriate to consider first the structure of polymer-based materials. Ion-exchange materials of different nature including the so-called homogeneous membranes and gel ion exchangers are in fact inhomogeneous.^{1, 11–13} There are different forms of inhomogeneity, *e.g.*, a structural, chemical and physical one, which can manifest themselves on both the macro- and microscopic level. Sometimes, such inhomogeneities are created in a targeted manner in the course of synthesis procedures (macroporous ion exchangers, granulates, heterogeneous membranes). In other cases they appear spontaneously. Inhomogeneity of a material strongly affects the transfer mechanism and many physicochemical properties of ion exchangers, as well as the operating characteristics of membrane systems.

An ion exchanger, which is in equilibrium with atmosphere, is called dry (air-dry). However, even in this case the material contains some amount of water (nearly two water molecules per

A B Yaroslavtsev N S Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation. Fax (7-095) 954 12 79. Tel. (7-095) 978 85 27. E-mail: yaroslav@rfbr.ru

V V Nikonenko, V I Zabolotsky Kuban State University, ul. Stavropol'skaya 149, 350040 Krasnodar, Russian Federation. Fax (7-861) 269 95 01. E-mail: nikon@chem.kubsu.ru

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ionogenic group for sulfonated cation exchanger and 3 mass % or about 2%–3% of the maximum water uptake for perfluorocarbon membranes).^{13, 14} The structure of the dry ion exchanger is determined by conditions of the polymer synthesis and by structural rearrangement of the polymer due to the presence of ionogenic groups.

If ion exchangers are obtained by polymerisation and polycondensation, small highly cross-linked nuclei are first formed. Then nuclei merge together, thus forming an island structure;¹¹ the process can be accompanied by entanglement of polymer chains.¹² As a consequence, the polymer contains a large number of defects of various nature and size. These defects impart different levels of heterogeneity, from microscopic (atomic groups and molecules) to macroscopic (macropores, clusters of size 100 nm and larger), to the polymer structure.

In numerous studies carried out since the mid-1950s pores and other features of the heterogeneous structure of polymer matrices were detected both by direct observations (by electron microscopy, scanning electron microscopy,¹² small-angle X-ray scattering,^{13–16} Mössbauer spectroscopy,^{13, 17, 18} NMR spectroscopy^{19–22} and other methods^{13, 20, 21, 23–28}) as well as by indirect measurements (by mercury porosimetry,²⁹ reference porosimetry,^{30–32} differential scanning calorimetry,^{33, 34} etc.^{1, 34–37}).

Among the pioneering studies on the effect of charged ions on the ionomer structure was that reported by Eisenberg.³⁸ He chose an ion pair (an ionogenic group, *i.e.*, a partially or completely dehydrated fixed ion–counterion pair) as the main structural unit and showed that the dipole–dipole interaction causes association of the ion pairs to form the so-called multiplets containing no polymer chain segments. Due to steric hindrances the number of ion pairs in a multiplet is small, at most 6–8 according to Weiss *et al.*³⁹ and 2 according to Dreyfus.⁴⁰ The dipole–dipole attraction leads to aggregation of multiplets to yield larger associates (clusters). However, clustering induces a strong stretch of the elastic polymer matrix. The possibility for such a transformation to occur depends on several factors, *e.g.*, elasticity and degree of cross-linking of the polymer chains, concentration of ionogenic groups, etc. Ponomarev and Ionova⁴¹ studied changes in the strain energy, the energy of hydrophobic interactions between polymer chains and the Coulombic interaction energy upon clustering of ionogenic groups and showed that the process is energetically favourable if the concentration of ionogenic groups is not too low and the polymer network is sufficiently elastic. The newly formed cluster acts as an additional cross-link, thus making the polymer matrix more rigid.

Dreyfus⁴⁰ considered a simple model, which allows assessment of the structure and estimation of the size of dry clusters, as well as determination of their arrangement in membrane (Fig. 1). The model assumes an ideal flexibility of polymer chains. The only factor which limits an increase in the density of ionogenic groups is

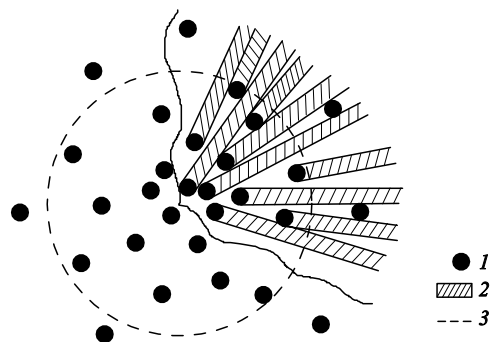


Figure 1. Schematic representation of a dry cluster in an ion-exchange membrane containing elastic hydrophobic polymer chains.⁴⁰ Multiplets (1), polymer chain segments or bundles (2) and approximate cluster boundary (3).

the size of the polymer chains. For perfluorocarbon membranes the radius of the dry ionic cluster is 1–2 nm.⁴⁰ This is in agreement with the results of the small-angle X-ray scattering experiments.¹⁵

Hydration of ion exchangers causes essential changes in their structure. A consequence of hydration of ions and hydrophilic regions of the polymer matrix is swelling of the ion exchanger. This leads to an increase in the mobility of polymer chains, which, in line with the formation of a network of hydrogen bonds, facilitates additional aggregation and brings about clustering and formation of other structural elements with more or less homogeneous structure and composition. Because of this in studies on membrane systems such aggregates are called 'phases'. In spite of the fact that this term is not rigorous, we will use it in the text below. One phase is the hydrophilic 'gel' phase, which comprises the system of micropores formed by the rather closely spaced fixed and mobile ions and hydrophilic segments of the polymer chains. The second, hydrophobic, phase includes aggregated hydrophobic polymer chains and their bundles, as well as segments of an inert binder (*e.g.*, polyethylene), which is added to increase a membrane's mechanical strength. The electrically neutral solution, which fills voids, mesopores and macropores upon swelling, can be treated as the third phase.

As perfluorocarbon sulfonated cation-exchange membranes pass from the dry state to the swollen state with a water content of 20 mass %, the intensity of small-angle X-ray scattering by clusters increases by nearly an order of magnitude.¹³ The inter-cluster distance increases from 2–3 to 4–5 nm.^{13, 15, 42–44} Analogous results were obtained¹⁶ for polyphosphazene membranes (a promising material for fuel cell applications).⁴⁵ As water penetrates into the cluster, its volume increases, thus causing a stretch of the elastic matrix. In this case hydrophobic segments of polymer chains can be displaced from the cluster volume, thus forming the hydrophobic phase. Equilibrium is attained when the energy liberated upon hydration of ions becomes equal to the energy required to stretch the matrix.^{42–44, 46} As a result, the hydrated cluster looks like an inversed micelle.

The cluster–network model proposed by Gierke *et al.*⁴² treats spherical clusters. The fixed ions are at the cluster's periphery, which provides a minimum value of the surface energy and excludes contact of the polymer with water. Counterions neutralise the charge of the fixed ions, thus forming an electrical double layer (Fig. 2). The interior of the cluster is filled with aqueous electrolyte solution. For simplicity, Hsu and Gierke⁴² assumed that, depending on the energy state, there are two kinds of water, the 'inner' water and the 'surface' water. The latter fills the first and second outer layers of the cluster and constitutes the hydration shells of the fixed ions and counterions. The state of the inner water does not differ from the state of water in free solution.

The cluster diameter can be evaluated from the water uptake of the membrane. Assuming that clusters occupy the sites of a cubic lattice separated by 5 nm, the number of clusters per cubic centimetre of the membrane is 8×10^{18} while the number of water molecules per cluster at a water content of 15 vol. % is nearly 10^3 . At a membrane capacity of 1 mmol cm^{-3} , the number of fixed ions in the cluster approaches a value of 70. The cluster diameter is

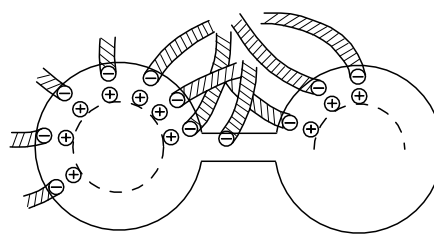


Figure 2. Schematic representation of the structure of a swollen perfluorinated membrane according to the cluster–network model of Gierke.⁴²

~ 4 nm.⁴² It increases as the membrane's exchange capacity increases and as the degree of cross-linking of the polymer matrix decreases.^{15, 16}

This model also permits consideration of channels connecting adjacent clusters (see Fig. 2). Such channels were shown to be thermodynamically stable.⁴² However, the free energy of the system changes only slightly upon channel formation (-11 J cm⁻³); therefore, channels continuously appear and disappear. According to Timashev's figure of speech,¹³ they are 'scintillating'. The calculated channel diameter (1.4 ± 0.2 nm) is consistent with the experimental data ($1.2-1.3$ nm).⁴⁶

As the concentration of fixed ions and the water content in the membrane increases, the cluster diameter increases while the intercluster distance decreases. A feature of this situation is a marked trend to a 'collapse' of the system of hydrated clusters to form a through pore network.⁴⁰ A fraction of clusters 'merge' together, the channels connecting adjacent clusters are shortened, their diameters increase and the membrane structure becomes less regular. The transport properties of highly hydrated perfluorocarbon membranes with relatively high concentrations of fixed ionogenic groups are similar to those of the 'gel' hydrocarbon membranes. At a low content of water the properties of the two types of membranes differ appreciably in, *e.g.*, the character of dependence of the specific conductivity and diffusion permeability on the electrolyte concentration, *etc.*⁴⁷

The cluster-network model by Gierke was subjected to criticism^{13, 48, 49} because it provides no explanation for new results obtained by X-ray diffraction, Mössbauer spectroscopy, *etc.* To interpret these results, a channel model of the structure of the amorphous part of a perfluorocarbon membrane was proposed.¹³ This model assumes the presence of a comb-like periodic layered system of conducting pores (channels) with a wall-to-wall distance of 3–4 nm. Tovbin, Vasyutkin and Dyakonov^{48, 49} modified this model and developed a three-dimensional structural model of a perfluorinated membrane, which treats two kinds of pores, *viz.*, slit-like and cylindrical ones. The larger slit-like pores with a wall-to-wall distance of 3–5 nm are formed by close-packed polymer chains, are 10–17 nm long and 5–10 nm wide. Regular packing of polymer chains that form the 'walls' of the slit-like pores is periodically distorted by transient regions characterised by chain bending and entanglement. Such transient regions can be represented as sets of cylindrical pores formed by segments of bending polymer chains; the characteristic pore diameter and pore length are 1.5 and 2.5 nm, respectively. The role of these pores is analogous to that of the cluster-connecting channels in the Gierke model. The characteristic sizes of the structural elements in the models by Gierke and by Tovbin–Vasyutkin are in good agreement while the models themselves differ in interpretation of the cluster and channel shape.

The results obtained in a large number of experimental studies carried out to date allow definite conclusions about the structure of swollen hydrocarbon membranes. One of the pioneering works was reported by Gnusin⁵⁰ who studied inhomogeneous distribution of the concentration of ionogenic groups by microscopic observations. Similar results were also obtained by spectroscopic methods,^{13, 17, 22, 51, 52} contact reference porosimetry^{30–32} as well as by other methods.^{34–37} Figure 3 presents the results obtained for a heterogeneous cation-exchange membrane MK-40 by contact reference porosimetry^{31, 53} and mercury porosimetry.³⁴ The pore radius distribution curve is bimodal. Its maxima correspond to two types of pores, that is, the micropores and mesopores of radius about 10 nm and macropores of radius of the order of nearly 1000 nm. The first type of pores is localised within particles of the KU-2 cation-exchange resin employed for the preparation of the membrane, while the second type of pores represents the space between the resin and binder (polyethylene) particles.

According to Vol'fkovich *et al.*,³¹ micropores (of radius 1–2 nm) and mesopores (of radius 2–10 nm) in the structure of hydrocarbon membranes involve the space between individual polymer chains and their bundles. The volume of macropores (of

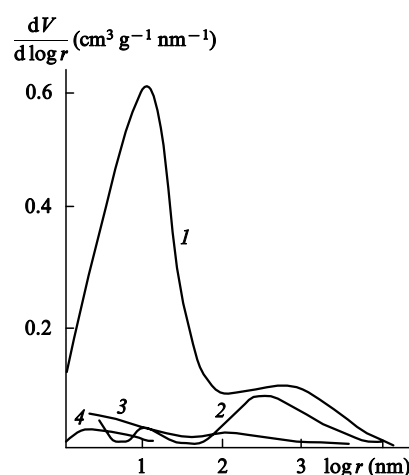


Figure 3. Pore radius distribution curves for a MK-40 membrane obtained by contact reference porosimetry (1),⁵³ mercury porosimetry (2),³¹ (3)³⁴ and sorption technique (4);³⁴ V is the total volume of the pores of radius r .

radius exceeding 10 nm) is the space between large bundles of polymer chains and between these bundles and polyethylene binder particles. Large pores have puckered walls, the relative fraction of such pores can serve as a measure of inhomogeneity of ion exchangers. However, the total volume of large pores is much smaller (sometimes by an order of magnitude³¹) than that of the small pores, which determine the ion-exchange and sorption properties of an ion exchanger. For instance, more than 80% of pores in the MA-100 homogeneous membrane have radii less than 10 nm, while the maximum volume fraction falls to the pores of radius 4.5 nm.³¹

2. Structure of inorganic ion-exchange materials

The major distinction between inorganic systems and the polymeric systems considered above is a higher degree of structural ordering in the former material. Exchange of a particular type of ion by another one usually occurs with retention of the lattice framework. A feature of the structure of ion-exchange materials with a rigid three-dimensional framework is the high degree of retention of the type of coordination polyhedra characteristic of a certain sort of ion. Most inorganic ion-exchange materials possess cation-exchange or bifunctional properties. The latter group is mostly represented by hydrated oxides of polyvalent elements.

Among inorganic ion-exchange compounds, it is possible to identify the following classes: complex and hydrated oxides and salts of polyvalent metals. Detailed description of each class has been documented.^{2, 54, 55} In this Section we will consider the structure of some of the most widely used inorganic ion exchangers. From this point on for more systematic presentation it is convenient to divide the ion exchangers into nanomaterials, layered materials and materials with a three-dimensional framework.

A strong impetus to the development of research on nanomaterials has been noted recently. This is mainly due to the specific properties of such materials^{56–60} and to advances in the synthesis, investigation and applications of fullerenes.^{61–64} The geometry of small particles is to a great extent determined by the condition for a minimum surface tension energy. Therefore, a nearly spherical shape is the most typical. The developed surface of nanoparticles contains numerous uncompensated bonds, which can be stabilised upon sorption of various ions and molecules.⁵⁵ However, these species are weakly bound to the nanoparticle cage, which makes possible reversible dissociation and surface migration.⁵⁵ In combination with high surface diffusion coefficients this determines good transport properties of such materials.^{60, 65, 66}

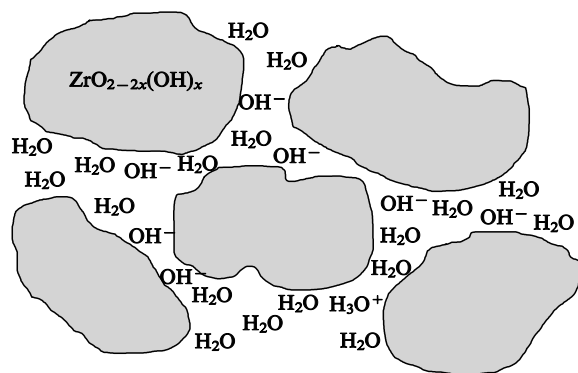


Figure 4. Schematic representation of the structure of hydrated zirconia.^{54, 55}

This type of ion-exchange material is often called a globular hydrate.⁵⁵ Typical representatives of such materials are hydrated oxides of polyvalent metals. Ion transport in them mainly occurs within the intergrain space containing a large number of water molecules (Fig. 4). These compounds are characterised by relatively low ion-exchange capacity, which can vary by several orders of magnitude on heating or prolonged storage as a result of olation, oxolation and crystallisation processes. In some cases heat treatment at temperatures of up to 400 °C can improve the exchange properties of these compounds due to shortening of distances between hydroxyl groups and particle's surface.⁶⁷

Structural peculiarities of amorphous hydrated oxides are due to the inhomogeneity of the bonds formed by OH groups and, as a consequence, by their ability to dissociate by acid or basic mechanisms with appreciably different dissociation constants. Therefore, the exchange capacity of hydrated oxides, which manifests itself when contacting an aqueous solution, strongly depends on the proton concentration in the solution.^{54, 68} In addition, these materials can change their properties from anion-exchange to cation-exchange with an increase in the pH value of the solution. The relation between cation- and anion-exchange properties of hydrated oxides is determined primarily by the electronegativity of the structure-forming cation. For instance, double hydroxides of divalent and trivalent elements^{69, 70} as well as hydrated yttrium oxide⁷¹ are anionites. Depending on the particular conditions, hydrated zirconium and tin oxides possess both cation- and anion-exchange properties,⁵⁴ while hydrated antimony(V) oxide is a cation exchanger.⁷²

Globular hydrates also comprise tungstophosphates of some monovalent metals, which possess cation-exchange properties. The number of water molecules that form a monolayer on the particle surface usually varies from 7 to 12 per formula unit. Both heteropolyanions and protons are sorbed on the surface of such compounds, which is equivalent to the deposition of acid salts in which the content of hydrogen ions can exceed 1.0 per formula unit.⁷³ According to NMR studies, monovalent cations on the surface of particles at room temperature are in the highly mobile state.^{73, 74} It is these ions that can be exchanged with ease upon contact with aqueous solutions of salts.

The advantage of layered compounds is the high concentration of accessible sorption sites or ion exchange groups. Among this class of inorganic ion-exchange materials, hydrogen phosphates and arsenates of polyvalent elements [$\text{MH}_x(\text{ZO}_4)_2 \cdot n\text{H}_2\text{O}$] ($\text{Z} = \text{P}, \text{As}$) are most widely used. The structure of a typical representative of this group of compounds, zirconium hydrogen phosphate, is presented in Fig. 5. Cations of small radii can migrate in the large interplanar space (interplanar spacing $d = 7-8 \text{ \AA}$) with ease in the direction parallel to that in which layers are aligned.^{76, 77} Because of this the exchange capacity of such compounds is most often much higher than that of globular hydrates. For instance, a typical value of the ion-exchange

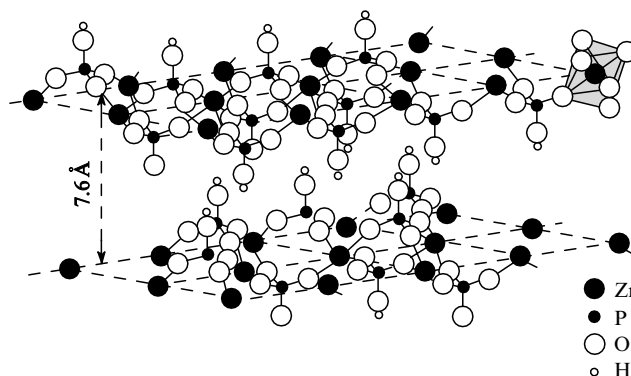


Figure 5. Crystal structure of zirconium hydrogen phosphate.⁷⁵

capacity of, *e.g.*, hydrogen phosphates of tetravalent elements is 4–8 mequiv g^{-1} (see Refs 78–83). Due to the nonequivalence of hydrogen atoms and steric hindrances to arrangement of the second cation in the matrix, exchange processes in hydrogen phosphates of tetravalent elements most often involve two stages. Besides, in contrast to most polymeric membrane materials, exchange in these systems often occurs by movement of the interphase boundary, the composition of each phase being changed slightly in the course of exchange.^{55, 84} Hydrogen tantalum phosphate has a somewhat lower exchange capacity (2 mequiv g^{-1}).⁸⁵ At the same time the cation mobility in this compound is much higher than that in the hydrogen phosphates of tetravalent elements.^{86, 87}

Another group of layered compounds possessing ion-exchange properties comprises hydrated oxyphosphates of pentavalent metals $\text{H}_2\text{XO}_2\text{PO}_4 \cdot n\text{H}_2\text{O}$ ($\text{X} = \text{V}, \text{Nb}, \text{Mo}$). For instance, the niobium compound contains two hydroxyl groups;⁸⁸ however, only one proton in them can be replaced by a cation in the reaction with alkali.^{89–92} Exchange processes in uranyl phosphate ($\text{H}_2\text{UO}_2\text{PO}_4 \cdot n\text{H}_2\text{O}$) occur similarly.^{93, 94} No less important is the ability of the compounds under study to be intercalated with alkali metal cations or hydrogen, which is accompanied by reduction of a fraction of the polyvalent cations and the formation of variable-composition compounds $\text{M}_x\text{VOPO}_4 \cdot n\text{H}_2\text{O}$.^{95–97} The latter also possess ion-exchange properties^{98–100} and, in addition, high conductance, which is of great importance for the occurrence of some practically valuable transfer processes.

Layered ion exchangers comprise a giant class of clay materials built of blocks whose composition approximately corresponds to $\text{Si}_2\text{Al}_4\text{O}_{20}^{4-}$. The electroneutrality of the compound is ensured overall by the incorporation in the interplanar space of alkali or alkaline-earth metal cations or protons. A large proportion of cations located within the interplanar space can be readily exchanged. The total ion-exchange capacity of such materials can be as high as 1.5 mequiv g^{-1} . For the H-form of the materials with a nearly ideal composition the ion-exchange capacities with respect to cations and anions are approximately equal.^{2, 101–103} Many layered inorganic ion exchangers are characterised by low solubility and their synthesis is, as a rule, accompanied by the formation of strongly supersaturated solutions. This leads to the formation of small particles, which are less thermodynamically stable; however, the exchange reactions on their surfaces usually occur much faster. Therefore, often researchers restrict themselves to the synthesis of materials built of rather small particles, which makes the 'boundary' between layered ion exchangers and nanomaterials diffuse. An intermediate position between the two above-mentioned classes of compounds is occupied by fibrous materials.^{104, 105}

The exchange processes in the layered compounds considered above are, as a rule, accompanied by substantial changes in the interplanar spacing due to the different radii of the exchanging cations and to the change in the degree of hydration.⁸⁵ However,

not all compounds obey this regularity. In particular, practically valuable inorganic membrane materials are β -aluminates having a composition $M_{1+x}Al_{11}O_{17+x/2}$ (M^+ is a proton or the ammonium, alkali or monovalent metal cation). They also have a layered structure. A peculiar feature of their structure is that the four-layer blocks of composition $(Al_{11}O_{16})_n$ with close-packed oxygen atoms are linked by oxygen atoms of the fifth layer containing a quarter of the oxygen atoms in each of the four above-mentioned layers. Because of this the interplanar spacing varies only slightly in the course of exchange. Besides, cation exchange in such materials occurs relatively slowly at ambient temperatures. Therefore, most often the exchange processes are carried out in nitrate melts of β -aluminates at temperatures of at least 300 °C.^{106–115} These compounds can be considered as a transient form between layered ion exchangers and materials with a three-dimensional framework.

Inorganic ion-exchange materials with a three-dimensional framework demonstrate the largest variety of structures. Transfer in such compounds is due to the presence of long continuous channels. Since ion transfer can occur only through migration of defects (vacancies or interstitial ions), a fraction of sites 'reserved' for the mobile ions should be vacant.⁶ Some examples of these compounds are provided by complex phosphates and silicates $A_xB_2(YO_4)_3$, where A is the univalent cation, B is the trivalent or tetravalent cation and Y = P or Si. Sodium-containing representatives of this type of material[†] are characterised by high cation mobility.¹¹⁶ High cation mobility was also found in other structurally similar compounds containing protons, ammonium, lithium and some other cations (see, e.g., Refs 117 and 118). The three-dimensional crystal lattice of the compounds belonging to the NASICON structural type is formed by the XO_6 octahedra (X is the trivalent or tetravalent metal) and PO_4 tetrahedra linked in such a way that three-dimensional channels extending along the crystallographic axis c are formed in the structure.¹¹⁹ It is these channels where all the atoms of type A are located. However, if they are all occupied in $Na_4Zr_2(SiO_4)_3$, a total of 25% and 75% of sites remain vacant in $Na_3Sc_2(PO_4)_3$ and $NaZr_2(PO_4)_3$, respectively. In this connection at temperatures above the superionic phase transition temperature (320 K) a fraction of lithium atoms in the $LiZr_2(PO_4)_3$ structure cannot be located by the diffraction techniques.¹¹⁹ Besides, it was found that such materials can be doped with heterovalent admixtures. For instance, it is possible to replace a fraction of phosphorus atoms by silicon, vanadium or niobium atoms.^{120, 121} The largest increase in conductivity can be achieved by replacing a fraction of the cations occupying the X sites by trivalent metal cations with a simultaneous increase in the content of the alkali metal cations A (see, e.g., Refs 122–125). The conductivity (cation mobility) of such systems can be several orders of magnitude higher than the conductivity of the initial phases.

Most often cation exchange in the NASICON compounds is carried out by treating the initial phase with salt melts.^{126–128} Compounds with the three-dimensional framework also comprise zeolites that are widely used as sorption materials and catalysts,^{102, 129–135} some complex oxides and many other inorganic materials that have been reviewed.^{2, 54, 55} It should be mentioned that a large number of novel inorganic ion exchangers are synthesised and studied yearly.^{136–142} High selectivity and stability of inorganic ion-exchange materials are prerequisites for the development of investigations in this area.^{2, 102, 143, 144}

Recently, extensive research on the synthesis and properties of mixed ion exchangers based on inorganic matrices with chemically bound organic fragments, which contain functional groups or link individual layers and thus confine the volume of the interplanar space, has been carried out. Such ion exchangers are most often synthesised using hydrogen phosphates of tetravalent elements as

matrices.² This allowed preparation of a large number of cation- (see Refs 145–148) and anion-exchange materials¹⁴⁹ possessing specific properties. Studies on the synthesis of similar materials based on other classes of compounds have also been carried out.¹⁵⁰

Polymer-based composite materials with heterogeneous inorganic admixtures can be considered as a new class of ion-exchange materials. They exhibit specific physical and chemical properties and can be divided into two types, viz., materials with an inert and with an ion-exchange polymer matrix. In the first type of system the mobile cations are generated by the inorganic component.^{151–155} Such materials are formed, e.g., in the reaction of a polymer matrix with alkali metal halides or pseudohalides. The rubbery phase of the polymeric component provides a high ion mobility.^{156, 157} The maximum conductivity of these composites is attained at an optimum ratio between the concentrations of the salt molecules and monomer units (this ratio is usually 0.2 to 0.4). In some cases the optimum value is much smaller.^{151, 158, 159} In the initial stage of doping a sharp increase in the cation mobility is due to an increase in the concentration of charge carriers. Further increases in the cation mobility are accompanied by a substantial increase in the degree of crystallinity of the polymer and reduction of the mobility of charge carriers.¹⁵¹ The effect of various microcrystalline oxides,^{156, 157, 160} phosphates¹⁶¹ and other heterogeneous admixtures to solid polymer electrolytes on the ion-exchange properties of the composite materials under study has been investigated.

The second type of material employs an active ion-exchange membrane capable of sorbing both cations^{162–164} and anions¹⁶⁵ as the polymer component. The list of currently used inorganic dopants includes a variety of compounds, namely, hydrated oxides of polyvalent elements (aluminium, titanium, silicon, antimony),^{162, 166, 167} heteropolyacids^{163, 168, 169} and other compounds.¹⁶⁴ The characteristic size of the dopant species can vary from several to several hundreds of nanometres.¹⁶⁸ Apparently, in most cases they form islands in the membrane. For instance, a small-angle X-ray scattering study¹⁷⁰ revealed that the average distance between the dopant species in the Nafion– SiO_2 system is about 5 nm. The advantages of the composite membranes are mechanical strength, selectivity and the possibility of increasing the ionic conductivity of some systems, which can be as high as 10^{-3} – 0.2 S cm⁻¹ (see Refs 162, 165, 171).

III. Ion diffusion in solids

1. General laws

The rates of diffusion processes in various solids are substantially different. In the vast majority of compounds such processes proceed at relatively low rates; nevertheless, this does not make them less significant. For instance, very slow geochemical processes cause changes in the composition and structure of the Earth's crust.¹⁷² Raising the temperature permits a substantial increase in the ion and molecular mobility. At high temperatures, solid-phase reactions between rather stable (at first glance) oxide phases proceed at a rather high rate.⁵ Ion exchange and membrane processes are due to cation and anion diffusion.⁵⁵ The mechanism and rate of transfer in ion-exchange and membrane materials to a great extent determines the possibility of their practical use. Selective electrotransport of cations and anions through cation- and anion-exchange membranes, respectively, permits, e.g., desalination of liquid mixtures.

Two mechanisms, diffusion and convection, underlie the ion transfer processes. In this review we will mostly consider the first mechanism. The rate of diffusion processes is determined by the product of the charge carrier mobility and their concentration. The first factor depends on the nature of the mobile ion and the matrix (the material in which transfer occurs).^{173–175} In most inorganic compounds it is possible to select one type of ion having high mobility, which allows one to treat them as unipolar electrolytes. The highest mobility is possessed by small ions, which can

[†] They were called NASICON (an abbreviation of Na Super Ion CONductor).

travel with ease through faces of adjacent coordination polyhedra. At the same time, such ions must be capable of forming and cleaving chemical bonds, which implies a relatively low polarising ability. For this reason only small singly charged ions can possess a high mobility in inorganic systems at moderate temperatures (below 700–800 K). Among anions, these are only the fluoride and oxygen (at elevated temperatures) ions. Usually, cations of smaller radius also have a higher mobility. The highest ion mobility is attained for a number of compounds of monovalent metals (copper, silver and sodium).¹⁷³ Having similar radii, the first two cations offer the advantage of high polarisability of their electron shells.

The transport properties of most inorganic compounds are due to (i) the presence of vacant structural sites, in which the energy of the mobile ions is similar to the energy of the structure-forming ions, and (ii) the ratio of the cation size and the face size of the coordination polyhedron through which cation migration occurs.^{174, 175} In the case of proton diffusion (small radius, $\sim 10^{-5}$ Å) the latter factor is insignificant. More important for proton transfer is the system of interatomic distances and the proton-acceptor ability of electronegative lattice-forming atoms.^{176, 177}

Ion transfer in solids occurs through the migration of defects (vacancies or interstices) and the ratio of the number of defects to the number of mobile ions determines the concentration of charge carriers, which is the most important characteristic. All materials possessing high rate of ion transfer are characterised by high concentration of charged point defects.^{173, 177, 178} Such an approach is applicable to a wide range of systems. For instance, water is a poor conductor first of all due to the low concentration of charge carriers (hydrated protons or hydroxide ions). The addition of acids or alkali causes the formation of defects, thus leading to a sharp increase in the conductivity of the system.¹⁷⁹ Analogously, the concentration of defects in the low-temperature modification of silver iodide (β -AgI) is relatively low, while it increases by several orders of magnitude in the superionic phase of this compound.¹⁸⁰ The concentration of defects in superionic compounds can be as high as 10^{18} cm⁻³ (see Refs 172 and 181). It is this parameter whose value determines the ability of a substance to provide fast ion transport.

The reaction of defect formation in an ionic crystal M^+X^- with Frenkel defects can be described by the following equation¹⁸²



where M is the cation, V is the vacancy, the subscripts M and i correspond to the atom occupying the cation site and the interstice, respectively, and the superscripts (a point and a prime) respectively denote the positive and negative charge of the species with respect to the stoichiometric charge of a given lattice site. Let N_i and N_v be the mole fractions of the ion interstices and cation vacancies in the bulk of the crystal. The product of these quantities can be expressed through the equilibrium constant (K_F) or the Gibbs free energy (ΔG_F) of the reaction (1)

$$N_i N_v = CK_F = C \exp\left(-\frac{\Delta G_F}{RT}\right), \quad (2)$$

where C is the number of interstices per site of a regular lattice (e.g., for crystals with the rock salt structure one gets $C = 2$). Since the crystal is electrically neutral, the concentrations of vacancies and interstices in the crystal have equal values. Therefore, we can write

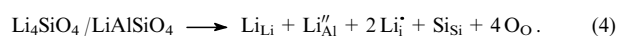
$$N_i = N_v = (CK_F)^{1/2} = C^{1/2} \exp\left(-\frac{\Delta G_F}{2RT}\right). \quad (3)$$

In some materials the energies of the atoms occupying the lattice sites and the defect sites are nearly equal. In particular, the energies of the cations occupying five different sites with the

coordination numbers of 5, 8 and 9 in the structure of sodium β -aluminate are similar.¹⁸³ Because of this at room temperature nearly half the sodium ions are located at sites with a higher energy, which makes the notions 'sites' and 'interstices' undefined. At the same time in the case of $NH_4Al_{11}O_{17}$ arrangement of a large NH_4^+ cation at different sites leads to a larger energy difference. Therefore, in $NH_4Al_{11}O_{17}$ almost all ammonium ions occupy the so-called Beavers–Ross sites. Clearly, in ammonium β' -aluminate, $(NH_4)_{1+x}Al_{11}O_{17+x/2}$, the excess NH_4^+ ions should occupy the interstices. This should lead to a decrease in the concentration of cation vacancies [see Eqn (3)]. However, structural studies point to a sharp increase in the number of cation vacancies with increasing concentration of interstitial ammonium ions. For instance, on average 23% of regular sites in $(NH_4)_{1.2}Al_{11}O_{17.1}$ are vacant, while the interstices are occupied by 0.43 ammonium ions per formula unit.¹⁸⁴ As the ammonium ion arrives at an interstice, it displaces adjacent cations from regular lattice sites to the interstices with similar energies. The formation of relatively large structural domains (clusters) characterised by the predominant population of interstices appears to be energetically favourable. It is these clusters in which the majority of excess cations is located.

The rate of ion transport can also be considerably increased by doping ionic crystals with heterovalent admixtures. Doping causes an increase in the concentration of cation vacancies or interstices. For instance, heterovalent replacement of the phosphorus or tetravalent metal atoms in high-defect solid solutions based on phases with the NASICON structure (see above) by cations of lower valence with simultaneous introduction of an excess of alkali metal results in a sharp increase in the concentration of interstitial mobile ions, which is accompanied by an increase in the ionic conductivity.^{116, 122, 185} A study of a lithium-containing compound revealed the formation of clusters containing cation interstices alternating with the domains of stoichiometric composition, which is similar to β -aluminates of alkali metals. This allowed Abrahams and Bruce¹⁸⁶ to conclude that ion transfer in such materials involves migration of clusters containing a large number of interstices.

Replacement of silicon by phosphorus in a silicate of composition $Li_{4-x}Si_{1-x}P_xO_4$ also results in the formation of one cation vacancy in the lattice. A feature of the Li_4SiO_4 – $LiAlSiO_4$ system is the formation of a continuous series of solid solutions of composition $Li_{4-3x}Al_xSiO_4$ and an individual compound $Li_5AlSi_2O_8$. West *et al.*¹⁸⁷ showed that individual compounds in this system exhibit the lowest conductivity. Interstitial lithium ions are the main type of defects, which determines the conductivity of the Li_4SiO_4 -based solid solutions



In contrast to this, cation vacancies dominate in the solid solutions based on $LiAlSiO_4$



The cooperative phenomena contribute largely to transfer processes in condensed media.¹⁸⁸ They have a particularly strong effect on proton transfer, which always occurs by successive proton jumps from one electronegative atom to another and by rotation of proton-containing groups.¹⁸⁹ Water molecules located near a hydrophobic polymeric ion-exchange matrix form relatively weak hydrogen bonds and readily pass into the rotational mobility state. A rotating water molecule should be treated as a neutral spherical species rather than a dipole. Hydrogen bonds formed by this molecule are cleaved, which facilitates the mobility of the nearest neighbours. Their rotation, in turn, induces the mobility of other surrounding molecules and, finally, of the whole system. For instance, a fraction of the hydrogen bonds formed by water molecules and proton hydrates in $H_3PW_{12}O_{40} \cdot 29H_2O$, in which the anion O atoms having a low proton-acceptor ability act as proton acceptors, are very weak. The high rotational mobility of these fragments, which, in turn, function as acceptors of

protons of other H-bonds, propagates over the whole proton hydrate sublattice due to the cooperative effect. Therefore, its transition to the highly mobile state occurs at low temperatures.¹⁹⁰ A similar transition to the mobile state at low temperatures has been reported for layers of water molecules sorbed on the surface of some inorganic compounds.¹⁷⁶

Vibrations of both solution particles and functional groups of ion exchanger induce alternating weakening of some hydrogen bonds and strengthening of some others in the system. Strengthening of hydrogen bonds brings about a decrease in the activation energy for proton transfer and accelerates proton hopping, whereas the weakening of bonds enhances the rotational mobility. These processes are separated in space, so that proton transfer acquires a cooperative character. The cooperative nature of proton transfer has also been noted for salts of polyfunctional organic acids,^{191, 192} for chains of the acid $-(\text{H}_2\text{O})_n-$ anion type¹⁹³ and for complex biomolecules.^{194, 195} There are grounds to believe that the cooperative mechanism of transfer can also be involved in the case of some alkali metal cations.¹⁹⁶ It should be mentioned that all the systems listed above are characterised by relatively weak binding, which seems to be important for efficient cooperative processes. The higher the structural disorder and the weaker the bonds formed there, the larger the vibrational amplitude and the higher the rate of transfer. It is the weakness of bonds formed and the ease of their rearrangement that result in a large vibrational amplitude and the highest efficiency of cooperative processes.

In this connection we will return to the polymeric membrane materials considered above. A salient feature of such systems is a decrease in the ionic conductivity with a decrease in the mobility of polymer chain segments, which is accompanied by an increase in the viscosity of the polymer.¹⁵¹ Taking into account this fact, Druger *et al.*¹⁹⁷ proposed a percolation model of transfer with allowance for correlation between cation hopping and rotation of segments of polymer chains, which induces reorientation of cation's coordination polyhedra.

Diffusion in polymeric membranes and ion-exchange materials is usually described assuming the three most probable ion transfer mechanisms, *viz.*, the vacancy, relay and solvation ones.^{51, 198, 199} According to the vacancy mechanism, the mobile ions migrate from one fixed (immobile) molecular group to another one. Migration occurs if at least one neighbouring group is unoccupied by an ion. The relay mechanism involves 'displacement' of an ion bound to the fixed group by a 'free' ion present in the channel. The 'displaced' ion goes to the conductive channel or displaces the next bound ion, thus maintaining the relay transmission. The third solvation mechanism deals with the motion of ions in solution and is to a great extent analogous to transfer along interstices in ionic crystals.

The first and third mechanisms can be realized simultaneously, since the counterion having escaped its potential well cannot go beyond the bulk of the ion exchanger (this corresponds to the formation of Schottky defects in crystals²⁰⁰). This relay mechanism occurs in the case of a narrow channel (pore), where the vacancy mechanism is impossible for steric considerations.^{201, 202}

The depth of the potential well is determined by the energy of the coulombic interactions between hydrated ions, by the chemical interaction between the ion and the molecular group it is bound to and by the energy necessary to stretch the polymer network and thus to provide the possibility for an ion to escape.⁵¹ For some transfer mechanisms the barrier height also depends on the energy of formation of ion vacancies and dopant ions.²⁰⁰ According to quantum-mechanical calculations by Shaposhnik *et al.*,^{203, 204} insertion of water molecules between the counterion and the fixed ion leads to substantial weakening of coulombic interactions between them. At the same time one should take into account the energies of the hydrogen bonds formed by water molecules with the counterions and fixed ions, which is responsible for the crucial role of hydrogen bond cleavage in ion trans-

port. The potential barrier is determined by the elementary jump length, λ , of the diffusing ion. In ionic crystals, ion hopping from one interstice to another occurs; therefore, the λ value is determined by the lattice constant.²⁰⁰ For ion-exchange materials, λ is most likely determined by the distance between corresponding molecular groups and depends on the ion-exchange capacity.⁵¹ In conventional ion-exchange membranes the average distance between such groups is 0.5–1.0 nm.^{13, 51} Probably, ion transfer from one fixed group to another involves a number of elementary jumps. In this case, at least in systems with a high concentration of ionic salts in channels, the role of transfer agent can be played by the mobile ions likely charged with the fixed groups (coions) or by the solvent molecules.

When estimating the self-diffusion coefficient of multiply charged ions, Shaposhnik *et al.*^{203, 204} pointed out that the probability of a fluctuation, which makes possible simultaneous abstraction of an ion from several fixed groups it is bound to, is very low. Assuming that the ion escapes from the potential well in several steps, they concluded that the diffusion coefficients of the doubly charged ions must be nearly 4 times lower than those of the corresponding singly charged ions.

2. Transfer processes and interfaces

Most of the membrane and sorption processes are heterogeneous, so interfacial phenomena are of great importance in this case.²⁰⁵ Frenkel²⁰⁶ and Chebotin and Perfil'yev²⁰⁷ pointed out that the grain boundaries and the surfaces of solid particles are sources of excess point defects, the concentration of which for ionic crystals is determined by the surface potential. Most often cations and anions are located on the surface of crystals under different conditions. Apparently, that is why cation vacancies or interstices are mainly sorbed on the surface, while defects of the opposite sign are concentrated within a thin near-surface layer. Because of this the so-called 'surface' charge appears within the Debye layer (~ 1 – 3 nm thick). The volume density of the 'surface' charge tends to zero with the distance from the interface to the interior of the crystal.^{208–210} The magnitude of the charge is determined by the morphology, crystal chemistry considerations and sorption properties of the surface. The electrical double layer at the organic ion exchanger–solution interface is formed analogously.^{11, 173}

The concentration of defects and the surface potential of silver chloride polycrystals were estimated by Maier²¹¹ from the ionic conductivity of this compound. The results of calculations are in good agreement with the data obtained using independent methods. In particular, the surface potential of silver chloride and silver bromide changed from -0.1 to -0.25 eV on heating from 298 to 550 K.^{212, 213} According to calculations, at room temperature the concentration of cation interstices in these compounds must be three orders of magnitude higher than in the bulk of the crystal.²¹² Enhancement of the translational mobility of ions and intensification of the diffusion processes on the surfaces of crystals are due to weak binding of the surface atoms and high imperfection of the surface.^{65, 66, 214}

The contribution of the surface component to transfer processes is most significant for nanomaterials, since the linear size of nanoparticles can be comparable with the thickness of the Debye layer. In this case the bulk of the particle is characterised by an increased concentration of defects and the material as such must possess an abnormally high conductivity.²¹⁵ A detailed description of ion transfer in nanomaterials can be found in reviews.^{60, 216}

In the early 1970s Liang²¹⁷ discovered that the ionic conductivity of the low-temperature modification of silver iodide placed in contact with finely dispersed alumina increases by several orders of magnitude despite the fact that the latter compound did not possess conducting properties. This appeared to be of increasing interest due to the potential use of composite electrolytes in compact power sources with high capacity.²¹⁸ A number of experimental studies were carried out, aimed at increasing the ionic conductivity of silver, mercury, lithium and monovalent copper halides by doping them with finely dispersed

powder of an inert phase, for the most part finely dispersed alumina, silica and titania.^{219–227} At about that time Shahi and Wagner^{228, 229} and Hartwig and Weppner²³⁰ reported an increase in the ionic conductivity of two-phase solid electrolyte mixtures (AgI–AgBr, LiI–NH₄I). In succeeding years the number of studies in this research area increased significantly.

An increase in the conductivity upon heterogeneous doping of ionic compounds is primarily determined by a substantial increase in the contribution of the surface component. Numerous attempts to explain this phenomenon have been undertaken. For instance, Stoneham *et al.*²³¹ postulated that the formation of the highly conducting phase is due to the presence of trace amounts of water. However, experimental data supported the assumption that an increase in the conductivity of binary systems of the AgI–Al₂O₃ type is first of all determined by an increase in the concentration of defects in ionic salts containing mobile ions.²²⁰

Suppose that the admixture (phase B) possesses the properties of a base, is chemically inert towards the ionic compound M⁺X[–] and forms no solid solutions with M⁺X[–]. It is known that two phases are in equilibrium if the chemical potentials of all components (including ions) in each phase are equal to one another. Therefore, sorption of the M⁺ and X[–] ions on the surface of B is possible until the ion activities are equal to those in the bulk of M⁺X[–]. For instance, only silver ions incapable of penetrating alumina particles are in the mobile state in the AgI–Al₂O₃ system; however, these ions can be efficiently sorbed at the interface. Because of this, cation vacancies are concentrated in the adjacent layer of the solid electrolyte, thus imparting a negative charge to it (Fig. 6a). By analogy with the situation which takes place when a solid contacts an electrolyte solution,^{232, 233} an electrical double layer is formed at the AgI/Al₂O₃ interface. A theory for this phenomenon has been developed by Maier *et al.*^{208, 234–248} Defect formation can be described by the following equations:²⁰⁸

$$M_M + V_B = M_B + V'_M, \quad (6)$$

$$M'_B + V_i = M'_i + V_B, \quad (7)$$

where the subscript B denotes the interfacial sorption site.

To describe the thermodynamics of interfacial processes, the functions ΔG_{VB} and ΔG_{iB} were introduced. The difference between the values of these functions at the interface and at the surface of a pure crystal equals the Gibbs free energy of migration of a metal ion from MX to the surface of the B phase. If $\Delta G_{VB} < \Delta G_{iB}$, a fraction of ions escape from the bulk and appear at the interface due to sorption. This causes a sharp increase in the concentration of vacancies within the Debye layer. The change in the concen-

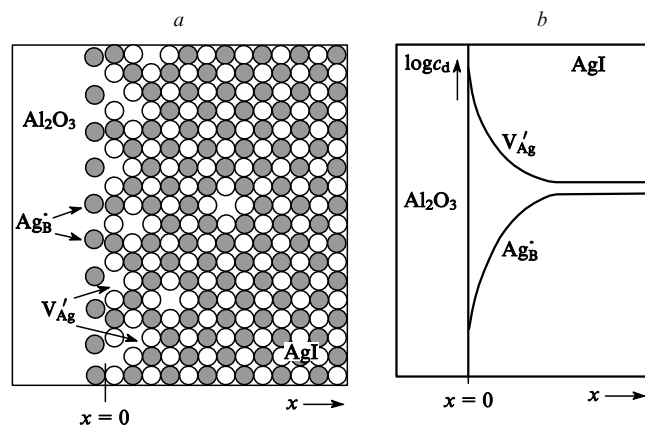


Figure 6. Scheme of defect formation at the AgI/Al₂O₃ interface (a) and changes in the defect concentration (c_d) within the boundary layer (b);⁹ x is the distance from the surface of the Al₂O₃ particles (phase B) into the interior of the AgI particle.

tration of cations along the normal to the interface is analogous to that shown in Fig. 6b. If the phase B possesses the properties of a weak base, it does not possess the ability to sorb cations and can tear them away (adsorb anions), which leads to an increase in the concentration of interstices in the near-surface layer. In both cases for a rather strong interaction the concentration of a particular sort of defect increases, which affects the physical and chemical properties of composite systems.

Various types of interactions at solid/solid interfaces have been reported.^{181, 240} In particular, the systems comprised of alumina and lithium iodide (or silver chloride, or a divalent metal fluoride) are characterised by sorption of mobile monovalent ions (Li⁺, Ag⁺, F[–]) at the interface. As a consequence, the concentration of vacancies within the Debye layer sharply increases.^{208, 243, 249} The interaction of the silver chloride surface with ammonia vapour causes an increase in the concentration of cation vacancies due to the formation of relatively strong cationic complexes at the interface.²⁴⁰ In contrast to this, interaction of silver chloride or calcium fluoride with Lewis acids (BF₃ or AsF₅) results in the formation of strong surface anionic complexes. In this case the concentration of interstitial silver ions or fluoride ion vacancies within the Debye layer increases sharply.^{240, 242, 244} The interaction of silver iodide with silver bromide or silver chloride also causes a substantial increase in the conductivity of the system^{225, 250, 251} due to the formation of heterogeneous (AgI/AgCl) contacts, which is accompanied by an increase in the concentration of cation vacancies and interstices in the near-interface region. This kind of interphase interaction is analogous to the formation of an electrical double layer near the surface of solids immersed in electrolyte solutions.^{232, 233} Sorption of oxygen atoms on the oxide surfaces also causes the formation of cation vacancies in the near-surface layer.²⁴⁵

As mentioned above, ion exchangers and membrane materials can be represented as multicomponent and multiphase systems comprised of very thin interlayers, channels or voids filled with a charged solution (micro-, meso- and macropores) and an inorganic or polymer matrix containing functional groups. Due to the interaction between the solution and matrix, spatially separated charges appear. Most often, the size of channels and pores, in which ion transfer occurs, is of the order of several nanometres (see Fig. 3). Since this size is comparable to the characteristic thickness of the Debye layer, rather intense sorption–desorption processes occur involving the overall pore system. Even in the case of contact with neat solvent the concentration of charged particles formed as a result of dissociation of functional groups or sorption of one sort of ions (solvent constituents; in the case of water these are the H⁺ or OH[–] groups) in the conducting channels is high. Therefore, transfer processes in these channels can be highly efficient. Besides, since changes in the concentration of charged species are most pronounced within the grain boundary Debye layer (Fig. 7), the ion distribution over the channel thickness is nonuniform. The rate of ion transport differs correspondingly.

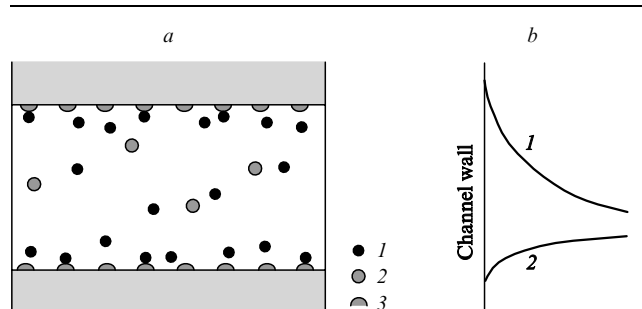


Figure 7. Counterion and coion distribution in the membrane channel (a) and changes in their concentrations near the channel wall (b); counterions (1), coions (2) and ionogenic groups (3).

The electric potential and ion concentration distributions in the pores of ion-exchange materials are described in the framework of the Gouy–Chapman theory and related models based on it.^{252–255}

The effect of homogeneous and heterogeneous contacts on the rate of chemical transport is ambiguous. On the one hand, a considerable increase in the concentration of charge carriers within the Debye layer accelerates transfer along the boundary. On the other hand, ion transfer between two phases can be complicated because of the low concentration of charge carriers at the interface.^{9, 248, 256} Besides, interfacial phenomena strongly affect the kinetics of various processes that occur involving the solid phase. Nonlinear phenomena, such as oscillating catalytic processes,²⁵⁷ oscillations of the electrochemical potential on the surface of metallic electrodes,^{258, 259} *etc.*, can be observed at the gas–solid and liquid–solid interfaces. Therefore, it is of importance to allow for all interactions between the membrane material and the environment in the course of ion transfer.

Let us consider transfer of the component M through an ionic compound $M^{z+}X^{y-}$ through which both ionic and electronic conduction can occur. If the driving force is weak, one can assume that the flux of the component M is proportional to the electrochemical potential gradient ($\Delta\mu_M$). Directed transfer of only one sort of ions would lead to charge separation in the membrane bulk, which requires a large expenditure of energy. Therefore, chemical transport usually involves unidirectional diffusion of differently charged ions including electrons or counterdiffusion of likely charged ions. Generally, the flux of any sort of ions can be calculated from stoichiometric ratios. For instance, the flux of metal ions is given by the Wagner equation²⁶⁰

$$J_M = -\frac{\sigma \Delta\mu_M}{(ze n_M)^2}, \quad (8)$$

where σ is the ambipolar conductivity of the crystal

$$\sigma = \frac{\sigma_M \sigma_B}{\sigma_M + \sigma_B} \quad (9)$$

(σ_M and σ_B are the ionic conductivity of the material with respect to a given sort of ion and the electronic conductivity, respectively), e is the electron charge and n_M is the stoichiometric coefficient. Equation (8) is also applicable to calculations of transport through grain boundaries.²⁵⁶

Analysis of the relations listed above suggests that the rate of mass transfer is controlled by the concentration of defects possessing a lower mobility. If the limiting factor is ion transfer, chemical transport in systems with multiple boundaries characterised by an increased concentration of defects occurs at a higher rate. Acceleration of transfer involves more intense chemical transport along grain boundaries (Fig. 8 *a*).

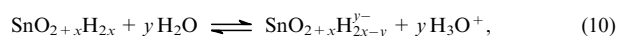
In some cases mass transfer along grain boundaries accelerates due to the specific interaction between them. In particular, a study²⁶¹ of electrotransport of multiply charged cations across the

interface between two oxide phases revealed that the properties of ceramics obtained in the synthesis of some molybdates and tungstates of divalent metals in an electric field are significantly different from the properties of ceramics obtained by sintering of oxide powders. This first of all manifests itself as a change in the adhesive properties of the interfaces between the initial reagent and product, as well as an increased concentration of diffusant on the product surface. Besides, it was shown that diffusion of molybdenum and tungsten in such systems occurs faster compared to diffusion of calcium, strontium and lead, which contradicts the commonly accepted electrotransport models. Neiman and Guseva²⁶¹ assumed that molybdenum and tungsten diffuse as constituents of ‘multiparticle defect complexes’ and pointed to a marked dependence of the transfer rate on the substrate porosity. Based on the aforesaid, it was concluded that MoO_3 (WO_3) interact with the reaction product as wetting agents, thus forming a thin layer of the ‘surface phase’, which accelerates ion transfer.

Studies on the synthesis of tungstates and molybdates in an electric field involving unidirectional diffusion of MoO_3 and WO_3 revealed an abnormally strong effect of the electric field on the reaction kinetics, as well as a ‘non-Faraday behaviour’ of the reaction and a nonmonotonic dependence of the reaction rate on the voltage applied.^{262–264} Similar phenomena were also observed in studies of the interaction of (i) molybdenum and tungsten oxides with trivalent bismuth oxide²⁶⁵ and vanadium and niobium oxides,^{266, 267} (ii) V_2O_5 and Nb_2O_5 with rare-earth element oxides,²⁶⁸ (iii) Bi_2O_3 with transition-metal oxides²⁶⁹ and (iv) indium, gallium and chromium oxides with Al_2O_3 and ZrO_2 .^{270, 271}

Following a parallel between transfer in solids and fluids, it is appropriate to discuss the interrelation between anomalous transport properties of grain boundaries (see above) and high ionic mobility in globular hydrates whose structure was described above.

Water molecules filling the intergrain space of these compounds are bound to the surface only by weak coordination and hydrogen bonds. Therefore, water molecules are in a highly mobile state.^{66, 71, 74, 189} At the same time, defect formation occurs on the surface of the hydrated particle (see above). This process is accompanied by passage of a fraction of the surface cations and anions into the newly formed solution, which, under some assumptions, can be treated as an individual phase. Ionic constituents of this phase also possess high mobility. Therefore, they can exchange with ease, as solid particles contact the surrounding real solution. (This is also the reason for the conducting properties of such compounds.^{54, 71, 101}) For instance, the following process is to some extent possible:



since hydroxyl groups in $\text{SnO}_2 \cdot n\text{H}_2\text{O}$ can undergo dissociation by the acid mechanism.

The intergrain space of a globular hydrate is filled with a solution of composition $y\text{H}^+ \cdot n\text{H}_2\text{O}$, which is responsible for high proton conductivity of this compound (it can be as high as $3 \times 10^{-4} \text{ S cm}^{-1}$ at room temperature). This solution is an analogue of the charged defect layer near the surface of the oxide phase. Proton transfer in the solution filling the intergrain space of globular hydrates is similar to that occurring in aqueous solutions and proceeds by the Grotthus mechanism.¹⁷⁵ Related phenomena are also responsible for the conductivity of finely dispersed zirconium hydrogen phosphate (proton mobility on the surface of this compound is four orders of magnitude higher than in the bulk phase⁶⁶) and insoluble alkali metal tungstophosphates.^{74, 120}

The above-mentioned structural features of globular hydrates determine fast ion transport and the occurrence of chemical reactions involving only active surface groups. For the most part the exchanging ions migrate in the intergrain space along grain boundaries. Typical examples of chemical transport in globular hydrates are provided by numerous ion-exchange reactions occur-

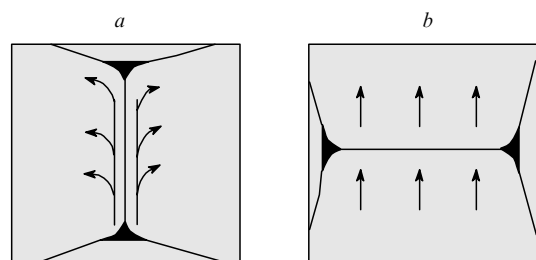


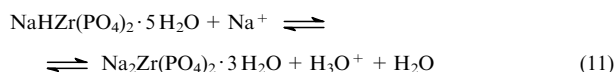
Figure 8. Schemes of mass transport along (*a*) and normal to (*b*) the interface.²⁵⁶

ring in hydrated oxides^{54, 55, 71, 101} and hydrates of heteropolyacids.^{74, 120, 272}

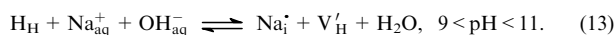
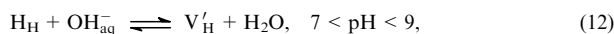
Similar reactions are also observed in the course of chemical transport in the case of conventional polymeric membrane materials.^{9, 273} Defect formation in them occurs mostly at the interface between the polymer matrix and solution filling the conducting channels.

If a transport process involves mass transfer across the interface between two crystals (Fig. 8b), an additional potential difference is produced, which hinders the process. This phenomenon is analogous to the *p-n*-junction in semiconductors. Jamnik and Maier²⁵⁶ showed that, all things being equal, diffusion through the system containing an interface oriented normal to the flow direction is substantially hindered. A large proportion of the transferred mass is concentrated at the interface between two crystals.

However, real processes involving chemical transport along the normal to the interface are much more diverse. The interphase interaction can also cause an acceleration of mass transfer in this direction. In particular, studies on the proton/alkali-metal-cation exchange reactions in titanium and zirconium hydrogen phosphates revealed a strong dependence of the reaction kinetics on pH value of the solution contacting the solid phase. The exchange rate is limited by two-dimensional counterdiffusion of the exchanging cations through the newly formed product layer.²⁷⁴ The second stage of exchange is controlled by proton diffusion. Changes in the pH value in the course of the exchange reaction



cause a decrease in the calculated cation diffusion coefficient (*D*) in the $\text{Na}_2\text{Zr(PO}_4)_2 \cdot 3\text{H}_2\text{O}$ layer by three orders of magnitude and more (Fig. 9).^{275, 276} For alkali solutions this is due to defect formation on the surface of crystals,²⁷⁵ which to a first approximation can be described by the following quasi-chemical reactions:



The former process is predominant in weak alkaline solutions. It is accompanied by the formation of a negatively charged surface layer with a high concentration of proton vacancies. The charge of the layer can be compensated upon sorption of cations on the surface of the solid phase. At higher pH ($9 < \text{pH} < 11$), the concentration of vacancies increases and this charge compensation mechanism is no longer efficient. Therefore, insertion of sodium ions into the interstices or abstraction of anions from the

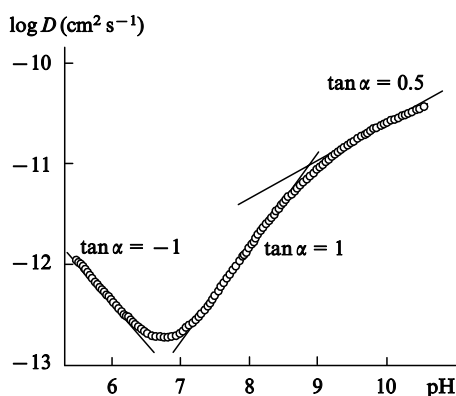


Figure 9. Calculated coefficient of cation diffusion in a $\text{Na}_2\text{Zr(PO}_4)_2 \cdot 3\text{H}_2\text{O}$ layer plotted vs. the pH value of the contacting solution.

surface occur simultaneously. The change in the main mechanism of defect formation is accompanied by changes in the slope of the plot of the logarithm of the diffusion coefficient vs. the pH value (see Fig. 9). Proton vacancies formed in the course of the process migrate into the interior of the crystal along with the oppositely charged sodium cations. In this case the concentration of proton defects in the bulk of the solid phase is related to their concentration on the surface.⁷⁶ In turn an increase in the concentration of charge carriers causes an increase in the diffusion coefficient.

At $\text{pH} < 7$, the slope of the plot of the logarithm of the diffusion coefficient vs. the pH value changes its sign (see Fig. 9). This means that proton interstices become the main type of defects in this range of pH values. They can be formed in the reaction



As we approach the equilibrium position in the second stage of the H^+/Na^+ exchange on zirconium hydrogen phosphate (it is attained in the region $4 < \text{pH} < 6$ ⁷⁶), the proportion of proton interstices increases and approaches the equilibrium value when two phases, $\text{NaHZr(PO}_4)_2 \cdot 5\text{H}_2\text{O}$ and $\text{Na}_2\text{Zr(PO}_4)_2 \cdot 3\text{H}_2\text{O}$, contact each other. Thus, defect formation occurs mainly at the interface between two solid phases while the proton interstices diffuse into solution through the $\text{Na}_2\text{Zr(PO}_4)_2 \cdot 3\text{H}_2\text{O}$ layer.^{76, 275}

Using a relation proposed⁷⁶ for nonlinear diffusion allowed a description of the defect distribution throughout the sample bulk (excluding the electrical double layer) in different stages of ion exchange (Fig. 10). Proton interstices are the main type of defects in acid media (Fig. 10a). The exchange process is determined by counterdiffusion of proton interstices and sodium ions. In the case of alkali solutions the diffusion layer can be divided into two regions (Fig. 10b). In the region adjacent to the unsubstituted $\text{NaHZr(PO}_4)_2 \cdot 5\text{H}_2\text{O}$ phase, counterdiffusion of proton interstices and sodium ions predominates, whereas counterdiffusion of proton vacancies dominates in the region near the alkali solution. In the latter case the exchange is determined by parallel diffusion of sodium ions and proton vacancies. At a point characterised by equal concentrations of proton vacancies and interstices, they annihilate and the main type of charge carriers changes.

A significant effect of anions present in solution on the kinetics of H^+/Na^+ ion exchange on zirconium hydrogen phosphate has

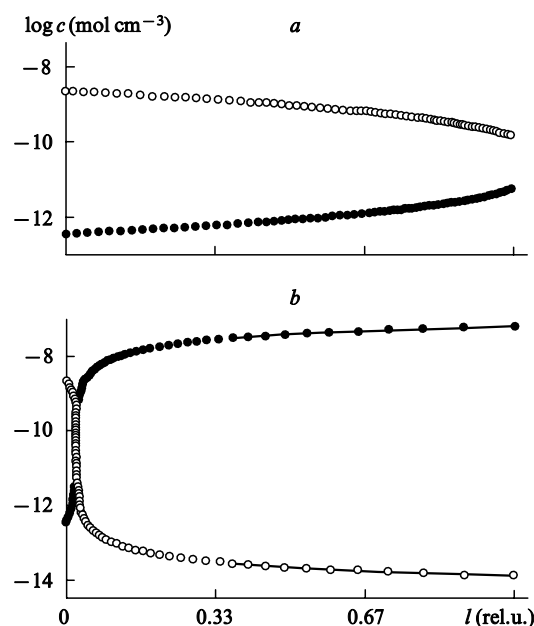


Figure 10. Change in the defect concentration (*c*) with the length of the diffusion layer of $\text{Na}_2\text{Zr(PO}_4)_2 \cdot 3\text{H}_2\text{O}$ (*l*) contacting a solution with pH 4 (a) and 11 (b):⁷⁶ interstitial sites (1) and vacancies (2).

been reported.^{277,278} The rate of exchange increased with an increase in the sorption ability of anions on the surface of zirconium phosphate in the series $\text{NO}_3^- \approx \text{ClO}_4^- < \text{SO}_4^{2-}$ and $\text{I}^- < \text{Br}^- < \text{Cl}^-$. The increase in the rate of exchange is due to the necessity of compensating the charge of proton vacancies on the surface of the double phosphate. A possible mechanism involves desorption of phosphate ions from the surface, which becomes easy because of sorption of anions bearing a smaller charge on the free surface sites.^{277,278}

These effects are much less pronounced in the case of the interaction between exchange products with different degrees of substitution. Such effects were detected in studies of the kinetics of ion exchange and ionic conductivity in the $\text{NaHZr}(\text{PO}_4)_2 \cdot n\text{H}_2\text{O} - \text{H}_2\text{Zr}(\text{PO}_4)_2 \cdot \text{H}_2\text{O}$ and $\text{Na}_2\text{Zr}(\text{PO}_4)_2 \cdot m\text{H}_2\text{O} - \text{NaHZr}(\text{PO}_4)_2 \cdot n\text{H}_2\text{O}$ systems and by analysing the ^{23}Na NMR spectra.^{84,87}

IV. Transport equations

1. The basic systems of equations

In deriving transport equations using the thermodynamics of nonequilibrium processes the membrane material is considered as a 'black box', since initially no information on its thermodynamic, structural and kinetic parameters is available. In the equilibrium state the electrochemical potential, $\tilde{\mu}_i$, of the i th component has a constant value at any point of the system. If the electrochemical potential gradients, $d\tilde{\mu}_i/dx$, differ from zero (for simplicity we consider a one-dimensional transfer along the normal to the membrane surface), fluxes (J_i) of the i th particles appear in the system. At small deviations from the equilibrium, the fluxes and forces inducing them are linearly related.^{279–281} With allowance for the fact that the force $d\tilde{\mu}_j/dx$ exerted on particles of the j component can cause transfer of the particles of the i component (e.g., electromigration of ions causes transfer of water, or electroosmosis), we get the Onsager equation

$$J_i = - \sum_j L_{ij} \frac{d\tilde{\mu}_j}{dx}. \quad (15)$$

Determination of the phenomenological transfer coefficients, L_{ij} , is complicated by the fact that the number of these coefficients is rather large even for simple systems. For instance, for a membrane contacting a binary electrolyte solution one has to know six transfer coefficients. In addition, the local coefficients L_{ij} are functions of the local concentration of the so-called 'virtual solution'. The virtual solution was first introduced by Kedem and Katchalsky²⁸² and was called the 'Corresponding Solution'. This is a hypothetical solution, which is in equilibrium with a certain membrane layer.

The generalised electrochemical potential, $\tilde{\mu}_i$, in Eqn (15) can be represented as a function of the concentration (or activity a_i), electric potential ϕ and pressure p of the virtual solution

$$\tilde{\mu}_i = \mu_i^0 + RT \ln a_i + z_i F \phi + \bar{V}_i p, \quad (16)$$

where z_i is the charge, F is the Faraday number and $\bar{V}_i$ is the partial molar volume of the ions i .

To determine the local L_{ij} values characterising a thin membrane layer of thickness dx from the experimental integral values of the transfer coefficients characterising the whole membrane, the membrane must be macrohomogeneous,^{283,284} i.e., the L_{ij} values must be independent of the layer coordinate dx provided that each layer dx is in equilibrium with the same solution. Figure 11 presents the dependences of the L_{ij} coefficients on the concentration of the equilibrium NaCl solution obtained for a perfluorocarbon membrane Nafion-120 containing sulfonic acid groups. These coefficients were calculated²⁸⁵ using the data reported by Narebska *et al.*^{286,287} who carried out six experiments on measurements of the specific conductivity, apparent transport

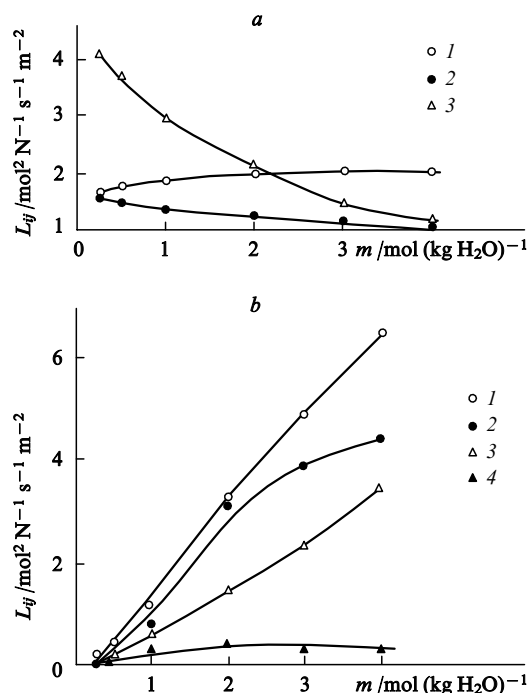


Figure 11. Phenomenological coefficients L_{ij} for a Nafion-120 membrane plotted vs. concentration of the equilibrium NaCl solution;²⁸⁵ (a): $10^{10} L_{++}$ (1), $10^9 L_{+w}$ (2), $10^8 L_{ww}$ (3); (b): $10^{11} L_{--}$ (1), $10^{10} L_{-w}$ (2), $10^{11} L_{+-}$ (3), $10^{11} l_1$ (4) ($l_1 = L_{+-} - m M_w L_{-w}$, where m is the molality of the equilibrium solution, M_w is the molecular mass of water); the subscripts '+' and '-' refer to the cation and anion, respectively, and the subscript 'w' refers to water.

numbers, salt diffusion, osmotic and electroosmotic fluid flows, as well as the fluid flow due to the hydrostatic pressure drop.

The choice of fluxes (J_i) and corresponding thermodynamic forces (F_i) in the transfer equations of nonequilibrium thermodynamics is not arbitrary: if J_i and F_i are chosen correctly, the sum of their products must be equal to the dissipative function (product of the absolute temperature and the rate of entropy production per unit volume of the membrane^{279–282})

$$T \frac{ds}{dt} = \sum_i J_i F_i, \quad (17)$$

where $s = S/Ad$, S is the entropy of the adiabatic system comprised of the membrane and two adjacent solutions, A is the surface area and d is the membrane thickness. In our case the thermodynamic force has the form

$$F_i = - \frac{d\tilde{\mu}_i}{dx}.$$

It is of importance that we can choose the forces and fluxes, since this allows an appropriate description of various aspects of membrane transport phenomena. For instance, the Onsager equation, Eqn (15), is convenient for theoretical analysis since the equilibrium condition corresponds to the absence of external forces ($d\tilde{\mu}_i/dx = 0$); the well-known Nernst–Planck equation (see below) also follows from Eqn (15); finally, the contribution of coupled effects can be estimated by comparing the L_{ij} values,²⁸⁶ since these coefficients are of the same dimension. At the same time the L_{ij} coefficients are related in a complex manner to the measurands (membrane conductivity, diffusion permeability, etc.). The use of equations similar to Eqn (15) presents some difficulties in description of transfer phenomena with a pronounced convective component.²⁸⁸

A large number of equations were proposed^{288–292} in addition to the Onsager equation to allow for the coupled effects. For instance, the Stefan–Maxwell equations can be treated as an empirical generalisation of the transfer equations for ideal gases.²⁹³ One can also derive these equations from the statistical mechanics equations in the framework of the microscopic approach. The possibility of using particle velocities instead of the flux densities and applying the pressure gradient in explicit form as the driving force also makes them convenient for the description of convective transfer.^{294–296}

The so-called ‘frictional’ model of mass transport is based on an analogy between the motion of particles (ions, molecules) in a continuous medium and the motion of bodies in a viscous fluid. Spiegler²⁸⁹ was the first who applied this theory to membranes; more recently, it was developed by other researchers.^{297, 298} Other applications (transfer in ionic solutions and melts) were generalised in a monograph.²⁹⁰ Studies by Meares *et al.*²⁹⁷ and by Narebska *et al.*^{286, 287} showed that the friction coefficients, f_{ij} , are also concentration dependent, though to a somewhat lesser extent compared to the L_{ij} coefficients.

2. The Kedem–Katchalsky system of equations

Let us analyse the Kedem–Katchalsky system of equations, which is of prime interest for a practical description of transfer through membranes.^{282, 283, 299} The Kedem–Katchalsky equations are written in the form²⁸⁵

$$J_v = -L_p \left(\frac{dp}{dx} - \sigma_s RT c_s v \frac{d \ln a_{\pm}}{dx} \right) + \beta I, \quad (18)$$

$$J_i = -c_i L_p (1 - \sigma_s) \frac{dp}{dx} - \omega \frac{d\pi}{dx} + \frac{It_i}{z_i F} = \quad (19)$$

$$= -c_i L_p (1 - \sigma_s) \frac{dp}{dx} - P \frac{dc_i}{dx} + \frac{It_i}{z_i F},$$

$$\frac{d\varphi}{dx} = -\frac{I}{\kappa} - \frac{RT}{F} \left(\frac{t_+}{z_+} \frac{d \ln a_+}{dx} + \frac{t_-}{z_-} \frac{d \ln a_-}{dx} - \right. \quad (20)$$

$$\left. -\beta c_s v_i F \frac{d \ln a_{\pm}}{dx} \right) - \beta \frac{dp}{dx}.$$

Here J_v is the volume flux density of the solvent; J_i is the flux density of the ions i ; I is the current density; c_i and c_s are the molar concentrations of the ions i and the salt in the virtual solution within the membrane, respectively; $a_{\pm}$ is the mean ionic activity, π and p are the osmotic and hydrostatic pressures in the virtual solution, respectively; v_i is the stoichiometric number of the ion i and φ is the electric potential.

The conducting properties of a membrane are characterised by six local transport coefficients. These are the specific conductivity, κ ; diffusion permeability, P or ω ; hydraulic permeability, L_p ; the transport number of the counterions, t_+ ; electroosmotic permeability, β ; and the Staverman reflection factor, σ_s , which varies from zero to unity for non-rejecting to perfect membranes, respectively.

The convenience of the practical application of Eqns (18)–(20) can be demonstrated taking Eqn (20) as an example. Here, we can distinguish with certainty between three components of the electric potential gradient, *viz.*, the ohmic (first term), diffusion (second and third terms) and the streaming potentials due to the osmotic and hydrostatic pressure drop driven transfer (fourth and fifth terms, respectively).

It should be noted that the above-mentioned systems of transfer equations including the Onsager and Kedem–Katchalsky equations are mathematically equivalent,¹ since passage from one system to another can be done by simply substituting variables.

3. The Nernst–Planck equation

The Nernst–Planck equation is most widely used in the theory of transport in membranes. This equation has a somewhat simpler form compared to the equations used in theory of nonequilibrium processes but takes into account only two main components of transfer, namely, diffusion and electromigration. It can be derived from the Onsager equation (15) assuming that the cross-coefficients are equal to zero.^{289, 290} It is of interest to consider diffusion on the microscopic level by applying the random walk theory to particular ions or vacancies.³⁰⁰ This permits an alternative examination of the Nernst–Planck equation.

Suppose that hopping occurs by jumps of equal length λ and that the i th ion can execute stochastic jumps in any direction irrespective of the preceding jumps, the hopping probability for any direction being constant. Then, the particle flux density along some direction is described by the Fick equation with the self-diffusion coefficient D

$$D_i = -\frac{\omega \lambda^2}{6}, \quad (21)$$

where ω is the hopping frequency, which depends on the escape frequency of the ion from the potential well (v) and on the number, n , of the nearest potential wells accessible to the ion through a single jump

$$\omega = vn; \quad (22)$$

n is the number of the nearest sites accessible to a given ion in the crystal structure or the number of fixed functional groups in an organic ion exchanger. For the vacancy mechanism of transfer n equals the number of ions in the nearest environment of a vacancy.

In the case of stochastic self-diffusion in a constant external electric field, E , directed along a particular axis x ,

$$E = -\frac{d\varphi}{dx},$$

the resultant flux of the ions i through a unit of area can be defined in the same manner as in Eyring’s theory of absolute reaction rates

$$J = \frac{\lambda}{2\sqrt{3}} nv \left[c_1 \exp\left(-\frac{zF\Delta\varphi}{2RT}\right) - c_2 \exp\left(\frac{zF\Delta\varphi}{2RT}\right) \right], \quad (23)$$

where c_1 and c_2 are the ion concentrations on the left and on the right with respect to the barrier under study. If the electric field is not too strong ($|\Delta\varphi| \ll RT/F \approx 25$ mV at room temperature), by expanding the exponents in Eqn (23) in a series and restricting ourselves to the first two terms of the expansion, we get the Nernst–Planck equation

$$J = -D \left(\frac{dc}{dx} + zc \frac{F}{RT} \frac{d\varphi}{dx} \right). \quad (24)$$

In the absence of the concentration gradient ($dc/dx = 0$) Eqn (24) takes the form

$$J = -Dzc \frac{F}{RT} \frac{d\varphi}{dx}. \quad (25)$$

Using the ion mobility u , the parameter J can be represented in the form

$$J = -cu \frac{d\varphi}{dx}. \quad (26)$$

From Eqns (25) and (26) one can get the Nernst–Einstein relationship

$$u = D \frac{zF}{RT}. \quad (27)$$

The Nernst–Planck equation is of great importance for transport theory; however, it is of limited utility. The most important conclusions reported by Buck³⁰⁰ and other researchers^{13, 51, 301–311} who examined limitations of this equation are as follows.

1. The microscopic approach to the derivation of the Nernst–Planck equation implies averaging over a rather large number of jumps, *i.e.*, from the molecular standpoint a membrane should be a homogeneous medium. Application of the Nernst–Planck equation to thin biomembranes, membranes with narrow (on the molecular scale) conducting channels and mosaic membranes seems to be hardly probable. The energy profile of the ion moving across a biomembrane can exhibit only 3–4 barriers;^{301, 302} therefore, in this case the absolute reaction rate method is more appropriate for description of ion transport.^{300, 303}

2. The Nernst–Planck equation should also not be applied at times shorter than the time necessary for averaging fluctuations of the external force exerted on an ion.³⁰⁰ One of the fastest processes suitable for description by the Nernst–Planck equation is relaxation of the space charge in the electrical double layer at the interface between two electrolyte solutions or at the electrolyte solution/electrode interface.³⁰⁶ The relaxation time

$$\tau = \frac{\lambda^2}{D}$$

(λ is the Debye length) is of the order of 10^{-8} – 10^{-9} s for solutions with an electrolyte concentration of 10^{-2} – 10^{-3} mol litre⁻¹.

3. As mentioned above, transport processes can be controlled by ion diffusion across the interface,^{13, 51, 300, 304, 305} which is associated with a particular chemical reaction, rearrangement of the hydration shell, overcoming of the Coulomb barrier by multiply charged counterions, *etc.* In the last case the potential barrier can be much higher than in the bulk of the corresponding phase, while the potential jump $|\Delta\phi|$ at the interface (overvoltage at the interface) can be comparable with the overall potential jump in the membrane system. In this case the condition

$$|\Delta\phi| \ll \frac{RT}{F},$$

necessary for the approximated expression of the exponents in Eqn (23) is broken and, hence, Eqn (24) is no longer valid.

4. Equation (24) was derived assuming a stochastic motion of ions and that each succeeding jump is independent of the preceding one. However, this assumption is often not true. Particle diffusion in crystals,³⁰⁷ ion exchangers^{51, 301–303, 311} and solutions⁵¹ involves correlated successive jumps of individual species. In the case of low-concentration vacancy diffusion it is more probable for an ion to return to the initial site than to jump in another direction. Due to such a correlation the distance from the initial site travelled by the ion after n jumps will be shorter than the ion displacement caused by stochastic diffusion. In the Nernst–Planck equation the diffusion coefficient depends on the microscopic-scale transfer mechanism (self-diffusion or conduction). It seems plausible that this can be interpreted as a dependence of D on the nature of the driving force of transfer. This dependence, which is sometimes interpreted as violation of the Nernst–Einstein relationship, is taken into account using the apparent correlation coefficient

$$f = \frac{D_{id}}{D_{ie}}, \quad (28)$$

where D_{id} and D_{ie} are the experimental diffusion coefficients determined in the self-diffusion and conduction studies, respectively. The f value primarily depends on structural features and varies for ionic crystals from 0.5 to nearly unity.³⁰⁸ For the relay transfer mechanism the f value can be much less than 0.5. The f

values for a number of ion exchangers have been documented.^{1, 51, 308}

5. Stochastic diffusion and conduction studies revealed some differences between the interaction of an ion with the ionic atmosphere.^{309, 310} Diffusion is accompanied only by the relaxation drag effect, which is due to the finite time of annihilation and creation of the ionic atmosphere (relaxation time). In the case of conduction in an external electric field an ion moves through the ionic atmosphere moving in the opposite direction rather than in an immobile medium. Therefore, the ion experiences the drag effect due to both relaxation and electrophoresis.^{309, 310}

6. A significant drawback of the Nernst–Planck equation is that it does not include the parameters of water transfer and the streaming potential, which are important characteristics of biomembrane processes and electrodialysis of concentrated solutions.³¹¹ In addition, some coupled effects due to the ‘frictional’ interaction between the mobile and fixed ions and molecules are also ignored. In particular, this drawback sometimes precludes the use of the Nernst–Planck equation for characterisation of ion-exchange membranes.²⁸⁵

Notwithstanding the above-mentioned limitations, the Nernst–Planck equation has found a wide field of applications. It is used for the description of transfer in liquids, solids and gels, in the bulk of the corresponding phases and at the phase boundaries. Given the activity coefficients and cross coefficients, the field of applications of this equation is extended even more. If a phase boundary can be considered as a quasi-equilibrium one, the Nernst–Planck equation is transformed into the Boltzmann and Donnan equations. As applied to electric transfer and diffusion, it is transformed into the Ohm and Fick laws, respectively. The Nernst–Planck equation describes both steady-state and non-steady-state processes including such fast phenomena as the space charge relaxation. This equation can be readily combined with other equations, which describe conjugated chemical reactions, ion and molecular association and dissociation, adsorption and the space charge formation. Combining the Nernst–Planck equation and the equations describing the hydrodynamics of a solution adjacent to the membrane permits construction of mathematical models for assessment of the role of concentration polarisation in the membrane transfer processes.

4. Generalisation of the Nernst–Planck equation

Often it is convenient to use the ion transfer equation, which is analogous to the Nernst–Planck equation but includes some coupled effects. Such an equation is obtained by substituting Eqn (20) into Eqn (19) at $dp/dx = 0$ assuming a linear relation between individual ion activity coefficients and the average ion activity coefficient²⁸⁵

$$J_i = -P_i \frac{dc_i}{dx} - \frac{z_i}{|z_i|} u_i c_i \frac{d\phi}{dx}, \quad (29)$$

where P_i is the individual local membrane permeability to diffusion of the ion i and u_i is the mobility of the ion i in the membrane. Both coefficients are explicit functions of the experimentally measurable parameters (transport numbers, conductivity, diffusion permeability and electroosmotic permeability of the membrane). This significantly simplifies the determination of the coefficients in Eqn (29). The advantage of this equation is that it implicitly (through a membrane’s electroosmotic permeability) includes the effect of the streaming potential (and, hence, water transport) on the ion transfer. Finally, when using the virtual solution, there is no need to calculate the potential jumps at the membrane/solution interface and sometimes no need to determine the actual ion concentrations in the membrane.

Comparison of the Onsager and Kedem–Katchalsky equations allows one to relate the corresponding transfer coefficients.²⁸⁵ It is possible to obtain six relations for six pairs of coefficients. Some of the relationships are known. For instance, one of them expresses the specific conductivity of a membrane (the

Kedem–Katchalsky coefficient) through the L_{ij} coefficients in the Onsager equation.^{312–314} The following approximate equation between the Kedem–Katchalsky transport coefficients was obtained²⁸⁵ neglecting the cross-coefficients that describe the interaction of coions with counterions (L_{+-}) and water (mM_wL_{-w}) in one relationship

$$P = \frac{2RT\kappa t_{+ap}\gamma}{F^2c}, \quad (30)$$

where t_{+ap} is the apparent transport number of the counterions and γ is the activity factor.²⁸⁵

Equation (30) is a generalisation of the Nernst–Einstein relationship to osmotic and electroosmotic transport of water across a membrane. To use this equation, one should know the values of all parameters. These values are hard to determine. Nevertheless, many authors^{36,285,312–316} used and tested this equation under different conditions, mainly assuming that $t_w = 0$ and $t_{+ap} = t_+$. A rigorous study²⁸⁵ of the Nafion-120, MF-4SK and MK-40 membranes revealed that the coefficient l_1

$$l_1 = L_{+-} - mM_wL_{-w}$$

has a positive value (see Fig. 11b). This means that the first term (L_{+-}) describing the interaction between differently charged ions is larger than the second term (mM_wL_{-w}), which describes the interaction between coions and water. Following Kedem and Perry,³¹³ these membranes can be considered as hydrophobic. If $l_1 = 0$, both types of interaction are mutually cancelled out and relationship (30) should be exactly fulfilled. The case $l_1 < 0$ has been studied.³¹³

Using relation (30), Eqn (29) can be transformed into a transfer equation, which is even more similar to the Nernst–Planck equation,²⁸⁵

$$J_i = L_i \left(b_i RT \frac{d \ln c_i}{dx} + z_i F \frac{d\phi}{dx} \right), \quad (31)$$

where the L_i and b_i coefficients are explicitly expressed through t_i and κ . Here, the b_i coefficients tend to unity at c_i tending to zero and depend on the transport numbers of the ions and water.²⁸⁵ The distinction between Eqn (31) and the Kedem–Katchalsky equation [Eqn (19)] is that the former ignores the interaction of coions with counterions and water. The advantage of Eqn (31) is its applicability to polyionic systems.

It should be noted that the electric potential gradient in Eqn (31) includes the streaming potential due to convective transfer driven by the hydrostatic and osmotic pressure gradients [see Eqn (20)]. Therefore, Eqn (31) implicitly takes into account the effect of osmotic volume transfer on the ion transport. In the so-called ‘extended’ Nernst–Planck equation these components are included in an explicit form in the convective term^{11,317–320}

$$J_i = -D_i \left(\frac{dc_i}{dx} + c_i \frac{d \ln \gamma_i}{dx} + z_i c_i \frac{F}{RT} \frac{d\phi}{dx} \right) + c_i \vartheta, \quad (32)$$

where γ_i is the ion activity coefficient and ϑ is the linear velocity for transfer of the centre of mass of the fluid, while the concentration and electric potential refer to the whole membrane. In the calculations, ϑ is assumed to be proportional to the electric potential and hydrostatic pressure gradients;¹¹ it can also be found experimentally when determining the volume flux through the membrane.³²⁰

Equation (30) and analogous relations,^{315,316} which generalise the Nernst–Einstein equation, are used for characterisation of ion-exchange membranes;^{285,316,321} it is more easily to calculate the transport number, t_i , from the readily measurable κ and P values than to determine it by directly measuring the ion fluxes.³²²

5. Particle diffusion kinetics of ion exchange

The kinetics of ion exchange in systems containing inorganic ion exchangers are most often studied assuming that the process is controlled by diffusion within the grain, since diffusion in solutions occurs much faster. The quantitative description of diffusion processes is complicated by the necessity of collecting a fraction of particles (crystals) of a prescribed size, which can vary over a wide range in the course of the exchange. The interdiffusion coefficients of the ions involved in the process can also change as the process is developed. This can be due to both a gradual change in the concentration of the ions of different mobility in the material under study and to the change in the characteristic size of channels and pores in the ion exchanger matrix.⁵⁵ Changes in the defect concentration in the bulk of the ion exchanger with consumption of the active component in solution can also appear to be important.⁹ Nevertheless, in most cases the kinetics of exchange are described ignoring these factors.

Among the pioneering studies concerned with generalisation of the equations of transfer to objects of various geometry with inclusion of different boundary conditions was that reported by Barrer.³²³ Most often, the transport phenomena occurring when an ion exchanger contacts external solution are described by the relation proposed by Boyd *et al.*³²⁴ for diffusion in a homogeneous grain. The necessary conditions are as follows: (i) exchange occurs through the formation of a continuous series of solid solutions, *i.e.*, it does not involve any phase transitions and (ii) the grain/solution interface is in local thermodynamic equilibrium. The equation for a spherical grain has the form

$$F = 1 - \frac{6}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{n^2} \exp\left(-\frac{D t \pi^2 n^2}{R^2}\right), \quad (33)$$

where F is the fractional attainment of equilibrium, D is the interdiffusion coefficient of the ions within the grain, t is the time and R is the radius of the ion exchanger particles. The series in this equation rapidly converges for large values of F . Mention may be made that this relationship can be derived from the Fick law,^{11,325} which is a particular case of Eqn (19).

Formula (33) was used for the determination of the cation diffusion coefficients in various ion exchangers.⁵⁵ A somewhat modified relation in the differential form was proposed,⁸⁶ which includes an additional term to take into account changes in the defect formation conditions upon exchange.

In many inorganic ion exchangers the exchange processes are accompanied by changes in the phase composition. In this case the initial phase coexists with the newly formed one. The process involves a gradual movement of the interface into the interior of the grain. After solving the problem of motion of a particle in the crystal field with a periodic potential in the presence of a chemical potential gradient a relation was proposed for the determination of the diffusion coefficients from the data on the kinetics of ion exchange. In the case of two-dimensional diffusion (cylindrical grain approximation), *e.g.*, ion exchange in layered phosphates of some polyvalent metals, the relation has the form³²⁶

$$J = \frac{2\pi c D h \Delta\mu}{RT} \ln \frac{r_0}{r}, \quad (34)$$

where c is the concentration of the mobile ions, h is the characteristic size of the ionite particle, $\Delta\mu$ is the chemical potential difference of the exchanging ions between the surface of the crystal and the interface between the initial and newly formed phases, r is the grain radius and r_0 is the radius of the domain of the initial phase retained within the grain.

If exchange occurs through a flow of an alkali solution to crystalline α -zirconium hydrogen phosphate, the calculated interdiffusion coefficient varies by three orders of magnitude.⁷⁶ The reason is a dramatic change in the alkali concentration, which causes changes in the defect formation conditions. A relation proposed^{76–84} to describe all processes occurring in the system

and the concentration distribution of various defects in the product layer is more sophisticated than Eqn (34).

It should be noted that systems with organic ion exchangers often exhibit a mixed-diffusion type of exchange. The limiting stage of such a process can change with the solution concentration, namely, transfer in dilute solutions is controlled by the diffusion through the outer diffusion layer, while transfer in concentrated solutions is controlled by intradiffusion.^{11, 327–329} Nevertheless, experimental studies on ion exchange, counterdiffusion across a membrane or diffusion of one electrolyte (dialysis) provide information necessary for the determination of the diffusion coefficients^{330, 331} and selectivity of ion-exchange membranes.³³² In the case of organic membranes characterised by rather high permeability with respect to water one should take into account the osmotic transfer of water and the corresponding streaming potential.^{328, 329, 333}

6. Continuum models

Formal description of transfer processes involving treatment of a membrane as a ‘black box’ prevents the static and kinetic properties of membranes from being related to their structural features. Knowledge of such a relation is necessary to gain a better insight into the selectivity mechanism of membrane transport, dependence of the transport properties on the concentration, electric current, *etc.* This information is also necessary for chemists to obtain membranes with prescribed properties.

A large number of models relating the structural and kinetic properties of membranes have been proposed. These models can be divided into two large groups. These are the heterogeneous models, which treat a membrane as a multiphase system and characterise each phase by specific structural and kinetic parameters, and the continuum models, which concern continuous changes in the membrane properties taking into account only one phase (the membrane material can be multiphase; however, transfer in other phases is usually ignored).

The continuum models can be in turn divided into three groups:

(1) models, which treat a membrane as a single phase (charged gel); the static and kinetic parameters of the membrane (fixed ion concentration, ion diffusion coefficients, *etc.*) can continuously change with the coordinate and exhibit no explicit relation to the structural parameters;^{334, 335}

(2) capillary models,³³⁶ which are also known as the space charge models^{253–255, 337–345} in which transfer is considered to be within capillary pores with charged walls;

(3) models based on percolation theory;^{346–348} in this case the ion transfer is simulated by flow of a fluid through a system of voids connected by narrow channels.^{13, 346}

The capillary models provide the most detailed information on the transport parameters and are based on information on the membrane structure. They were first developed to describe the electrokinetic phenomena in microcapillaries with charged walls.^{254, 336} More recently,^{253–255, 337–345} they were improved and adapted for the description of the membrane transfer phenomena. These models permit the inclusion of rather subtle effects, *viz.*, changes in the dielectric constant with the distance from pore walls,³³⁷ adsorption,^{254, 341–343 *etc.*}^{255, 344, 345} and consideration of various pore geometries (planar, cylindrical and spherical).³⁴⁰

The equation of transport in a pore schematically shown in Fig. 12 is written as the Nernst–Planck equation with the convective term (32) projected on the longitudinal (x) and normal (z) coordinates.^{337, 339} The diffusion coefficient of the ions in the solution confined within the pore is usually assumed to be equal to the diffusion coefficient in free solution. The cross-sectional distribution of the local concentration, $\bar{c}_i$, of the ions i in the pore is described by the Poisson–Boltzmann equation.^{253, 339, 340} The surface density of the electric charge, q , on the pore walls is $110–440 \text{ mC m}^{-2}$,^{42, 252, 349} while the pore radius varies from 0.5 to 5 nm.³³⁹

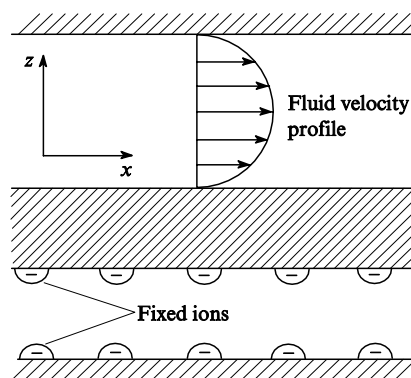


Figure 12. Schematic representation of the structure of a membrane containing parallel cylindrical pores with charged walls. The hatched area represents the insoluble polymer matrix.

The convective transfer rates, $\mathcal{Q}(r)$, were found by numerical solution to the Navier–Stokes equations.^{253, 255, 337–340, 344, 345} Determination of Onsager’s L_{ij} coefficients for the Nafion-120 membrane allowed^{338, 350} one ‘to bridge the gap’ between the two approaches, irreversible thermodynamics and model description. The parameters of the model (effective pore radius, fixed ion concentration per unit volume of the solution confined inside a pore and tortuosity factor) were chosen based on the results of the porosity, exchange capacity, membrane conductivity and membrane hydraulic permeability measurements.

The percolation theory^{13, 347, 348} is well adapted for the description of transfer in a system with a developed network of channels exhibiting both high and low ion transfer ability (clusters and cluster-connecting channels in perfluorinated membranes, respectively). This theory provides an explanation for the dependence of the membrane conductivity (κ) on the water content (w).^{351, 352} At low water content both clusters and channels are low hydrated and their mass-transfer resistance is so high that the former virtually do not contact one another. As the water content increases, a more and more increasing number of clusters becomes connected by channels, thus forming a network penetrating throughout the whole membrane. There is a threshold water content (percolation threshold, w_0) corresponding to the insulator–conductor transition. At $w < w_0$, the membrane conductivity is zero while at $w > w_0$, it increases exponentially.^{347, 348} A theoretical estimate of the exponent is 1.5 ± 0.2 for the three-dimensional system.³⁴⁸ The pre-exponential factor is determined by peculiarities of the ion–ion and ion–molecule interactions and by diffusion processes between two adjacent clusters.^{42, 351, 352} The percolation models for ion transfer and water transport in ion-exchange materials were developed by Timashev.¹³

7. Heterogeneous models

Analysis of the ion exchanger structure (see above) showed that the material contains more or less homogeneous regions, which are conventionally called phases.³⁵³ One phase comprises the electrically neutral solution, which fills both macroscopic structural defects (macropores, cavities, cracks) and central parts of mesopores (clusters in perfluorinated membranes also belong to this type of defect). The second phase, which is called ‘gel’,^{11, 354–356} is formed by an ensemble of micropores and the outer parts of mesopores containing fixed and mobile ions, water and polymer chains. Sometimes, the third (inert) phase, which is comprised of entangled hydrophobic polymer chains (the case of perfluorinated membranes) or inert binder used to improve the mechanical strength (*e.g.*, heterogeneous membranes MK-40 and MA-40) is taken into consideration.

The aim of simulation of transfer in a multiphase membrane is to determine particular physicochemical properties of each phase

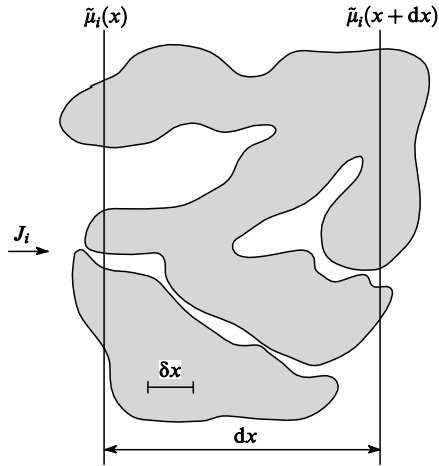


Figure 13. Schematic representation of a two-phase microheterogeneous membrane.

The shaded area is the gel phase; shown are two length scales, a microscopic (δx) and a macroscopic one (dx).

and then to obtain characteristics of the whole membrane as functions of the properties of the individual phases. Let us consider a macroscopic volume, *e.g.*, a layer containing all phases of the membrane, which are in equilibrium with one another. The thickness of this layer, dx , is small as compared to the membrane thickness (Fig. 13). In the framework of the thermodynamics of nonequilibrium processes the equations of transfer for each phase k and for the whole layer of thickness dx can be written in the form

$$J_i^{(k)} = -L_i^{(k)} \frac{\delta \tilde{\mu}_i}{\delta x}, \quad (35)$$

$$J_i = -L_i^* \frac{d\tilde{\mu}_i}{dx},$$

where $\delta \tilde{\mu}_i$ and $d\tilde{\mu}_i$ are the changes in the electrochemical potential between points separated by the distance δx within the phase k and by the layer dx , respectively. The problem can be formulated in the following way: to determine the effective coefficient L_i^* for the membrane layer as a function of the $L_i^{(k)}$ coefficients, which characterise individual phases, and the geometric parameters, which describe the shape and mutual position of the phases.

Search for the functions relating the effective conductivity to the corresponding characteristics of individual phases for various transfer phenomena (conduction, diffusion, heat transfer, *etc.*) has been ongoing for many years. As long ago as 1873 Maxwell³⁵⁷ reported a solution to the problem of conduction in a conducting medium containing widely separated spheres whose specific conductivity differs from that of the medium. Studies by Rayleigh,³⁵⁸ Landau and Lifshitz,³⁵⁹ Bier, Lichnecker and Roter (see references cited in Ref. 360) and other researchers^{361–366} who contributed largely to the solution to this problem should be pointed out. The results obtained were generalised in a hypothesis called the ‘generalised conduction principle’,³⁶¹ according to which the function relating L_i^* to $L_i^{(k)}$ is independent of the nature of both the force exerted on the heterogeneous system and the substance transferred.

The structure of ion-exchange membranes was described using various approaches,^{11, 354–356, 363} which were analysed in some reviews.^{9, 362, 364} In the early stage, heterogeneous structural–kinetic models for the description of the shape and mutual arrangement of phases included a rather large number of parameters, which made their use difficult. Gnusin and Grebenyuk³⁵⁴ proposed the so-called three-channel model for charge transfer in inhomogeneous membranes. They distinguished three types of conducting channels: gel segments, gel-connecting channels and the mixed channel. The model permitted a correct description of

the concentration dependence of a membrane’s specific conductivity; however, it required knowledge of three independent geometric parameters. More recently, Gnusin *et al.*³⁶⁵ developed a two-parameter procedure for description of the geometry of the system. Yet another stride taken towards the development of heterogeneous models was the passage from a particular type of force (electric or diffusion) exerted on the system to the generalised force in the form of the electrochemical potential gradient.³⁶⁶ A so-called ‘microheterogeneous model’, which included both improvements mentioned above, was developed.^{36, 366–369}

The basic principles of the ‘heterogeneous interstitial solution’ model³⁷⁰ are similar to those of the microheterogeneous model described below. For simplicity, let the ion exchanger be a two-phase system comprised of the gel phase and the gel-connecting channels filled with the equilibrium solution, the volume fractions of the phases being f_1 and f_2 , respectively. By writing the equation of transfer for each phase and using the continuity condition for the electrochemical potential at the interface one can obtain the equation in the framework of the microheterogeneous model^{36, 366}

$$L_i = [f_1 \bar{L}_i^\alpha + f_2 (L_i^*)]^{1/\alpha}, \quad (36)$$

where $\bar{L}_i$ and L_i^* correspond to the gel phase and to the solution phase, respectively, and α is the structural parameter. The relation (36) is a generalisation of particular expressions obtained for two limiting cases, *viz.*, parallel ($\alpha = 1$) and series ($\alpha = -1$) arrangement of the phases with respect to the transfer direction; in intermediate situations, the α value lies in the range $-1 < \alpha < 1$.³⁶⁶ The L_i and $\bar{L}_i$ parameters can be expressed through ion diffusion coefficients in the corresponding phases, D_i and $\bar{D}_i$

$$L_i = \frac{D_i c_i}{RT},$$

$$\bar{L}_i = \frac{\bar{D}_i \bar{c}_i}{RT},$$

while the ion concentrations in the gel phase, $\bar{c}_i$, can be found from the corresponding concentrations in the solution phase, c_i , using the Donnan equation.

The diffusion coefficients in the interstitial solution are assumed to be equal to those in free solution. The model permits calculations of the ion concentrations in the gel phase, $\bar{c}_i$, and the effective membrane conductivities, L_i^* , as functions of the electrolyte concentration in the interstitial solution.

The advantage of the model is the possibility of description of the static and transport properties of a membrane using one set of structural and kinetic parameters (see above). In this connection it is of interest to calculate the d.c. and a.c. specific conductivities of the membrane (κ_d and κ_a , respectively). The relation between κ_d and κ_a was studied by Gnusin *et al.*^{366, 367} who derived and experimentally tested the following approximate formula

$$\kappa_d = \bar{\kappa}^{f_1} (\kappa^* t_i)^{f_2} = \kappa_a t_i^{f_2},$$

where $\bar{\kappa}$ and κ^* are the specific conductivities of the gel phase and the interstitial solution, respectively, and t_i is the transport number of the ions i in solution. The κ_a values can be calculated using an approximate relationship, which is valid at $\alpha \rightarrow 0$,³⁶⁶

$$\kappa_a = \bar{\kappa}^{f_1} (\kappa^*)^{f_2}, \quad (37)$$

according to which the $\log \kappa_a - \log \kappa^*$ curve must be linear with a slope of f_2 . Indeed, as can be seen in Fig. 14, Eqn (37) permits the correct description of the experimental data. The f_2 values calculated using Eqn (37) and those determined in the electrolyte sorption, contact reference porosimetry and differential scanning calorimetry studies have been compared.^{34–36} The similar values of this parameter determined by independent methods indicate

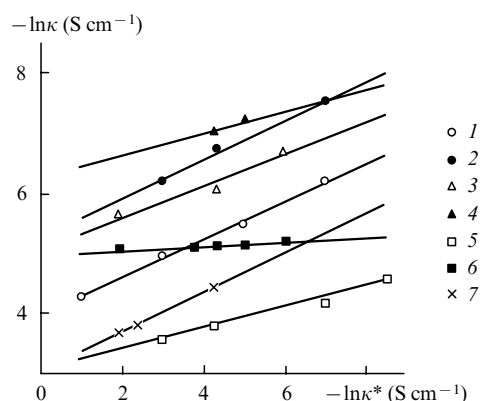


Figure 14. Plot of the a.c. specific conductivity of ion-exchange membranes vs. the specific conductivity of solution.³⁶ Membrane in solution: C-60/65 in HCl (1); Amberplex C-1 in NaCl (2) and KCl (3); Amberplex A-1 in NaCl (4); AMF C-103 in NaCl (5); MF-4SK in NaCl (6) and Nepton CR-61 in KCl (7).

that the microheterogeneous model correctly describes the structure of ion-exchange membranes and that the electrically neutral solution characterised by the volume fraction f_2 does exist within the membrane. Equation (37) and the microheterogeneous model has been used by many researchers for estimation of the degree of heterogeneity of organic ion-exchange membranes.^{371–373}

Summing up, mention should be made that capillary and microheterogeneous models considered above use all transport equations and all relations between the transport coefficients, which were obtained in the framework of the thermodynamics of nonequilibrium processes. Additional parameters, which depend on the membrane structure, allow one to relate the transfer coefficients to the structural – kinetic parameters of the membrane and to the concentration of the equilibrium solution.

V. Limiting stages of transfer and diffusion layers

1. Change in the electrochemical potential and limiting stages of transfer

As mentioned above, directed diffusion in membrane materials is driven by the electrochemical potential gradient produced in the system for various reasons.

A peculiar feature of heterogeneous processes is a nonuniform change in the electrochemical potential gradient along the normal to the interfaces. The systems comprised of membrane or ion-exchange materials usually have a multilayer structure. Often, membranes themselves contain some layers; e.g., bipolar organic membranes³⁷⁴ and membranes with a modified surface layer^{375,376} comprise two layers. In any case the membrane is surrounded by two diffusion layers of the solution (see below). Under intense current regimes in solution a macroscopic space charge appears near the membrane surface.^{377,378} This charge can also be considered as a layer which resists mass transfer. The electrochemical potential changes differently on going through different layers of the system; the layers characterised by maximum potential jump exhibit the highest mass-transfer resistance.

Let us consider the interaction between the compounds A and B, which involves the formation of a new phase AB due to the diffusion of A across the product layer and the movement of the AB/B interface. Different types of changes in the chemical potential of the component A, $\Delta\mu_A$, in this system are shown in Fig. 15. If a reaction is controlled by the diffusion across the product layer, it is this layer that contributes predominantly to the change, $\Delta\mu_A$. If the coefficient of diffusion through this layer can be considered constant, the chemical potential of a quasi-stationary process decreases uniformly, since the ion fluxes through any cross-section must be equal (Fig. 15a). However, more often

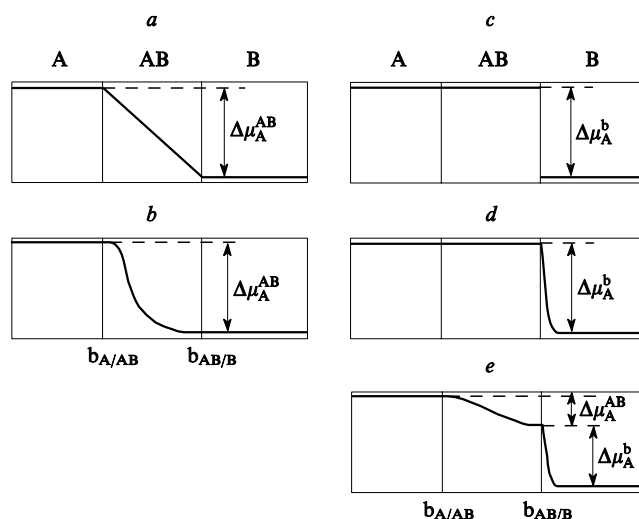


Figure 15. Change in the chemical potential along the normal to the interface for solid-phase reactions.⁹

The reaction is controlled by: diffusion, $D = \text{const}$ (a); diffusion, $D = \text{var}$ (b); mass transfer through the interface (c); relaxation processes in near-surface layer (d); change in the chemical potential due to diffusion and relaxation processes (e).

(taking into account the phenomena considered above) the interaction between the product and the initial components causes an increase in the defect concentrations at the A/AB and AB/B interfaces. This violates a uniform decrease in the chemical potential. If differently charged defects (e.g., cation interstices and vacancies, as in the ion-exchange process described above) are generated at the oppositely lying interfaces, the chemical potential changes to the greatest extent at a point corresponding to the minimum value of the overall diffusion coefficient with respect to both types of defects (Fig. 15b).⁷⁶

Even higher chemical potential gradients can be achieved for the reactions controlled by interfacial processes (Fig. 15c,d). The rates of such processes are determined by the surface area of the interphase boundary and by the properties of the phases. It is commonly accepted that the surface processes controlling the rates of chemical reactions can proceed by two main mechanisms, that is, activated diffusion across the interface and relaxation resulting in a structural rearrangement. The chemical potential decreases primarily at the moving interface in the former case (see Fig. 15c) and in a narrow near-interface region within a certain initial component in the latter case (see Fig. 15d). Real systems usually exhibit a combination of the case shown in Fig. 15c or Fig. 15d with a decrease in the chemical potential within the product layer (Fig. 15e). It was concluded³⁷⁹ that high activation energies for ion transfer across the interface are hardly probable, since the interface has an increased energy and the diffusion processes in the near-interface region are accelerated. Therefore, in the text below emphasis is placed on the relaxation processes in the region adjacent to the reaction product.

An increase in the chemical potential difference for the ions A at the AB/B interface causes acceleration of their transport across the interface and the formation of a supersaturated solution of A in the near-interface region of the phase B. Passage of the solution to the AB region requires its ordering and a change in the geometry of the environment. In particular, the formation of a large number of linear dislocations and point defects at the interface in the case of interaction between the crystalline phases AB and B and a solid solution is due to different lattice parameters of these phases. For the reasons described above transformation of the A–B solid solution into a chemical compound is accompanied by transfer of the ions A and B within the solution. Such a process inevitably requires the overcoming of some activation

barriers and a time delay (induction period). According to Schmalzried and Janek,³⁷⁹ the average time taken to transfer the silver ions across the α -AgI/ β -Ag₂S interface is five orders of magnitude shorter than the corresponding times of the individual phases. The structural rearrangement region can be as thick as ~ 10 nm,³⁷⁹ which exceeds the thickness of the Debye layer and corresponds to several tens of crystallographic planes.

The flux of the ions A across the AB/B interface (J_A) is given by the Nernst–Planck equation. The J_A value can be determined from electrochemical experiments (e.g., 2.3×10^{-5} mol cm² s⁻¹ for the α -AgI/ β -Ag₂S interface at 260 °C³⁸⁰). Mass-transfer resistance at the interface can be due to some other processes, namely, a chemical reaction (e.g., complexation), rearrangement within the hydration shell, overcoming of the Coulomb barrier by multiply charged counterions, etc.^{13, 51}

As the reaction passes, the thickness of the product layer (L_{AB}) increases, which causes an increase in the diffusion resistance of the AB layer and in the total change in the chemical potential within this layer ($\Delta\mu_A^{AB}$). The overall change in the chemical potential of the system equals the Gibbs free energy of the reaction (ΔG_{AB}); therefore, a change in ΔG_{AB} is accompanied by a change in the potential difference at the AB/A interface (see Fig. 15 e)

$$\Delta\mu_A^b = \Delta G_{AB} - \Delta\mu_A^{AB}.$$

Since we deal with a quasi-stationary process, the fluxes of A through the interface and through the AB layer must be equal to each other

$$J_A = -\frac{J_A^0 \Delta\mu_A^b}{RT} = -\frac{D_A^{AB} c_A^{AB} \Delta\mu_A^{AB}}{RTL_{AB}}, \quad (38)$$

where D_A^{AB} and c_A^{AB} is the diffusion coefficient and concentration of A in the AB layer, respectively. From this one can readily obtain the condition for equality of $\Delta\mu_A^b$ and $\Delta\mu_A^{AB}$, which corresponds to the change in the limiting stage of the reaction from interfacial relaxation to diffusion in the AB layer. This situation occurs as the AB product layer reaches some characteristic thickness at which the dependence of the mass of the product on the duration of the reaction changes from linear to parabolic. The characteristic thickness of this layer for, e.g., the formation of spinels, is of the order of 1 μ m,³⁸⁰ while the time taken to change the type of the limiting stage is of the order of several minutes.³⁸¹

Ion transfer in a complex multilayer system is controlled by those layers for which the electrochemical potential jump is comparable to the overall change in the electrochemical potential in the system. If the potential jump for a particular layer is small compared to the overall change in the potential, the electrochemical potentials at the left and right boundaries of the layer can be considered approximately equal. Then to a first approximation the boundaries can be treated as being in quasi-equilibrium with each other. This assumption essentially simplifies the determination of the fluxes of the solution components through the membrane. Usually the surface layers of a membrane are assumed to be in local thermodynamic equilibrium with the surface layers of the solution, which allows one to relate the boundary concentrations in the membrane to the boundary concentrations in the solution by the Donnan relations.^{1, 11, 327} Timashev and co-workers^{13, 304, 305} examined nonequilibrium boundary conditions applicable to, e.g., membranes with modified surface layers.

2. Diffusion layers

In some cases the rate of transfer across a membrane is controlled by mass delivery to (or rejection from) the membrane surface from the bulk of the solution through the boundary layer adjacent to the membrane (this layer is called the diffusion layer).

The concept of the diffusion layer was proposed by Nernst³⁸² who studied the dissolution of solids and assumed that the rate of

the process is limited by the diffusion across the non-stirring boundary layer of the fluid of thickness δ

$$J = -\frac{D(c_0 - c_s)}{\delta}, \quad (39)$$

where D is the diffusion coefficient of the solute, c_0 is the concentration in the stirring solution and c_s is the concentration of the substance at the interface with the solid.

Levich³⁸³ reported a consistent interpretation of the concept of the diffusion layer in the framework of his theory of convective diffusion. According to this theory, the flux density vector of a substance in a fluid has a diffusive and convective components

$$\vec{J} = -D\text{grad}c + c\vec{v}, \quad (40)$$

where c is the concentration of the substance and $\vec{v}$ is the velocity of the centre of mass.

Convective transfer within the diffusion layer is possible but tends to zero as the solid surface is approached. Nernst's conception of the boundary layer, in which mass transfer occurs by diffusion only, can be considered as a convenient idealisation. The thickness of the diffusion layer is determined by the coordinate of the intersection point of the tangents to the concentration profiles at the solid surface and in the bulk of the stirring solution.

The following expression was derived for calculating the thickness of the diffusion layer in the case of a laminar flow of a fluid in a channel formed by two plane-parallel plates

$$\delta = 1.02 \left(\frac{yDh}{\bar{v}} \right)^{1/3}, \quad (41)$$

where y is the longitudinal coordinate measured from the inlet of the channel, h is the distance between the plates and $\bar{v}$ is the average fluid flow velocity. Numerical test calculations carried out in the framework of the convective-diffusion model of electro-dialysis^{384, 385} showed³⁸⁵ that this formula is valid for relatively short channels ($y \leq 0.02\bar{v}h^2/D$). In this case the thicknesses of the diffusion layers adjacent to membranes are small compared to the intermembrane distance h (Fig. 16). On further increase in the channel length the horizontal plateau in the concentration profile becomes diffuse, the diffusion region fills the entire channel, and the concept of the diffusion boundary layer loses its meaning. According to numerical calculations,^{385, 386} the thickness of the diffusion layer formally determined from the intersection point of the tangents is nearly one third of the intermembrane distance.

Experimental studies on the concentration distributions in the desalination compartments of electrodialysis cells have been reported.^{387–389} When the solution flow hits barriers present in

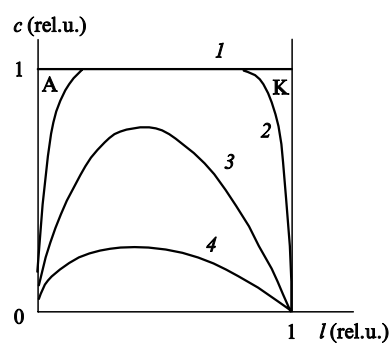


Figure 16. NaCl-Concentration profile in the desalination channel [combination of an anion-exchange (A) and a cation-exchange (K) membrane] of an electrodialysis apparatus at different values of dimensionless longitudinal coordinate $Y = yD/(\bar{v}h^2)$. Calculated using the convective-diffusion model;³⁸⁴ Y : 0 (1), 0.001 (2), 0.05 (3) and 0.2 (4).

the channel (separator, ionite granules), the diffusion layer is partially interrupted; its local thickness varies periodically.^{386, 390}

In the case of ion exchange and electrolyte diffusion across a membrane the concentration profiles are formed in both the ion-exchange material and the adjacent diffusion layers. The shape of the profiles depends on the dimensionless relative diffusion permeability of the membrane, p (Fig. 17),^{1, 391}

$$p = \frac{Pc^I\delta}{Dd},$$

where P is the diffusion permeability of the membrane, D is the electrolyte diffusion coefficient in the solution and d is the membrane thickness. At small p , the concentration and, hence, the electrochemical potential change primarily within the membrane (particle diffusion kinetics), while at large p this occurs within the diffusion layers of the solution (film diffusion kinetics). For organic membranes, the P/D ratio is of the order of 10^{-1} – 10^{-2} , while the δ/d ratio varies from 0.1 to 1; hence one gets $p \approx 10^{-3}$ – 10^{-1} . For most inorganic membranes $p < 10^{-2}$ and the change in the concentration within the diffusion layers can be neglected. The role of the parameter p is analogous to the role of the Biot or Helfferich criteria^{11, 327} used in ion exchange theory; sometimes, the reciprocal of p , or the relative electrodiffusion resistance of the membrane, is used.^{1, 391}

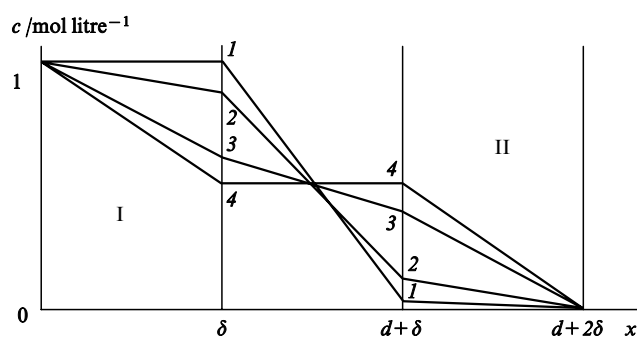


Figure 17. Concentration profiles obtained for the virtual solution in the membrane and in two diffusion layers (I and II) in the case of a binary electrolyte diffusion ($I = 0$).

Calculated using the microheterogeneous model for the MK-40–NaCl system, $\delta^I = \delta^{II} = \delta$; $p = 0.01$ (1), 0.1 (2), 1 (3) and 10 (4); $c^I = 1$ mol litre⁻¹; $c^{II} = 0$.³⁶⁸

However, a complete analogy between the electrolyte diffusion and ion exchange is possible only at a zero current. Due to the difference between the transport numbers of ions in the solution and in the membrane the flow of a current of density I causes desalination of the solution layer adjacent to one membrane surface (a diffusion layer depleted in electrolyte is formed), while the solution in the layer adjacent to the other membrane surface is concentrated.¹¹ As the potential jump increases, the electrolyte concentration at the depleted-diffusion-layer/membrane interface becomes much lower than in the bulk of the solution and the current density reaches the limiting value, I_{lim} . In an ideal system characterised by a constant thickness of the diffusion layer and local electroneutrality the current density must not exceed the I_{lim} value. However, in real systems, especially in dilute solutions, the current density can be several tens of times higher than I_{lim} .^{392–397} This is due to a number of phenomena^{394–405} involving electrodiffusion transport at high voltages: generation of the H^+ and OH^- ions upon irreversible splitting of water at the membrane/solution interface;³⁹⁴ coupled convection due to the concentration and (or) temperature gradients (gravitational convection)^{394–397} and the space charge density gradient (electroconvection);^{398–404} and the ‘exaltation’ effect.^{394, 405} It should be noted that exper-

imental and theoretical investigations of these phenomena are of importance for understanding and optimising the electrodialysis process under intense current regimes.^{394, 402}

The limiting current density is inversely proportional to the thickness of the diffusion layer δ .^{1, 11} This dependence is often used to determine the δ value from the limiting current density at the membrane surface^{406, 407} or from the limiting flux of a particular component.⁴⁰⁸ For dilute solutions the accompanying effects mentioned above cause a significant distortion of the shape of the current-vs.-voltage curve, thus hampering a correct determination of the limiting current and δ value.^{394, 406, 409} A method involving the use of an auxiliary electrode system to eliminate this problem has been developed.⁴⁰⁶

3. Limiting stages and mathematical description of multistage transfer

Determination of the limiting stages of a transfer process is of considerable importance for an understanding and practical implementation of the process. However, this is a complicated problem. As mentioned above, ion transfer across a membrane is generally a mixed-diffusion process,^{306, 327, 391} i.e., the resultant rate of transfer is determined by transport through both the membrane and the diffusion layers of the solution. As the current strength increases, the role of the depleted diffusion layer in controlling the kinetics of the ion transfer process becomes increasingly important irrespective of the p value and in the limiting case it is transfer through this layer that is the limiting stage of the process. Taking into account this fact, it is possible to explain many experimentally observed regularities of ion transport in membrane systems. For instance, the loss of transport selectivity of a particular type of the competing counterions across the membrane is due to the change from particle diffusion (or mixed-diffusion) kinetics at low currents to film diffusion kinetics at currents close to the limiting current.^{391, 410, 411} Even in the presence of a specially modified surface layer,³⁷⁵ which resists the transfer of two competing counterions in different manners, the transfer permselectivity can be significantly improved only at currents lower than the limiting current.^{410, 412}

Ion transfer is often complicated by the occurrence of chemical reactions, e.g., water splitting at the interface between two layers of a bipolar membrane^{392, 393, 413–417} or near the membrane/solution interface.^{392–394, 414–421} This is possible if currents close to or exceeding the limiting current flow in the system, in the case of association or dissociation of weak electrolyte ions and molecules (amino acids) accompanying the so-called facilitated transfer^{422–426} or in the case of electrodialysis of natural water (carbonates, phosphates).^{427–430} Water splitting in aqueous solutions is a slow process with a rate constant of 2×10^{-5} s⁻¹ (see Ref. 392) and can therefore be the limiting stage of transfer in membrane systems. However, the mechanism of this reaction is rather complicated. In the membrane’s bulk within a thin boundary layer 1–10 nm thick the reaction is accelerated, being catalysed by some functional groups (secondary and tertiary amines, weak acid carboxylic groups), heavy metal ions and by the electric field gradient of the electrical double layer,^{392, 414–417, 431, 432} which can be as high as 5×10^8 V m⁻¹ (see Ref. 392). As a result, the reaction rate can increase by nearly five orders of magnitude. In some cases this is the desired effect (in, e.g., production of acids and alkali from salts using bipolar membranes³⁷⁴), whereas in other cases this significantly complicates the technological process (in, e.g., desalination of solutions by electrodialysis^{356, 433}). The hydrocarbonate ions in the membrane can also catalyse water splitting, thus increasing the generation rate of the H^+ and OH^- ions (see Ref. 429). At the same time dissociation of some weak electrolyte anions at the membrane boundary can to some extent control the rate of electrodialysis.^{356, 433}

Thus, studies of transport inside a membrane only are insufficient for understanding the transfer processes in membrane systems. Transfer across the diffusion layers and interface (more

exactly, matching these processes and transport within the membrane) strongly affects the behaviour of the whole system. The three-layer mathematical models of transfer in membrane systems^{1, 369, 391, 410, 411, 434–441} give an adequate insight into the processes, since transfer is considered both within the membrane and in two diffusion layers adjacent to the membrane. The three-layer mixed-diffusion model was first proposed by Wills and Lightfoot⁴³⁴ for electrodiffusion of a binary electrolyte. Electrodiffusion of binary and ternary electrolytes across a homogeneous^{391, 434–437} and a microheterogeneous membrane^{369, 411} has been studied. Zholkovsky⁴³⁶ and Gnusin⁴²¹ included transfer of the H^+ and OH^- ions appearing due to splitting of water at the membrane/solution interface. The contribution of electroosmotic ion transfer has been reported.³¹⁹ Using a specific numerical procedure, Manzanares *et al.*³⁰⁶ included violation of the electroneutrality conditions within the diffusion layers and the membrane. The role of the modified surface layer was elucidated,⁴¹⁰ the bi-ionic potential was studied^{328, 329} and facilitated diffusion of amino acids across the membrane was investigated.^{422–425}

The authors of all the studies mentioned above used similar formulations of the mathematical problems, the differences being due to the desire for taking into account a particular additional effect. Transfer across both diffusion layers ($0 \leq x < \delta^I$ and $d + \delta^I < x \leq d + \delta^I + \delta^{II}$) and the membrane ($\delta^I \leq x \leq d + \delta^I$) (see Fig. 17) is described by the Nernst–Planck equations^{306, 391, 439} under local electroneutrality. It is also assumed that the membrane boundaries are in local thermodynamic equilibrium and that the continuity conditions hold for the electrochemical potential and fluxes. The concentrations of all types of the ions i at the outer boundaries of the diffusion layers (c_i^I and c_i^{II}) are specified, while the current density is considered known. In this case the problem posed is a boundary-value problem for a three-layer domain. Solving this problem involves determination of the fluxes, concentration and potentials as functions of the coordinate x .

A general analytical solution to the problem for a single-layer domain was proposed by Schlögl.²⁹² The system under study was also divided into three domains (see Fig. 17) and the corresponding solutions were matched.^{391, 435, 439} Garrido *et al.*³¹⁹ and Karlin⁴³⁷ proposed numerical methods suitable for the steady-state and non-steady-state cases. Sistat and Pourcelly⁴³⁹ reported an analytical solution to the problem for a binary electrolyte using the Lambert function. Lebedev *et al.*^{391, 411, 440, 441} modified the known ‘shooting’ method^{442, 443} in order to adapt it to multilayer domains. More detailed reviews of the methods for solving this type of problem can be found in Refs 411 and 438 and in the monograph.¹

The use of the local electroneutrality condition makes the models used rather accurate provided that the current density is lower than I_{lim} . However, many practically important processes (e.g., deionisation of water by electrodialysis^{356, 444} or operation of bipolar membranes³⁷⁴) require intense current regimes when the current density exceeds I_{lim} . Levich⁴⁴⁵ considered the problem of ion transfer across the electrode/solution interface and showed that the concentration of the electrically neutral electrolyte solution near the electrode surface (c_s) varies at low currents. Simultaneously, the thickness of the diffuse part of the electrical double layer changes; however, the Boltzmann equilibrium distribution of the ion concentrations in this part is retained. The thickness of the electrical double layer is inversely proportional to $\sqrt{c_s}$ and, therefore, increases with a decrease in c_s . An analogous conclusion was also drawn by the authors of Refs 446 and 447 who extended the range of the current strengths to $I = I_{lim}$. Rubinstein and Shtilman³⁹⁸ first obtained a numerical solution to the Nernst–Planck–Poisson equations for the overlimiting current flowing across the diffusion layer adjacent to the ion-exchange membrane. They showed that at $I > I_{lim}$ the space charge region goes beyond the quasi-equilibrium electrical double layer at the interface. This causes a decrease in the effective

thickness of the diffusion layer, thus providing the ‘overlimiting’ increase in the salt ion current. The study³⁹⁸ has attracted considerable interest, since it gave a clue to the understanding of the mechanism of the ‘overlimiting’ current phenomenon. It was followed by a large number of studies concerning the role of the space charge in the formation of the ‘overlimiting’ current.^{377, 378, 398–404, 448–452} Considerable progress was achieved due to a rigorous and, at the same time, rather simple solution of the Nernst–Planck–Poisson equations by Urtenov *et al.*^{403, 448, 449} Assuming a quasi-uniform distribution of the space charge^{403, 404} instead of the electroneutrality condition, in some instances the system of differential equations was reduced to a cubic algebraic equation.⁴⁰³ This also permitted significant simplification of the method for solving the problem and studies of a three-layer system with two⁴⁵¹ and three types of ions.⁴⁵²

Simultaneously with the description of the structure of the diffusion layer at $I > I_{lim}$ many researchers^{394, 399–402} attempted to simulate the mechanism of the appearance of convective fluid flows under the action of the electric field on the space charge (these flows destroy the diffusion layer). Currently, the electroosmotic slip mechanism, which was first proposed by Dukhin *et al.*⁴⁰¹ who called it electroosmosis of the second kind (since the space charge responsible for the onset of convection appears as a result of the current flow), is thought to be the most probable. Rubinstein *et al.*^{377, 399, 400} reported a comprehensive analysis of electroconvection and showed that it appears in the near-surface region of both homogeneous and inhomogeneous membranes. The electroosmotic slip of a fluid can cause instability of concentration polarisation at the membrane, which manifests itself as oscillations of the electric potential jump, which transform into a random motion detected as an excess low-frequency electric noise at super-overlimiting currents. Urtenov *et al.*^{394, 449} reported numerical calculations of electroosmotic vortices assuming a constant bulk electric force calculated using the Nernst–Planck–Poisson equations. The results obtained are in good qualitative agreement with those reported by Rubinstein.

Mention should be made that electroconvection is not the only form of a coupled convective motion of a fluid under intense current regimes. Gravitational convection also plays an important role in membrane systems, especially at rather high solution concentrations and large intermembrane distance.^{396, 397} Under these conditions the Grashof¹ (or Rayleigh^{377, 400}) numbers can exceed their critical values and convective flows develop in the system, destroying the diffusion layer. The contribution of electroconvection to the overlimiting current is more significant for dilute solutions at short intermembrane distances.^{1, 394}

In conclusion it should be emphasised that concentration polarisation and transfer across the diffusion layer are of crucial importance for the formation of the properties of the whole membrane system. To follow how the properties of a membrane (in particular, its structure and kinetic parameters) affect the integral properties of the whole membrane system, one must know methods for description of the transfer processes occurring on different levels, namely, in a single membrane and in an assembly comprising a large number of membranes. In this case a hierarchic system of mathematical models⁴⁵³ (some of them were briefly outlined above) may appear to be useful.

VI. Methods of investigations of ion transport in membranes

Conventionally, there are two avenues of research on the ion transfer in membranes. One of them involves comparison and optimum choice of membranes for various processes.^{356, 454} Here, the main problem is the choice of the basic physicochemical (static and transport) characteristics of membranes, which would provide the greatest body of information, have unambiguous and clear physical meaning and be determined in not very time-consuming experiments without using sophisticated equipment.

On the other hand, measurements of physicochemical characteristics of membranes are required for basic research on the mechanism and quantitative description of ion transfer.

Numerous studies on the methods of chemical and thermodynamic research on ion exchange have been reported to date.^{11,327} The diffusion layer characteristics are successfully determined by laser interferometry,^{388,389} voltammetry,^{409,420,455} chronopotentiometry,^{372,409,456} using electrochemical noise^{396,397,457} and impedance measurements,^{416,417,456} *etc.* The electrochemical methods of investigations of the properties of ion-exchange membrane systems were reviewed by Pourcelly *et al.*⁴⁵⁶

In this Section we will dwell only on the methods for measuring the conducting and selectivity properties of membranes, due to which they occupy a special position among a variety of modern materials. These properties include first of all the conductivity, diffusion permeability and transport numbers of ions.^{285–287,458,459} Below we briefly outline the electrochemical, ion exchange and spectroscopic methods used in this field of research.

1. Conductivity and transport numbers

Methods for measuring the ionic conductivity of solids are most often used for the description of the transport properties of various membrane materials, from inorganic salts and oxide systems to polymeric membranes. The area of their application extends from obtaining thorough knowledge of the nature of ionic mobility and its relation to the structure and surface to the practically valuable studies on fabrication of various electrochemical, membrane devices and power sources, in particular, fuel cells that have been the subject of intensive recent research.^{4,460–462} In this connection it will be recalled that the well-known membrane polymeric material Nafion belongs to the proton solid electrolytes exhibiting the best conducting properties.^{463,464}

The ionic conductivity is most often studied by impedance spectroscopy, which involves complex measurements of the ohmic and capacitive resistance of membranes. By plotting the impedance or admittance hodograph for a wide frequency range it is possible to determine the ionic conductivity of the material under study. Now we will outline the methods employed and point to some recent studies. Conduction studies of inorganic membranes,⁴⁶⁵ various polyelectrolytes^{159,461,462,466–469} and composite membranes^{469,470} most often involve measurements of their impedance. Detailed description of the measuring techniques, measuring cells, as well as analysis of the results obtained using different types of equivalent circuits has been documented.^{456–458,471–478} In particular, the use of impedance spectroscopy allows measurements of the diffusion coefficients of electrolyte in the diffusion layer and determination of the rate constants for water splitting in membrane systems.^{414–417,439,479–482}

Since the conductivity of most membrane materials is strongly dependent on the water content,^{351,458,461,462} considerable efforts have been made to control the water vapour pressure and maintain it at a constant level. However, even this approach precludes the choice of conditions identical to those realised in studies of the transport properties in aqueous electrolyte solutions. To ensure such conditions, experiments often involve conductivity measurements of membranes separating two electrolyte solutions containing the working electrodes.^{456,458,477–478} The additional resistance of the solution is included by carrying out measurements for the same cell without the membrane (difference method). In some instances the solution resistance is comparable or higher than the membrane resistance. This causes a marked increase in the measurement error. Besides, interpretation of the results obtained is complicated by an additional contribution of the resistance of the membrane/electrode interfaces to the measured value and by possible deformation of the membranes in the cell.^{458,478} Methods of solving this problem have been documented.^{458,476–478}

A version of the difference method is the probe technique, which involves measurements using a four-electrode cell (two polarising and two working probe electrodes).⁴⁷¹ The use of two additional silver chloride or calomel electrodes permits simultaneous a.c. and d.c. measurements.³⁶⁷

The membrane d.c. frequency spectra measured under non-equilibrium conditions can also serve as a source of valuable information. To this end, a six-electrode cell can be used. One pair of electrodes is employed for the d.c. polarisation of the membrane under study, the other pair is used to induce an alternating sinusoidal electric field, while the third pair of electrodes acts as the potential probes. For simultaneous measurements of the membrane's voltage-vs.-current curve the cell is additionally equipped with two reversible reference electrodes. The use of such a measuring complex allows essential extension of the capabilities of membrane conductometry.⁴⁷⁷

A simple and rather accurate method for measuring the conductivity of ion-exchange materials representing both films and pieces of arbitrary geometry is the isoconductivity point technique.^{354,355,458} It involves conductivity measurements of the solution with and without the ion exchanger in the conductometric cell.

Membrane selectivity depends on the mobility and concentration of ions in a given material. The basic characteristics of the ion-selective properties of a membrane are the transport numbers, which are defined as the electric charge transferred by a given type of ion in the absence of the pressure and concentration gradients. The fundamentals of the method for determination of the transport numbers of various solid and liquid objects were developed by Turbandt.⁴⁸³

The selectivity is often estimated by the e.m.f. method in a cell containing reversible electrodes and a membrane separating two solutions of different concentration.⁴⁸⁴ In practice the so-called effective transport numbers, *i.e.*, the fraction of the charge transferred in the presence of the concentration and pressure gradients, are most often determined.^{485,486} To optimise the experimental design, it was proposed to use strong currents flowing over a short period of time;⁴⁸⁴ closed cells with a concentration drop changing its sign in the course of the experiment;^{444,487} devices for automatically maintaining the component concentrations at the cell inlet at a constant level,^{394,488,489} *etc.*⁴⁴⁴ To calculate the 'true' transport numbers, it was proposed to extrapolate the effective transport numbers to an infinitely strong current, since in this case the diffusion (not convection!) contribution to the flux can be neglected.⁴⁷¹

A more detailed description of methods for measuring the transport numbers can be found in monographs.^{307,308,444,472} It is appropriate to mention that liberation of some substances (*e.g.*, oxygen) at electrodes in the case of volumetric control of the transfer process requires a rather high voltage. This can introduce errors into the results obtained as compared to those obtained under the conditions of impedance spectroscopy measurements.

Other electrochemical methods of investigations of transfer phenomena can also be rather informative. These include thermoelectric measurements, thermally stimulated depolarisation, Hall effect studies, *etc.*^{472,474}

2. Spectroscopic methods

Various spectroscopic methods are often used in studies of transfer phenomena, ion and molecular mobility. One of them is vibrational spectroscopy.^{165,490} However, NMR spectroscopy is the most important and promising. The advantages of this method are a broad range of characteristic frequencies and the possibility of description of the local environment of a given sort of atom. Since the energy of the dipole–dipole interactions is inversely proportional to the cubed distance between the dipoles, the shape and width of the line of a given nucleus are determined by its nearest environment only. This allows one to distinguish between the crystallographically nonequivalent positions in the crystal structure and to characterise the nearest environment of a given

type of nuclei.^{491–494} In the case of a solid the rotation of the interatomic vector about the direction of the magnetic field at a frequency close to or higher than the resonance frequency causes averaging of the internuclear coupling. First of all, this manifests itself as line narrowing in the NMR spectra.⁴⁹⁵ Analysis of changes in the widths or in the second moments of the NMR lines permits information on the rotational mobility in solids to be obtained.^{180, 494} Translational mobility of ions and molecules also leads to line narrowing, though the effect is much more pronounced in this case. The lines of the nonequivalent nuclei involved in the fast exchange merge together. Such studies allow determination of the characteristic frequency and the activation energy for this type of mobility.^{494, 496, 497} The most valuable information on the cation mobility is provided by NMR relaxation in solids. Here, the researcher can immediately determine the frequency of rotational mobility and describe the processes of ion and molecular transfer. It should be noted that the activation energy for mobility extracted from the NMR data is often different from the data of electrochemical (in particular, impedance spectroscopy) measurements. The reason is that NMR spectroscopy gives the description of the local nuclear environment (see above), whereas the conductivity is undoubtedly an integral characteristic of a material. The predominant contribution to the overall process of transfer across the membrane may come from a low fraction of the atoms and ions possessing the highest mobility, *e.g.*, those located on the material's surface. Numerous examples of NMR studies of transfer processes have been documented.^{87, 166, 494, 496–502}

Another promising method for investigation of transfer phenomena in membranes is Raman spectroscopy,^{456, 503–506} which allows measurements of the vibrational spectra of the membrane components. This method provides particularly valuable information when the membrane contacts solutions of weak electrolytes. By Raman spectroscopy one can determine the concentrations of various ions (polychromates,⁵⁰³ sulfates and hydrosulfates⁵⁰⁴), nitric acid and nitrates⁵⁰⁵ in the membrane and in solution, as well as study poisoning of membranes in electroanalysis.⁵⁰⁶

3. Ion exchange rate and diffusion permeability measurements

The pioneering quantitative studies on the kinetics of ion exchange were carried out by Boyd, Adamson and Myers³²⁴ who proposed a model, which treated an ionite grain as a homogeneous sphere. More recently, this model has been extensively used by Barrer and Falconer.^{507, 508} Up to now the results obtained in that time for the diffusion-controlled processes in a grain or film (adjacent diffusion layer) have been widely used in the same form to describe the kinetics of ion exchange. Processes involving diffusion in the ionite grain as the rate-determining stage predominate.

There are processes to which the above-mentioned model is inapplicable. Tunitskii *et al.*⁵⁰⁹ and Helfferich^{510–512} extended this model to the diffusion of ions possessing different mobilities and to the processes complicated by the occurrence of chemical reactions. According to another model proposed for ion exchange in a heterogeneous grain due to the movement of the interface between the initial and the newly formed phases, diffusion across a variable-thickness layer of exchange products occurs.^{76, 274, 513}

A salient feature common to all these models is that the experimental data are obtained after disturbance of the equilibrated system by adding a reagent, which either contains a certain type of exchanging ion or, on the contrary, reduces their concentration due to complexation or formation of a weakly dissociating compound (*e.g.*, water). Then, the system relaxes to the equilibrium state. Here, the measured quantity is the continuously varied concentration of a particular sort of ions in the solution or in the ionite phase. In this connection such methods are called non-steady-state ones. The solution composition can be analysed by various analytical methods including potentiometric, polaro-

graphic and some other techniques.^{161, 273, 274} It is commonly accepted that the drawback of this approach is the variable composition of the solution, which causes the driving force of the process to change and complicates its mathematical description.

To eliminate these problems, either the ratio of the solution volume to the ionite volume is increased or the so-called methods of infinitely large volume are used (a large volume of solution is rapidly passed through a thin ionite layer). The course of the process is assessed by analysing the changes in the composition of the sorbent phase.^{55, 514, 515} This approach permits obtaining exact results but is very labour-consuming, which significantly limits the area of its application. In addition, the need for carrying out a continuous experiment can come into conflict with the necessity of frequent monitoring of the composition of the solid or liquid phase. More detailed studies of diffusion processes are also carried out using the methods based on the layer-by-layer analysis of cylindrical or conical ionite samples.^{516–519}

Much less time-consuming are the isoconcentration methods involving compensation of the changes in the solution composition due to some external action. For instance, Haagen⁵¹⁹ who proposed this method studied the H^+/M^+ exchange reaction resulting in the formation of acid in solution. The acid formation changes the colour of an indicator. By adding the necessary amount of alkali the acid is neutralised and the colour is restored. The exchange rate can be estimated from the amount of alkali, which should be added during some time interval. More recently, this method was improved, namely, it was forced into the regime of automatic compensation of the liberating product and a number of novel methods for detection of disturbance of the system's equilibrium was implemented. Some other techniques were developed, which significantly extended the area of application of this method.^{520, 521}

Using planar membranes, one can investigate the transfer processes induced by various driving forces, namely, the concentration, pressure or electric potential gradients. The method of studying the diffusion processes induced by the concentration or the chemical potential difference of a particular sort of ion is the most similar to those considered above. A membrane is placed between two half-cells containing solutions with different concentrations of the permeate.^{522–524} The method permits studies of the transfer processes proceeding at substantially different rates, as well as the processes occurring under quasi-steady-state or strongly nonequilibrium conditions.⁵²⁴ This is first of all due to the possibility of varying the solution concentrations, cell volumes and the geometric parameters of the membrane (surface area, thickness). Besides, the chemical potential difference of a certain type of ion can be substantially increased by using reagents which react with these ions, thus resulting in the formation of complex, weakly dissociating or insoluble compounds.⁵²⁴ A method for measuring the partial fluxes of particular types of ions through the membrane upon changes in the concentration and electric potential differences on each side of the membrane has been developed.⁵²⁵ To improve the accuracy of the measurements, the pH value and the concentration of ions in the solutions circulating through both half-cells are automatically maintained at a constant level.

Studies of transfer through the membrane volume and elucidation of the role of the membrane surface require reliable data on the diffusion layer adjacent to the surface. Unfortunately, experiments with conventional flow cells are inappropriate for taking into account the role of the diffusion layer, since the layer thickness varies with coordinate and can be calculated only for plane-parallel geometry. Bobreshova *et al.*^{526, 527} developed the rotating membrane disk method, which significantly simplifies the solution to this problem, since it provides uniform accessibility of both sides of the membrane surface to mass transfer and permits calculations of the thickness of the diffusion layer. This method allows one to analyse the polarisation characteristics of the

membrane system and relatively easily distinguish between different stages of mass transfer.

Experimental methods for measuring the diffusion permeability of membranes can be conventionally divided into two groups: methods without and with solution flow. A non-flow cell for the first group of methods comprises two compartments separated by the membrane under study. One compartment is filled with an equilibrium solution with a prescribed electrolyte concentration, while the other compartment is filled with deionised water. The diffusion flow of electrolyte through the membrane can be assessed from, e.g., an increase in the conductivity of the solution in the compartment filled with deionised water.⁵²⁸ A drawback of such cells is that the electrolyte concentrations in both compartments vary with time. This limits the lower bound of the concentration to 0.01 mol litre⁻¹. The flow cell methods make possible extension of the concentration range and reduction of the lower bound of the concentration down to 10⁻⁴ mol litre⁻¹.³⁶⁸

The method for determination of the self-diffusion coefficients of the ions in membranes using radiotracers should be pointed out (for a review of related methods, see Ref. 129). As a rule, the self-diffusion parameters of the labelled ions can be measured with high accuracy.

Studies of the interdiffusion of ions in an external electric field and without it permit the determination of both the diffusion and electromigration mobility of the ions. If the dependence of these ion coefficients on the water content in the membrane is known, it is possible to draw some conclusions about the membrane microstructure. For instance, it was shown^{529, 530} that an increase in the concentration of the solution in which the perfluorocarbon membrane is immersed (or a decrease in the membrane's water uptake) is accompanied by breakdown of large clusters into smaller ones and by shortening of the narrow cluster-connecting channels characterised by unidirectional diffusion of various ions. For cross-linked polystyrene sulfo cation-exchange membranes the above-mentioned coefficients are virtually independent of the solution concentration,⁵³⁰ which is thought to be indicative of a rigid network microstructure of the membrane.

VII. Conclusion

Progress of membrane science is favoured by the wide use of membrane and ion-exchange materials in various industrial processes, water treatment, air cleaning, separation processes and the production of highly efficient power sources, etc. Various practically valuable applications require specific materials, which can operate in various media in different temperature regimes and possess high selectivity and chemical stability and specific mechanical properties. Because of this, a large number of novel membrane materials are synthesised and studied yearly, as well as new avenues and methods of application being proposed. In particular, the synthesis of novel composite membrane materials with prescribed properties has been the subject of considerable recent research. However, in all cases the ability of membranes to provide fast ion or molecular transfer is particularly important. From this standpoint the determining role is played by the methods for description of transfer phenomena.

The greatest body of information on the structure of and transfer processes in membranes can be obtained using complementary experimental methods of investigation. Notwithstanding common patterns of transfer phenomena in various inorganic and high-molecular-mass ion-exchange and membrane materials, it is impossible to correctly describe them without knowledge of the structural peculiarities and properties of these systems as well as phase transformations occurring in the course of exchange. In most cases of crucial importance is the use of different methods for theoretical description of these phenomena. At the same time interpretation of the experimental results and, hence, to a great extent their value are often limited to the existing mathematical models of the phenomenon under study. This particularly concerns the non-steady-state methods of investigation of transfer

phenomena (chronopotentiometry, impedance), which have been rapidly developing recently. Description of these phenomena requires setting up of and solution of sophisticated mathematical problems. However, taking into account impetuous development of computational methods, rapid progress in this field also seems to be possible.

There is a great variety of transfer phenomena in membrane systems. However, the limited size of this review precluded consideration of many important problems in this area of study. Nevertheless, the authors hope that it will attract the attention of researchers to this field of investigation from both theoretical and practical standpoints.

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Solid-phase method for tritium labelling of biologically active compounds

V P Shevchenko, I Yu Nagaev, N F Myasoedov

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Abstract. The solid-phase method for conducting hydrogenolysis, hydrogenation and isotope exchange reactions is described. The potential of the solid-phase method for tritium labelling of various organic compounds including lipids, nucleotides, amino acids, peptides, *etc.* is demonstrated. The influence of the reaction conditions on the yield and on the molar radioactivity of the labelled specimens is considered. It is shown that the results obtained can be interpreted by the dependence of tritium spillover on the nature of the initial compound and other factors. The bibliography includes 158 references.

I. Introduction

Organic compounds labelled by tritium (a radioactive isotope of hydrogen) are widely used in research in chemistry and biology, in medicine and agriculture. The range of such compounds manufactured by various companies comprises hundreds of names and is being constantly extended and updated. Among labelled compounds, physiologically active substances are especially abundant, first of all, because of their use in biology and medicine. The structures of labelled products needed for various purposes become more complicated with time. Therefore, labelling procedures have to be modernised not only to prepare each of the main classes of organic compounds but also to introduce a label into various compounds of the same class.

The steadfast attention to the problem of synthesis of tritium-labelled compounds is due to the fact that tritium has an appropriate half-life (12.26 years) and high molar radioactivity. High-performance liquid chromatography allows one to isolate specimens with a radiochemical purity of 96%–98% even in the case where highly rigorous conditions are used for labelling such that the yield of the labelled compound is only several percent. Specific binding to receptors of tritium-labelled preparations is virtually free from isotope effects; this accounts for high sensitivity of this method and permits accurate determination of the rate constants for binding. Tritium-labelled compounds are also used in pharmacokinetic studies to determine the target organ

in which a drug is mainly accumulated and the rates of excretion of this drug from the organism. Tritium compounds are also needed to study metabolism and substrate specificity of enzymes and to search for new efficient enzyme inhibitors. Recalling also the fact that tritium-labelled specimens are at least 10 times less expensive than ^{14}C -labelled ones, one can understand why every aspect of related to the preparation of tritium isotopomers of biologically active compounds arouses considerable interest.

The methods for introduction of a tritium label can be divided into two main groups, namely, various versions of isotope exchange and chemical methods (usually, tritiation, dehalogenation, selective tritiation and dehalogenation).

This review considers the solid-phase method for tritium labelling. In view of the specific nature of solid-phase (without a solvent) synthesis, hydrogenation and isotope exchange are considered as particular cases of hydrogenolysis.¹ According to this method, an organic substance is applied on a support (sorbent) where a metal catalyst has been applied preliminarily, and this system is heated under a tritium gas atmosphere. Solid-phase hydrogenolysis proved to be the process of choice for introducing a tritium label into organic compounds. Using these reactions, tritium-labelled lipids, peptides, proteins, nucleic acids, carbohydrates, glycoproteins, nucleoproteins, lipoproteins, glycolipids, alkaloids, terpenoids and many other classes of biologically active compounds have been obtained rather easily.

Plentiful data on the reactions of various compounds applied on a support with activated hydrogen species formed on the metal catalysts have been reported. The enhanced mobility of activated hydrogen on inert supports has been discovered.² The flow of activated hydrogen species from one phase to another has been called hydrogen spillover. It is hydrogen (tritium) spillover that determines the possibility of solid-phase hydrogenolysis. Therefore, before considering the factual information on solid-phase reactions involved in tritium labelling of organic compounds, we give an account of the main data concerning the spillover of hydrogen, which would be useful for understanding the main features and the mechanism of hydrogenolysis.

II. Key information on hydrogen spillover

In most cases, solid-phase reactions are carried out under rigorous conditions, namely, at temperatures above 200 °C (usually, at 300, 500 °C or higher). For the majority of biologically active substances, the use of high temperatures is inadmissible; these substances are studied at lower temperatures. The regularities of the occurrence of solid-phase reactions established in low- and high-temperature experiments are different. Therefore, the data

V P Shevchenko, I Yu Nagaev, N F Myasoedov Institute of Molecular Genetics, Russian Academy of Sciences, pl. Kurchatova 2, 123182 Moscow, Russian Federation. Fax (7-095) 196 02 21. Tel. (7-095) 196 02 12 (V P Shevchenko, I Yu Nagaev). Tel. (7-095) 196 00 01. E-mail: img@glas.apc.org (N F Myasoedov)

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available from the literature concerning the nature of activated hydrogen species and the conclusions concerning processes related to hydrogen spillover on supports (high-temperature experiments) require critical analysis to be applied to the introduction of tritium into biologically active compounds (low-temperature experiments).

The activity of metal catalysts in the isotope exchange decreases in the series $\text{Pt} > \text{Pd} > \text{Ni}$.³ The chemisorption of H_2 usually occurs at 200–300 °C.⁴ The products of dissociation of molecular hydrogen on platinum migrate to the support in which a dynamic equilibrium is established between the atomic and protic forms of hydrogen.^{5,6} The number of active species, for example, for silica gel, amounts to $\sim 10^{12} \text{ g}^{-1}$ (see Refs 7–9). It was found that silica gel bearing activated hydrogen species is able to catalyse hydrogenation of alkenes. Under these conditions, hydrogenation mainly takes place on the sites generated owing to hydrogen spillover from the gas phase.^{7–11}

Hydroxy groups, oxides or carbon can act as hydrogen acceptors.¹² For example, a study by FT IR spectroscopy has shown the occurrence of isotope exchange between deuterium and hydrogen of the OH groups on Y zeolite (ZeY).¹³ It has also been shown¹⁴ that the OH groups of the support exchange with tritium under hydrogenation conditions. The reaction between the spillover species and the CH_3O fragments of the substrate molecules has been found to give OH groups and CH_4 .^{15,16}

The destruction products formed in reactions can serve as carriers of the active hydrogen species from the initiator to the acceptor.^{17–20}

The diffusion coefficients of hydrogen are determined using various methods including temperature-programmed desorption²¹ and adsorption²² methods, electron microscopy²³ and NMR.^{24,25} The diffusion over the surface of the support can occur over a distance of up to 90–200 nm from the metal catalyst (platinum) particles.^{24,25}

A mathematical model of spillover has been considered in several publications.^{26–28} This model assumes that the activated species are formed on the source metal and the support conveys these species to the substrate and back. One-, two- and three-dimensional diffusion kinetic models for hydrogenolysis of a supported organic substrate have been constructed.²⁸ The models take into account the concentration gradient of the spillover hydrogen and poisoning of the catalyst during the reaction. It was shown that hydrogenation is almost localised in the reaction areas around the crystallites of the metal catalyst and, hence, there exists some ratio of the catalyst, the support and the substrate optimal for this particular reaction. Data supporting both the atomic and protic natures of the spillover species can be found in the literature. Currently, most researchers hold the opinion that the spillover involves hydrogen atoms.^{18,29,30} It was found¹⁸ that the rate of disappearance of the EPR signal from perylene corresponds to the rate of absorption of H_2 by the Pt/ZrY system. It is noteworthy that direct EPR monitoring of atomic hydrogen on most supports is possible only at temperatures below –170 °C. Thorough analysis of the shape of the peak and the chemical shift in the ^1H NMR spectra has shown³⁰ that hydrogen migrates over the SiO_2 surface as $\text{H}^\bullet$ radicals. The adsorption sites for these radicals may be represented by SiO or Si groups.

It has been shown by EPR that tetravalent cerium is reduced to trivalent on the ZeY + Pt(black) system in the presence of hydrogen.³¹ Using *N-tert*-butyl- α -phenylnitron or 2,4,6-tri-*tert*-butylnitrobenzene, which served as traps for hydrogen, weakly bound hydrogen atoms participating in benzene hydrogenation have been detected.³²

It has been found that the exchange processes of $^2\text{H}_2$ with the OH groups of semiconductor supports do not differ much for *n*- and *p*-type semiconductors with applied platinum;³³ thus it can be concluded that spillover involves uncharged species.

The first step of spillover is homolytic cleavage of the H–H bond on the metal, regardless of whether hydrogen atoms or protons participate in the spillover. The rate-limiting step is either

the surface diffusion on the support or the transfer of particles from the catalyst to the support. Since the activation energies of these elementary steps are different, the limiting step of spillover may change upon temperature variation.⁷ The prevalent opinion is that hydrogen spillover is limited by diffusion over the surface of the support.⁶

The hypothesis according to which spillover proceeds by a proton mechanism has also been reported.^{11,34,35} Using reduction with temperature programming and IR spectroscopy, it was shown that, first, hydrogen quickly dissociates to atoms and then forms H^+ ions, which diffuse into the substrate bulk and slowly react with oxygen atoms of the support material.³⁶ In a number of studies,^{37–39} the increase in the electrical conductivity of TiO_2 in a hydrogen atmosphere was attributed to proton diffusion to the titanium dioxide. The electrical conductivity of TiO_2 attached to platinum is the first to increase and then this also takes place for TiO_2 without platinum.

The proton mechanism of spillover is also indicated by the correlation between the spillover rate and the proton affinity of the promoter,^{11,34} which can solvate the diffusing proton: water > methanol > ethanol > *n*-propanol > *n*-butanol. In the presence of these promoters, the spillover rate does not depend on the surface area of the applied platinum, whereas in the presence of, for example, acetic acid, which has a low proton affinity, this dependence does exist. In the latter case, the reaction rate can be determined by the rate of proton solvation.

Even those who support the atomic nature of hydrogen spillover have to admit⁴⁰ that no unambiguous spectroscopic data indicating that $\text{H}^\bullet$ act as activated hydrogen species have yet been obtained. In some cases, experimental evidence for both mechanisms is found for the same catalyst systems under the same reaction conditions.⁴⁰ Depending on the type of testing or the particular spectroscopic technique used, either atomic hydrogen or protons are identified. The model proposed by Roland *et al.*⁴⁰ describes the spillover as the formation of an electron donor on the surface of the support. In this consideration, weakly chemisorbed hydrogen is regarded as atomic, while strongly chemisorbed hydrogen is taken as protons. Quantitative data obtained by spectroscopic methods do not allow one to identify unequivocally the nature of the activated species in the solid-phase catalytic reactions.

Tritium can also react with a substrate in either atomic or ionic form. However, the results of the hypothetical interactions of the electrons generated in parallel with the formation of protons with either gaseous hydrogen or with the substrate molecules have not been considered in the literature. The latter process could also be interpreted as a specific case of electrochemical reaction. Electrons are free to migrate over the crystallite of the metal catalyst or over the support (for example, graphite). However, if the substrate is an insulator, the electron conductivity may prove to be negligibly low.

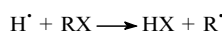
It is worth mentioning that the conductivity in the metal crystallite decreases as the temperature rises, because electron scattering is enhanced upon disordering of the motion of atoms caused by their thermal excitation. Metalloids usually have positive temperature coefficients of conductivity.⁴¹ The interaction with electrons might be responsible for the disappearance of the EPR signal of perylene adsorbed on the Pt/ZrY system¹⁸ and for the reduction of tetravalent cerium to trivalent cerium.³¹ It was shown above^{6–10} that hydrogenation can be accomplished by gaseous hydrogen; this may be related to the presence of electrons arising upon the spillover of protons.

Research into the reactions of various organic molecules with atomic tritium formed upon heating of tritium gas to 2000 K on a tungsten filament has shown⁴² that, even when the target is cooled with liquid nitrogen, the degree of replacement of hydrogen in the molecule of an organic compound does not exceed 10%. In this case, the chemical and radiochemical yields of the exchange were exceptionally low compared to the yields of solid-phase reactions. Indeed, even at room temperature, atomic hydrogen reduces

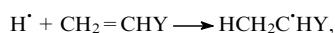
many metal oxides, reacts with sulfur, nitrogen and phosphorus, and also reacts with oxygen to give hydrogen peroxide; in addition, the hydrogen atoms easily recombine. The reactions involving radicals produce a variety of side products. Thus, if the label is introduced *via* a reaction with atomic tritium, the yields of labelled biologically active compounds would be very low. At temperatures used to carry out solid-phase reactions, atomic tritium generated in the reaction of tritium gas with the catalyst is converted into molecular tritium, which does not play any important role in the synthesis of labelled preparations. This seems to account for the stability of organic compounds in these reactions.

Probably, noticeable participation of atomic tritium in reactions could be expected at higher temperatures, which are not normally used in solid-phase labelling. Indeed, only at high temperatures can radical elimination as well as hydrogenation and dehalogenation involving atomic tritium compete with energetically more favourable recombination of tritium atoms.

It is of interest to analyse the data concerning the reactions of radicals with the substrate under conditions more appropriate for the investigation of these systems.⁴³ For example, it was found that radicals are more prone to undergo elimination than addition reactions.⁴³ This is due to the fact that the elimination



involves a linear reaction centre, which ensures the lowest activation barrier. During the addition



the reaction centre is a triangle; this, undoubtedly, increases the activation energy of this reaction. The intramolecular transfer of hydrogen atoms was studied by EPR (although, at low temperatures), and the kinetics of free-radical intramolecular transfer of protium and deuterium atoms was first studied by direct spectral methods using hydrocarbon groups grafted to the solid surface (silica gel) (Table 1).⁴⁴

Table 1. Rate constants for free-radical intramolecular transfer of protium and deuterium atoms.⁴⁴

Process	<i>T</i> / K	$10^{-5} k$ / s ⁻¹
$\begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}_3 \\ \quad \\ \text{CH}_2\text{C}^\bullet\text{H}_2 \end{array} \rightleftharpoons \begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}_2^\bullet \\ \quad \\ \text{CH}_2\text{C}^\bullet\text{H}_2 \end{array}$	246	66 ± 7
$\begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}_3 \\ \quad \\ \text{CH}_2\text{C}^\bullet\text{H}_2 \end{array} \rightleftharpoons \begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}^\bullet\text{CH}_3 \\ \quad \\ \text{CH}_2\text{C}^\bullet\text{H}_2 \end{array}$	295	12 ± 1
$\begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}_2^\bullet \\ \quad \\ \text{C}^\bullet\text{H}_3 \end{array} \rightleftharpoons \begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}^\bullet\text{H} \\ \quad \\ \text{C}^\bullet\text{H}_2\text{H} \end{array}$	373	5 ± 0.5
$\begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{C}^\bullet\text{H}_2\text{C}^\bullet\text{H}_2 \\ \quad \\ \text{CH}_3 \end{array} \rightleftharpoons \begin{array}{c} \diagup \text{Si} \diagdown \\ \quad \\ \text{CH}_2\text{CH}^\bullet\text{H} \\ \quad \\ \text{CH}_2^\bullet\text{H} \end{array}$	373	20 ± 2

It was shown that the radical centre can migrate; therefore, different polymerisation, isomerisation, *etc.* products can be formed not only at the sites of the initial formation of radicals.

It is of interest to analyse the regularities involved in homolytic and electrophilic substitution of tritium for hydrogen in aromatic compounds⁴⁵ in order to compare them with the regularities of isotope exchange. For electrophilic substitution, where H⁺ acts as the electrophilic species, *ortho*-, *para*- and *meta*-directors are distinguished in the molecule (Table 2). The proton addition is the slow step in this reaction. For example, on treatment of aromatic compounds with a mixture of trifluoroacetic acid and

Table 2. Rate constants for deuterium inclusion (rel.u.) into different positions of the aromatic ring with different substituents.

Position of the substituent	Rate of inclusion for the substituent			
	CH ₃	CH ₃ O	Cl	I
<i>ortho</i>	83	23 000	0.035	0.043
<i>meta</i>	1.9	0.25	0.002	0.003
<i>para</i>	83	55 000	0.160	0.112

heavy water, the rate of deuterium exchange was found to vary in parallel with the equilibrium degree of protonation.

Let us compare electrophilic alkylation of aromatic compounds with the corresponding radical reactions. Methylation of toluene and ethylation of bromo- and fluorobenzene by treatment with R⁺[Al₂Cl₇]⁻ proceed as typical electrophilic substitution reactions (Table 3). Homolytic methylation gives a different ratio of substitution products.

Table 3. Inclusion (%) of the CH₃ and C₂H₅ groups into *ortho*-, *meta*- and *para*-positions during alkylation of aromatic compounds.

Process	Inclusion position		
	<i>ortho</i>	<i>meta</i>	<i>para</i>
Methylation of			
toluene ^a	50–60	10–14	34–26
fluorobenzene ^b	57	37	6
bromobenzene ^b	67	23	10
Ethylation of			
fluorobenzene ^a	43	14	43
bromobenzene ^a	24	22	54

^a Electrophilic substitution. ^b Homolytic methylation.

As will be shown below, this type of specificity is also observed during solid-phase hydrogenolysis by tritium. It is evident that this type of process specificity cannot be interpreted when considering only the source or the mechanism of transport of activated species to the substrate. However, since these species have different properties (a radical and an ion), by investigating the reaction products and/or distribution of a label in them, one can draw conclusions in favour of a particular mechanism of hydrogen spillover.

III. Solid-phase reactions in the synthesis of tritium-labelled preparations

Solid-phase reactions proved to be fairly efficient for the introduction of a tritium label into organic compounds. When selective methods are used, the problem of optimisation of the conditions of introduction becomes especially topical. Highly labelled materials can be prepared in solid-phase processes such as selective isotope exchange, selective hydrogenation of unsaturated carbon–carbon and heteroatom–carbon bonds and selective reductive dehalogenation of one of the several halogen atoms or reductive dehalogenation for organic molecules containing labile unsaturated fragments.

It should be mentioned that the solid-phase reactions listed above are accompanied by side processes, which considerably influence the radiochemical characteristics of labelled specimens. For example, when substances applied on a catalyst are treated with tritium gas, the final molar radioactivity of the products depends appreciably on the isotope effects. The destruction of organic compounds not only hampers purification of labelled materials but also results in isotope dilution of tritium. Evidently, the reactions of organic compounds with the resulting protium –

tritium mixture decrease the degree of inclusion of tritium into the molecules of these compounds. A model has been proposed⁴⁶ that can be used to explain the influence of different factors on the degree of inclusion of tritium into organic molecules.

1. Solid-phase isotope exchange

Isotope exchange is the method of choice for introducing a tritium label, as it does not require the synthesis of precursors. In addition, isotope exchange allows one to prepare a labelled specimen using very small amounts (5–10 mg) of biologically active substances, which are often scarce and expensive. This method is inapplicable only when the starting compound is totally destroyed under experimental conditions.

The solid-phase catalytic isotope exchange is a complex process affected by numerous factors related to the properties of both organic compounds and the catalysts. For example, the efficiency of solid-phase isotope exchange depends appreciably on the melting point of the organic compound. In view of this fact, all compounds can be divided into two groups. The first one includes substances that behave like liquids at the chosen reaction temperature (in this case, the molecules can migrate over the support and with respect to one another); the second group comprises compounds that exist as crystals during the reaction (in this case, direct contact with the catalyst active sites is impossible and the degree of isotope exchange mainly depends on the efficiency of tritium spillover). Naturally, the regularities of insertion of the label into compounds of the first and second groups are dissimilar. Lipid-related compounds usually have low melting points, while nucleotides, nucleosides, amino acids, peptides and their derivatives have high melting points. Therefore, it is expedient to consider the regularities of labelling of compounds with different properties by this procedure and then to present data on the radiochemical characteristics of labelled specimens obtained under the optimal conditions for each class of compound.

a. Study of the dependence of the degree of solid-phase isotope exchange on the nature of organic compounds

Let us consider the results of experimental studies of the influence of the nature of organic compounds on the kinetics of their labelling and the dependence of the molar radioactivity of the resulting preparations on the reaction temperature.

Experiments on introducing a label into crystalline L-valine and L-alanine showed that the degree of isotope exchange smoothly increases with an increase in the temperature and the kinetic curves reach a plateau.^{47, 48}

A similar situation is observed in introduction of the label into adenine, guanine, xanthine, hypoxanthine (Table 4), deazaguanine and 3-indolylacetic acid.⁵¹

Table 4. Relative molar radioactivity of adenine, guanine, xanthine and hypoxanthine (5% Pd/CaCO₃, τ = 60 min) at various temperatures.^{49, 50}

$T/^{\circ}\text{C}$	RMR (%)			
	adenine	guanine	xanthine	hypoxanthine
20	1.4	1.3	0.8	1.7
120	1.8	1.7	2.4	—
140	16.8	6.5	20.9	13.1
150	34.7	16.7	50.0	—
160	54.7	25.7	67.4	16.7
180	100	71.9	96.5	63.0
200	—	91	100	100
220	—	100	—	98.8

Note. Here and in other tables, τ is the experiment duration; RMR is the relative molar radioactivity; the highest molar radioactivity attained in this series of experiments was taken to be 100%.

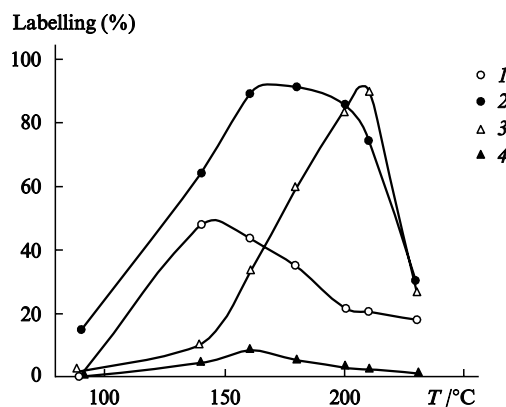


Figure 1. Degree of labelling of the substrate vs. the temperature of isotope exchange.⁵²

Reaction conditions: τ = 15 min; 5% Pt/C: hexadecane, 10:1 (1); 5% Pt/C: 6-ketopalmitic acid, 10:1 (2); 5% Pt/C: methyl stearate, 10:1 (3); 5% Pd/C: cetyl alcohol, 6:1 (4).

The kinetics of variation of the molar radioactivity of purine bases and amino acids are similar: the kinetic curves and the curves for the temperature dependence of the degree of labelling reach a plateau.

The curves obtained for low-melting compounds of lipid nature look quite different (Fig. 1). Similar types of dependence are also found in the case of other catalysts (Pd/BaSO₄, Rh/C),⁵² which differ in the ability to initiate the isotope exchange and in the temperature at which the highest molar radioactivity is attained. The appearance of maxima on these dependences can be explained in the following way. The molecules of, for example, a low-melting fatty acid, unlike those of high-melting compounds, can create a certain structured system around the active sites of the catalyst;⁵³ a layer of chemisorbed molecules functioning as ligands appears on the catalyst surface.^{54, 55} These systems are more stable against poisoning and deactivation. In view of the foregoing, the processes taking place on the catalyst surface during the solid-phase isotope exchange between tritium gas and low-melting compounds can be described by the following scheme. First, the adsorbed molecules of the substance undergo a redistribution on the catalyst surface to give ordered systems involving some of the substrate molecules and the catalyst active sites. The greater part of the molecules moves freely and comes in contact with these ordered structures. Therefore, the rate and the degree of exchange during labelling of such substances are higher than those in the case of high-melting compounds.^{52, 53} As the temperature and process duration increase, the degree of isotope exchange becomes higher but the rate of side processes also increases. Starting from certain temperatures, the structured chemisorbed layer is destroyed; this stops the isotope exchange and induces decomposition of, first, the fraction of the specimen with the highest degree of labelling.⁵³ This accounts for the appearance of maxima in the plots for the dependence of the molar radioactivity of fatty acids on the temperature and the duration of isotope exchange.^{52, 56}

This type of regularity has been observed when introducing the label into hexadecane, 6-ketopalmitic acid, methyl stearate and cetyl alcohol (see Fig. 1); the positions of the maxima and the patterns of temperature dependences of the molar radioactivity can be substantially different for different compounds.

All attempts to explain the appearance of the maxima by other reasons (for example, by high content of bound hydrogen in the activated carbon,⁵⁷ sublimation of a part of the compound from the catalyst surface, a decrease in the catalytic activity of the metal after thermal treatment^{58, 59}) have not been confirmed experimentally.

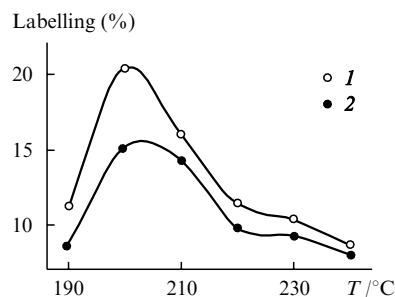


Figure 2. Degree of labelling of stearic acid vs. the temperature of isotope exchange (10% Pd/BaSO₄); (1) standard catalyst; (2) catalyst pre-calcined at 240 °C and 0.1 Pa.

Upon degassing and thermal deactivation of the catalyst, the degree of labelling of, for example, stearic acid really decreases but the general extremal pattern of the temperature dependence does not change (Fig. 2).⁶⁰ The proposed interpretation of the pattern of these curves would be confirmed if the maxima disappeared in the case of merely mechanical application of stearic acid onto the sorbent mixed with the standard catalyst. Indeed, with such application, the formation of the structured system of stearic acid molecules around the active sites of the catalyst would be appreciably hampered due to the short reaction time, and, hence, the degree of inclusion of tritium would be more uniform for all molecules of organic acid. Therefore, this modification of the conditions of the solid-phase reaction should entail some decrease in the degree of isotope exchange.

An experiment of this type has been carried out:⁶⁰ a methanol solution of stearic acid was mixed with the Alusorb or Silasorb sorbent in 1 : 10 ratio, the solvent was removed, and the residue was dried. Then the support–substance mixture was thoroughly triturated in a mortar together with the catalyst and the reactions with the aliquot portions of this mixture were carried out at different temperatures (Table 5). As can be seen from the data given in the Table, with an increase in temperature, the molar radioactivity of the specimen first increases, then decreases and subsequently varies insignificantly.

Table 5. Relative molar radioactivity of labelled stearic acid at various temperatures of isotope exchange (5% Pd/BaSO₄, catalyst : substance ratio is 20 : 1, $\tau = 15$ min) on the catalyst without a support and using an additional support.⁶⁰

$T/^{\circ}\text{C}$	RMR (%)		
	no support	Alusorb	Silasorb
190	42	46	47
200	71	76	80
210	82	81	82
220	100	79	81
230	48	75	84
240	36	82	83

Thus, the degree of labelling depends substantially on the aggregative state of the substrate under the solid-phase reaction conditions.^{52, 61}

A study of the dependence of the degree of labelling on the length of the carbon chain in homologues of fatty acids whose melting points are markedly lower than the temperature at which the isotope exchange is carried out showed a linear decrease in the molar radioactivity with a decrease in the chain length. Hence, the isotope exchange for this type of substance is a probability process. Some other features were noted. For example, the temperatures corresponding to the maximum degree of isotope replacement (T_{max}) were different for different homologues. For

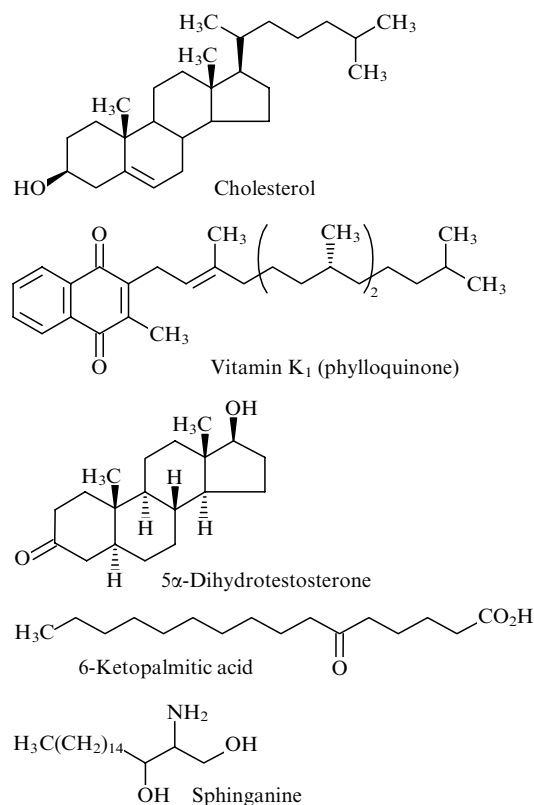
example, the T_{max} values for lauric (m.p. = 44 °C), myristic (m.p. = 58 °C), palmitic (m.p. = 64 °C) and stearic (m.p. = 70 °C) acids were 190, 200, 205–210 and 210 °C, respectively.^{52, 62}

Apparently, for representatives of one homologous series (for example, for fatty acids), T_{max} depends on the temperature of phase transition (melting). At a definite temperature, diffusion of these molecules increases so sharply that the efficiency of isotope exchange reaches a maximum and does not depend on the efficiency of hydrogen spillover. The conducting of these reactions at higher temperatures results only in activation of side processes.

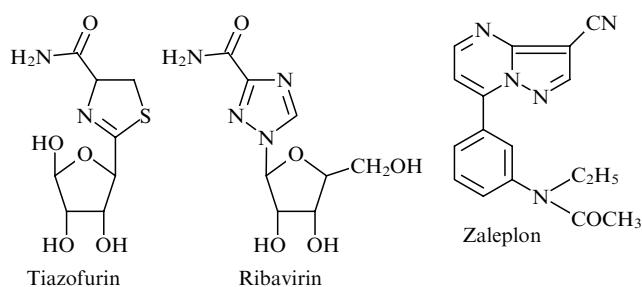
However, for high-melting sodium salts of acetic, propionic, and butyric acids, the molar radioactivity did not show this type of unambiguous dependence on the number of carbon atoms.⁶³ Evidently, the accessibility of the substance bulk during the isotope exchange reaction differs appreciably depending on whether the substance occurs on the support surface in the solid (crystalline) or in the liquid state.

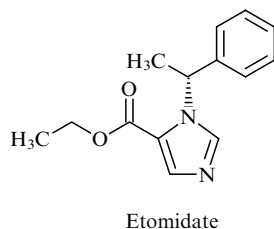
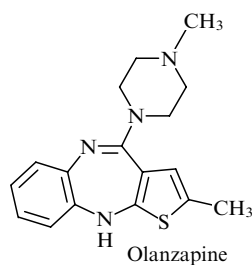
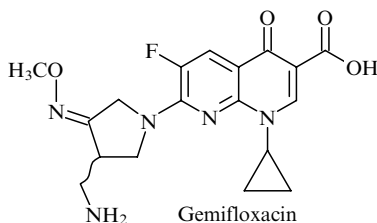
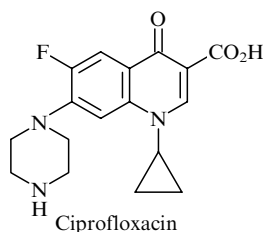
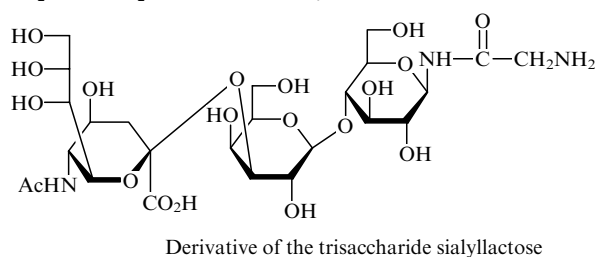
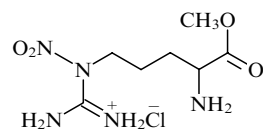
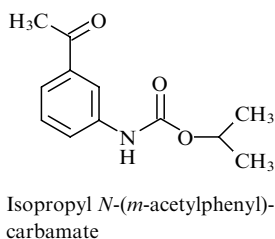
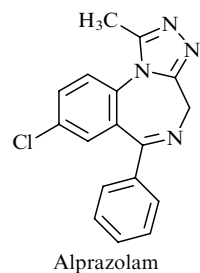
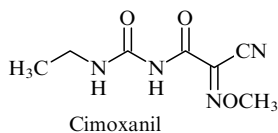
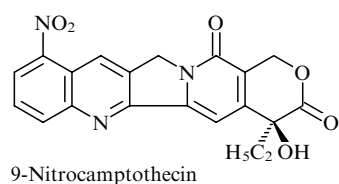
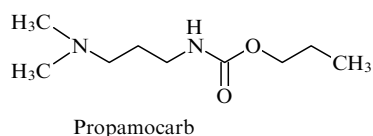
b. Introduction of a tritium label into lipophilic compounds and into low-molecular-mass bioregulators by solid-phase isotope exchange

Compounds of lipid nature vary appreciably in thermal stability and in stability against hydrogenolysis; they can be either polar or non-polar and either aliphatic or aromatic. Examples of such compounds are given below.



In this section, in addition to lipophilic compounds, we also consider other substances used in pharmacology. For example,





As a rule, these compounds are polyfunctional and contain fragments that are unstable under solid-phase reaction conditions. Many of these substances (called, for convenience, pharmaceuticals) possess hydrophobic properties, like compounds of a lipid nature.

To optimise the conditions of labelling in compounds of this type, the degree of isotope exchange has been studied as a function of the following variables: temperature (in the 60–240 °C region), the catalyst: substance ratio, the reaction time (in the range of 5–60 min), the nature of the catalyst (5% Pt/C, 5% Pd/C, 5% Rh/C, 5% Pd/BaSO₄) and some others.^{52, 56, 61–71} For example, it was found that the best conditions for introducing a

Table 6. Molar radioactivity (MR) of labelled sodium isobutyrate obtained with solid-phase isotope exchange carried out under various conditions.⁶³

Reaction conditions			MR /PBq mol ^{−1}
catalyst	τ /min	T /°C	
5% Pd/BaSO ₄	60	210	5.26
	60	190	3.85
	60	170	2.78
5% Pd/C	60	210	5.04
	60	190	5.44
	60	170	5.26
	30	170	5.30
	20	170	5.22
	15	170	4.85
	5	170	4.11

label into thermally stable isobutyric acid are as follows: 5% Pd/C, 30 min, 170 °C (Table 6).⁶³ Under more rigorous conditions, the yield of the labelled product decreased.

Study of the influence of the structure of compounds having similar physicochemical properties on the molar radioactivity of labelled specimens has shown⁶³ that the probability of inclusion of tritium, for example, in the methyl group of the isobutyric, propionic and butyric acids, is more than three times higher than the probability of its inclusion into methylene groups (Table 7). The reasons for this difference are considered below.

Table 7. Molar radioactivity of labelled organic acids prepared by solid-phase isotope exchange (5% Pd/C, T = 200 °C).⁶³

Compound ^a	MR /PBq mol ^{−1}	Amount of inserted label	
		per hydrogen atom	per methyl group
Acetic acid	1.20	0.40	1.20
Propionic acid	3.18	0.64	2.62
Butyric acid	3.74	0.53	2.62
Isobutyric acid	5.56	0.79	2.64

^a The corresponding sodium salts were used.

By solid-phase reactions carried out under the optimal conditions selected by the optimisation technique, labelled specimens with various structures have been prepared (Tables 8–10).^{50, 52, 53, 62, 65, 70–74}

Table 8. Molar radioactivity of aliphatic compounds.

Compound	MR /PBq mol ^{−1} (see ^a)	Ref.
6-Ketopalmitic acid	27.5–27.8	52
Methyl stearate	38.0–40.0	62
Cetyl alcohol	5.0–5.5	52
Hexadecane	17.0–17.5	62
Cholesterol	0.5–1.0	71
5α-Dihydrotestosterone	0.52–0.56	53
5α-Dihydrotestosterone enanthate	1.30–1.50	53
Sphinganine	7.78	69

^a The molar radioactivity of the specimen caused by introduction of one tritium atom is 1.08 PBq mol^{−1}.

Table 9. Molar radioactivity of aromatic compounds (palladium catalyst, $\tau = 15$ min).

Compound	$T/^{\circ}\text{C}$	MR /PBq mol ⁻¹	Yield (%)	Ref.
3-(3-Pyridyl)phenyl- isoxazole	60	0.0004	25	64
Alprazolam	175	0.15	4	74
Camptothecin	190	0.96	7	70
Tiazofurin	155	0.67	55	74
Ribavirin	160	1.11	80	74
Isopropyl- <i>N</i> -(<i>m</i> -acetyl- phenyl)carbamate	140	1.32	30	73
Gemifloxacin	180	0.34	5	53
Olanzapine	200	0.63	10	62
Zaleplon	180	0.19	2	62

Table 10. Conditions of tritium labelling of low-molecular-weight bioregulators.

Compound	Reaction conditions		MR ^a	Yield (%)	Ref.
	catalyst	$T/^{\circ}\text{C}$			
4-Ethyl-2,6,7-trioxa- 1-phosphabicyclo- [2.2.2]octane 1-oxide	5% Pt/C	170	1.15	14	50
Sodium salt of <i>N</i> -acetylneuraminic acid α -methyl- glycoside	5% Pd/CaCO ₃	200	0.46	25	76
Derivative of the trisac- charide sialyllactose	5% Pd/CaCO ₃	160	0.32	15	76
Propamocarb	5% Pd/BaSO ₄	135	0.56	58	73
Cimoxanil	5% Pd/CaCO ₃	90	0.006	30	73

^a Expressed in PBq mol⁻¹.

It has been noted above that the nature of the tritium active species can be traced most clearly in reactions with aromatic compounds. The susceptibility to electrophilic substitution is known^{45,72} to be different for different aromatic systems. It depends on the structure of the compound and on the presence of substituents; this was demonstrated, for example, by measuring the rate constants for the isotope exchange during the preparation of [8-³H]nucleotides of the adenine series. The data reported by Sidorov and Myasoedov⁷⁵ allow one to suggest that if the activated hydrogen species that react with an organic compound are represented by positively charged tritium ions, the degree of labelling should decrease in the sequence ribavirin, tiazofurin, zaleplon and alprazolam. Indeed, it was shown^{53,74} that ribavirin was labelled to a 7–8 times higher degree than alprazolam. Apparently, this is due to the fact that the highest probability of the electrophilic substitution is expected for the triazole fragment of ribavirin. Therefore, ribavirin should exhibit the highest molar radioactivity over the given series (see Table 9). Due to the presence of the sulfur atom in the thiazole fragment, tiazofurin is substantially deactivated and the electrophilic substitution is less efficient.

Not every substance withstands the conditions of the solid-phase isotope exchange to the same extent. The chemical yield of hexadecane and cetyl alcohol after the exchange is 80%, whereas labelled compounds containing free amines, neuraminic acid and so on are formed in less than 20% yields.^{61,69,76} The stabilities of the specimens can be sharply different even in the case of compounds with similar structures (see Table 10). For example,

the yield of the sodium salt of *N*-acetylneuraminic acid α -methylglycoside at 200 °C is almost twice as high as that of the derivative of the trisaccharide sialyllactose at 160 °C. It was shown⁷⁶ that the degree of inclusion of the label into the sodium salt of *N*-acetylneuraminic acid α -methylglycoside increases ~4-fold as the temperature rises from 160 to 200 °C (Table 11). If the derivative of the trisaccharide sialyllactose did not decompose at 200 °C, it would be possible to obtain a labelled specimen with a molar radioactivity of > 1 PBq mol⁻¹.

Table 11. Relative molar radioactivity of the labelled sodium salt of *N*-acetylneuraminic acid α -methylglycoside (the ratio catalyst : substance is 25 : 1) for different conditions of solid-phase isotope exchange.

Reaction conditions			Yield (%)	RMR (%)
catalyst	$T/^{\circ}\text{C}$	τ /min		
5% Pd/BaSO ₄	140	40	92	13
	180	5	75	39
5% Pd/CaCO ₃	140	40	95	16
	160	25	91	22
	180	5	74	46
	200	5	25	86
	220	5	8	100

The large scatter in the yields of labelled specimens is also typical of aromatic compounds. The compounds containing triazole, pyrazole and thiazole fragments are more stable during the solid-phase method of labelling than isoxazole derivatives; however, the yields of these compounds under the conditions optimal from the standpoint of higher molar radioactivity were 2 to 80% (see Table 9).

Thus, if the compound is stable, the solid-phase procedure gives labelled specimens with a very high molar radioactivity. For introducing a label into labile compounds, it is necessary to use modified procedures. There are two approaches for increasing the yield of such compounds: (1) organic compounds are applied onto an additional inert support and are mixed mechanically with the catalyst; (2) the catalyst is modified prior to the reaction.

c. The introduction of the tritium label into components of nucleic acids by solid-phase isotope exchange

The best catalyst for introducing a tritium label into purine bases is 5% Pd/CaCO₃ (Table 12). The dependence of the molar radioactivity on the reaction temperature for these compounds shows a gradual increase to 140 °C and a sharp growth in the range of 150–200 °C (see Table 4).⁴⁹ Apparently, the increase is due to the

Table 12. Molar radioactivity of the specimens obtained by tritium labelling of purine bases under various conditions.

Compound	Reaction conditions ^a		MR (see ^b)	Yield (%)	Ref.
	catalyst	$T/^{\circ}\text{C}$			
Kinetin	Pd/BaSO ₄	140	5.56	12.5	49
6-Benzyl- aminopurine	Pd/CaCO ₃	190	5.74	13	77
Guanine	Pd/CaCO ₃	200–210	0.83	75	75
Xanthine	Pd/CaCO ₃	200–210	0.93	75	75
Hypoxanthine	Pd/CaCO ₃	200–210	1.90	67	75
Adenosine	Pd/CaCO ₃	200–210	0.89	93	75
2'-Deoxy- guanosine	Pd/CaCO ₃	200–210	1.56	17	75

^a In all experiments, $\tau = 30$ min. ^b Expressed in PBq mol⁻¹.

fact that tritium atoms start to play a noticeable role in the isotope exchange, instead of the cations.

The introduction of a label into components of nucleic acids with different stabilities has been reported^{75, 78–80} (Table 13). It can be seen from the data presented in the table that high degrees of replacement of protium by tritium were attained in compounds with a rather simple structure. In the case of polymeric derivatives or compounds containing labile fragments, labelling had to be performed at relatively low temperatures, which substantially influenced the molar radioactivities of the labelled preparations. The major side products obtained according to this procedure were those resulting from hydrogenation, isomerisation and destruction processes.

Table 13. Molar radioactivity of purine and pyrimidine compounds and their derivatives prepared by solid-phase isotope exchange.^{50, 78–80}

Compound	<i>T</i> / °C	MR ^a	Compound	<i>T</i> / °C	MR ^a
Adenine	170	2.01	2',3'-Dideoxy-thymidine	120	2.44
Thymine	170	4.30	3'-Azidothymidine	120	2.33
Uracil	170	1.82	phosphonate		
Benzyladenine	190	6.67	Acyclovir	120	2.07
Deazaguanine	220	0.44	phosphonate		
7-Thia-8-oxo-guanosine	170	0.01	2',5'-ApApAp	200	2.15
Theophylline	160	0.92	3',5'-ApA	110	0.34
Furfuryl adenine	160	5.93	3',5'-ApApA	110	1.85
Guanosine	210	2.56	3',5'-pApApAp	110	1.00
2'-Deoxyguanosine	200	1.30	Poly-A (7-8S)	180	0.38 ^b
3'-Azidothymidine	120	1.11	Poly-U (12S)	180	0.44 ^b
Acyclovir	210	4.63	RNA 15S	180	0.45 ^b

^a Expressed in PBq mol⁻¹. ^b Specific activity /TBq g⁻¹.

To increase the molar radioactivity of labile compounds, additional supports were used; this made it possible to carry out the reaction at higher temperatures (Table 14).⁵¹ It can be seen from the data given in the table that an increase in the catalyst: compound ratio entails an increase in the degree of tritium inclusion with a simultaneous decrease in the yield of the labelled

Table 14. Relative molar radioactivity of labelled indol-3-ylacetic acid obtained by labelling under various conditions.⁵¹

Reaction conditions				RMR (%)	Yield (%)
I ^a	II ^b	III ^c	<i>T</i> / °C		
Catalyst: 5% Pd/CaCO ₃					
5 : 1	—	—	150	17.1	1.9
10 : 1	—	—	150	40.0	0.7
20 : 1	—	—	150	53.3	0.4
50 : 1	—	—	150	66.7	0.2
5 : 1	Al ₂ O ₃	10 : 1	200	100	12.5
Catalyst: 5% Pd/BaSO ₄					
5 : 1	CaCO ₃	10 : 1	200	84.4	3.2
5 : 1	CaCO ₃	50 : 1	200	—	—
5 : 1	Al ₂ O ₃	10 : 1	200	84.0	10.2
5 : 1	Al ₂ O ₃	50 : 1	200	44.0	6.0
Catalyst: 5% Pd/Al ₂ O ₃					
5 : 1	Al ₂ O ₃	10 : 1	200	55.6	5.3
5 : 1	Al ₂ O ₃	50 : 1	200	56.0	1.9

^a The catalyst : substance ratio /mg μmol⁻¹. ^b Additional support. ^c The additional support : substance ratio /mg mg⁻¹.

specimen. With the use of an additional support and a mixture of 5% Pd/CaCO₃ with indol-3-ylacetic acid supported on Al₂O₃, the yield of the desired product increased to 12.5%. According to ³H NMR data, the distribution of the label at 200 °C is uniform over all the stable positions of tritium in indol-3-ylacetic acid, which is indicative of a considerable contribution of atomic tritium to the labelling process.

The proportion of tritium in purine bases depends on the nature of the initial compound.⁷⁹ As can be seen from the data listed in Table 15, the presence of the phosphate group decreases the content of tritium in the purine moiety of the molecule. Possible interpretations of this finding are discussed below.

Table 15. Molar radioactivity and fraction of tritium (%) in the specimens obtained by labelling of purine bases.

Compound	MR /PBq mol ⁻¹	Fraction of tritium
Adenosine	4.44	48
Guanosine	2.56	30
Acyclovir	4.78	14
AMP	0.46	12
ATP	0.46	13
NAD	4.10	1.3
Coenzyme A	0.07	89

Note. Here and in other tables, AMP is adenosine 5'-monophosphate, ATP is adenosine 5'-triphosphate, NAD is nicotinamide dinucleotide.

d. The introduction of the tritium label into amino acids and peptides by solid-phase isotope exchange

Many amino acids are thermally more stable than nucleic acids. Data on the solid-phase introduction of the tritium label into some amino acids have been reported (Table 16).⁸¹ At 220 °C, the distribution of the label at the valine carbon atoms (α : β : γ) is described by a 1 : 1 : 6 ratio (τ = 20 min, the 5% Pd/C : compound ratio is 10 : 1). The distribution of the label (%) in [2,3-³H]alanine under the same conditions is given by⁸¹

Compound	<i>n</i> = 0	<i>n</i> = 1	<i>n</i> = 2	<i>n</i> = 3
CH _n ³ H _{3-n} C ³ HNH ₂ CO ₂ H	3	15	22	5
CH _n ³ H _{3-n} CHNH ₂ CO ₂ H	5	17	23	7

At high temperatures, the degree of isotope replacement is of the same order of magnitude at any atom of the amino acid.

Other data have been obtained at lower temperatures.⁸² The distribution of tritium in the (*R*)-4-hydroxy-[G-³H]-L-proline molecule was studied. This compound was synthesised by heating (150 °C) for 60 min of a mixture of 5% Rh/Al₂O₃ with the activated Norit carbon impregnated with an aqueous solution of amino acid and then freeze-dried (the catalyst : Norit : (*R*)-4-hydroxy[G-³H]-L-proline ratio was 10 : 50 : 1). The ratio of the activation energy (*E*_a) of hydrogen exchange at a given carbon

Table 16. Molar radioactivity, yield and optical purity of labelled amino acids prepared by solid-phase isotope exchange (200 °C, 60 min).⁸⁶

Compound	MR /PBq mol ⁻¹	Yield (%)	Optical purity (%)
Glycine	1.8	90	—
Serine	1.4	50	75
Alanine	3.2	65	82
Valine	6.5	85	94
Leucine	7.9	70	85
Isoleucine	8.1	75	88
Histidine	4.5	20	50
Tryptophane	3.6	30	70

atom to the activation energy (E) of hydrogen exchange in methane is as follows:

Position of the label	3 β	3 α	5 α	5 β	2	4
$E_a : E$	0.946	0.856	0.653	0.794	0.852	0.924
Content of the label (%)	1	6	59	21	9	4

When the solid-phase isotope exchange is carried out under relatively mild conditions, the following tendency can be traced: the lower the activation energy for the exchange at a given carbon atom, the higher the degree of replacement of protium by tritium.

In the case of amino acids, the use of an additional support also promoted an increase in the molar radioactivity (Table 17).⁴⁸ Activated carbon, alumina and calcium carbonate are used most often. This procedure made it possible to obtain labelled compounds having various stabilities with a high molar radioactivity.

Table 17. Molar radioactivity of biotin and amino acids prepared by solid phase isotope exchange using various additional supports.⁴⁸

Compound	Reaction conditions				MR /PBq mol ⁻¹
	I ^a	II ^b	III ^c	<i>T</i> /°C	
Catalyst: 5% Pd/CaCO ₃					
Biotin	10 : 1	Al ₂ O ₃	10 : 1	200	1.6
L-Phenylalanine	16 : 1	Al ₂ O ₃	5 : 1	200	3.03
Catalyst: 5% Rh/Al ₂ O ₃					
L-Methionine	10 : 1	Al ₂ O ₃	10 : 1	200	3.30
Catalyst: 5% Pd/BaSO ₄					
L-Histidine	10 : 1	CaCO ₃	10 : 1	220	4.60

^a The catalyst : substance ratio /mg μmol^{-1} . ^b Additional support. ^c The additional support : substance ratio /mg mg^{-1} .

The influence of the same additional support, in particular, carbon, prepared by different procedures on the degree of labelling has been studied⁸³ (Table 18). In an experiment, phenylalanine was applied on the Norit carbon or on fibrous carbon in a ratio of 1 : 10. The resulting blends were mechanically mixed with 5% Pd/C in 1 : 1 ratio. After treatment with tritium ($T = 130^{\circ}\text{C}$, $\tau = 25$ min), the yield and the molar radioactivity of labelled phenylalanine were determined.

It was found that with the use of 5% Pd/C, the yield was as low as 1% and with a mixture of 5% Pd/C with the Norit carbon, the yield was even lower, 0.1%. A higher yield and a higher molar radioactivity (at 140°C) were attained by using fibrous carbon.

Table 18. Yield and relative molar radioactivity of labelled phenylalanine obtained by solid-phase catalytic isotope exchange under various conditions ($\tau = 25$ min, $T = 130^{\circ}\text{C}$).⁸³

Reaction conditions		Yield (%)	RMR (%)
catalyst	support		
5% Pd/C	—	1	—
	Norit carbon	<0.1	—
5% Pd/CaCO ₃	fibrous carbon	16	100
	Norit carbon	2	29
5% PdO/ Al ₂ O ₃	fibrous carbon	39	44
	Norit carbon	1.5	17
5% PdO/ BaSO ₄	fibrous carbon	41	35
	Norit carbon	2	22
	fibrous carbon	35	47

Similar results were obtained upon mixing fibrous carbon – phenylalanine systems with 5% Pd/CaCO₃, 5% PdO/BaSO₄ and 5% PdO/Al₂O₃ (see Table 18). When fibrous carbon was used, the yields of phenylalanine were 15–20 times and the molar radioactivities were 1.5–2 times as high as those obtained in the presence of the activated Norit carbon, which is used most often in these reactions.

This result was attributed⁸³ to the fact that fibrous carbon consists of very thin graphite layers (30–500 Å thick) laid to form highly ordered structures;⁸⁴ therefore, it adsorbs approximately an order of magnitude more hydrogen than the usual carbon. In addition, the amounts of hydrogen adsorbed on and desorbed from graphite nanofibres at room temperature were substantially different, indicating chemisorption of hydrogen on carbon. This was confirmed by temperature-programmed desorption.⁸⁴ Hence, fibrous carbon as a support has certain advantages over other materials. A higher saturation by tritium molecules of the whole bulk of the reaction mixture should be favourable for the efficiency of its spillover and should lead to a higher concentration of the activated species of tritium directly in the reaction area.

The higher yield of labelled organic compounds makes it possible to obtain a plausible yield of labelled preparations at higher temperatures (35–45 $^{\circ}\text{C}$ higher than in the case of the standard procedure). This, in turn, makes it possible to increase substantially the molar radioactivity of the material; for example, in the case of phenylalanine, this value increases ~ 3 -fold.⁸³

The method according to which a mixture of the substance with the catalyst is treated before the reaction by transition metal salts also proved to be efficient for increasing the molar radioactivity of thermally unstable preparations. For example, rhodium salts were used in the labelling of amino acids.⁸⁵ As noted above, the molar radioactivity of labelled compounds can be increased by creating conditions for more efficient hydrogen spillover under which isotope exchange takes place throughout the whole bulk of the substrate or by increasing the thermal stability of the substance (in this case, the label can be introduced at a higher temperature). In order to elucidate the role of rhodium trichloride during labelling, it was used to impregnate the catalyst and the support both separately and jointly.

It can be seen from the data presented in Table 19 that the key role of RhCl₃ is not to stabilise the amino acid by complex formation but rather to decrease the destructive action of the activated tritium species on the substrate. When the catalyst was treated with rhodium trichloride and then mixed mechanically with the support (fibrous carbon or Al₂O₃) on which phenylalanine had been applied, the yield of the labelled product increased 3–6-fold. On treatment of the support with a solution with RhCl₃ and phenylalanine followed by freeze-drying of the resulting mixture and subsequent mechanical mixing with the catalyst, the yield of the labelled product increased only 2–4-fold. In both experiments, molar radioactivities of the same order were obtained. This fact indicates that in the case of using the conven-

Table 19. Yield and relative molar radioactivity of labelled phenylalanine obtained with different ways of modification of reaction ingredients by rhodium trichloride ($\tau = 20$ min, $T = 190^{\circ}\text{C}$, the ratio support : phenylalanine is 10 : 1, catalyst : support is 1 : 1, phenylalanine : RhCl₃ is 1 : 1).

Catalyst	Support	Yield (%)	RMR (%)
5% PdO/BaSO ₄	fibrous carbon	4.2	100
	fibrous carbon/RhCl ₃	14.8	18
	the same	20.5	21
5% PdO/BaSO ₄ /RhCl ₃	—	31.1	9
	Al ₂ O ₃	1.5	48
5% PdO/BaSO ₄	Al ₂ O ₃	8.9	83
	Al ₂ O ₃ , RhCl ₃	17.2	44
5% PdO/BaSO ₄ /RhCl ₃	Al ₂ O ₃	30.4	42

tional procedure (an aqueous solution of amino acid and RhCl_3 is freeze-dried with the catalyst), RhCl_3 not only stabilises labile compounds but, simultaneously, it modifies the initiator of hydrogen spillover. Apparently, co-precipitation of rhodium salts on palladium with subsequent heating under an atmosphere of tritium gas gives rise to bimetallic active sites, which acquire new properties of both an adsorbent and an initiator of hydrogen spillover. Phenomena of this type have been considered in detail⁸⁶ in a study of the influence of technetium on the efficiency of solid-phase isotope exchange.

Comparison of the catalytic activity of mono- (Pd or Pt) and bimetallic systems (Pd–Tc or Pt–Tc) showed a non-additive increase in the catalytic activity (synergism) in the case of bimetallic catalysts with respect to the activity of metal catalysts used separately under the same conditions.⁸⁷ Some researchers explain the synergistic effect by the fact that hydrogen is activated on one type of active sites and the reactions proceed on another type of active sites.^{88–91} This model assumes that the spillover of hydrogen between these sites is enhanced. Other researchers believe that the synergism is mainly related to the interaction of the atoms of one metal catalyst with the other.^{92–102} In this case, hydrogen becomes activated and reacts in the same phase, *i.e.*, the activated hydrogen species migrate from one metal atom to the other within the bimetallic active site.

In solid-phase experiments, the degree of labelling of amino acids was lower in the presence of bimetallic catalysts than in the presence of monometallic catalysts.⁸⁶ This implies that no activation of tritium spillover takes place on the bimetallic catalysts, and the activated tritium species merely migrate from one metal atom to the other within the common catalytic site. Indeed, the capacity for the sorption of hydrogen is lower for bimetallic catalysts than for monometallic ones,⁸⁷ which is usually related to the decrease in the efficiency of hydrogen spillover.

Thus, the increase in the stability of amino acids resulting from catalyst modification by rhodium salts is mainly due to the fact that the reaction of the molecules of these compounds with activated tritium species proceeds to a lesser extent on bimetallic catalysts than on monometallic ones. Therefore, in the case of solid-phase labelling in the presence of metal catalysts, the degree of decomposition of the initial substance decreases after treatment of the catalysts with rhodium salts, which allows the isotope exchange to be carried out at higher temperatures. Indeed, without rhodium salts, raising the temperature by 60 °C (a 5% PdO/ Al_2O_3 : amino acid ratio of 10:1, $\tau = 30$ min, a tritium pressure of 350 hPa) resulted in a ~20-fold decrease in the yield of glycine and a 5-fold decrease in the yield of ω -aminocaproic acid.⁸⁵

$T/^\circ\text{C}$	160	180	200	220
Yield of glycine (%)	66	21	5	3
Yield of ω -aminocaproic acid (%)	4.8	1.8	1.2	0.9

When the catalyst was treated with rhodium trichloride, the decrease in the yield of labelled amino acids with temperature rise was found to be markedly retarded (Table 20). This made it possible to introduce the label into thermally unstable ω -aminocaproic acid at 180 °C (molar radioactivity of the product was 0.85 PBq mol^{−1}, yield 45%).⁸⁵

Evidently, the degree of isotope exchange can also be increased by creating conditions for more efficient interaction of the activated tritium species with substrate molecules.

The tritium labelling of high-melting compounds can be enhanced using 4-dimethylaminopyridine (Table 21).⁸⁵ Many reactions involving protons can proceed only in the presence of this compound.¹⁰³ Apparently, after co-precipitation with the substrate, this molecule can facilitate the diffusion of tritium cations into the substance bulk and thus increase the probability of isotope exchange. The data presented in Table 21 confirm the legitimacy of this hypothesis. However, it is too early to draw more definite conclusions. Evidently, solid-phase reactions of this type can be carried out only at relatively low temperatures;

Table 20. Yield and relative molar radioactivity of labelled amino acids obtained by solid-phase isotope exchange under various conditions (the 5% Pd/ CaCO_3 : RhCl_3 ratio is 8:1).⁸⁵

Compound	τ/min	$T/^\circ\text{C}$	Yield (%)	RMR (%)
Glycine	20	200	83	30
	30	210	75	35
	60	210	73	37
	120	210	71	40
	20	240	45	70
	10	260	30	93
ω -Aminocaproic acid	15	170	42	80
	15	200	14	100

Table 21. Yield and relative molar radioactivity of phenylalanine obtained with various methods of application of 4-dimethylaminopyridine ($\tau = 20$ min, the 5% Pd/ CaCO_3 : substance ratio is 10:1, the phenylalanine: 4-dimethylaminopyridine ratio is 1:1, $T = 160$ °C).

Reaction conditions	Yield (%)	RMR (%)
Catalyst – phenylalanine mixture	31.4	38
Catalyst – phenylalanine mixture treated with 4-dimethylaminopyridine	20.0	56
Catalyst – 4-dimethylaminopyridine mixture treated with phenylalanine	14.4	85
Catalyst treated with a solution of phenylalanine and 4-dimethylaminopyridine	10.4	100

otherwise, tritium would be inserted into 4-dimethylaminopyridine, which would reduce the molar radioactivity of the labelled specimen and would markedly complicate isolation and purification of the target product.

As in the case of compounds of a lipid nature, the replacement of protium by tritium is usually higher for the methyl groups of amino acids than for the methylene groups or than the isotope exchange at a tertiary carbon atom (Table 22).¹⁰⁴

Table 22. Relative reactivity of amino acids in solid-phase isotope exchange and tritium distribution in labelled compounds ($T = 150$ °C).¹⁰⁴

Compound	Relative reactivity	Fraction (%) of the label at carbon atoms with different degrees of substitution		
		RCH_3	RR^1CH_2	$\text{RR}^1\text{R}^2\text{CH}$
Alanine	0.52	96	—	4
Asparagine	0.75	—	60	40
Aspartic acid	0.25	—	60	40
Threonine	0.76	73	9	18
Leucine	1.04	86	5	9
Isoleucine	0.95	86	5	9
Valine	1.0	92	—	8

Data on the label distribution in aromatic amino acids and on the relative reactivities of these substrates are summarised in Table 23.¹⁰⁴ It can be seen that the highest degree of isotope exchange is found for histidine, the major amount of the label being concentrated in the aromatic ring. The same is observed for other aromatic amino acids. The degree of isotope substitution depending on the nature of the amino acid varies in the sequence:¹⁰⁴ basic amino acids > aliphatic amino acids without ionic groups > acidic amino acids.

Table 23. Relative reactivities of aromatic and heteroaromatic amino acids and serotonin in the solid-phase isotope exchange and tritium distribution in labelled compounds ($T = 150\text{ }^{\circ}\text{C}$).¹⁰⁴

Compound	Relative reactivity ^a	Fraction (%) of the label at different positions		
		α -position	β -position	ring
Histidine	1.10	20	4	76
Phenylalanine	0.77	13	40	47
Tryptophan	0.96	11	24	65
Thyroxine	0.72	11	35	54
Serotonin	1.2	35	7	58

^a Valine was used as the reference.

Labelling of peptides is often carried out using procedures of liquid-state hydrogenation and dehalogenation of their precursors prepared by multistage synthetic protocols. In most cases, this is done using derivatives whose molecules include dehydroproline, iodophenylalanine or diiodotyrosine.¹⁰⁵ The molar radioactivity of the specimens obtained by this method was $0.77\text{--}2.35\text{ PBq mol}^{-1}$, depending on the precursor.

The synthesis of peptides is usually carried out either in solution or in the solid state. The synthesis of precursors is a very cumbersome and expensive stage. Therefore, solid-phase isotope exchange between the tritium gas and peptide usually proves to be more efficient.

Peptides are more labile compounds than amino acids. In addition, there exists the problem of racemisation of amino acid residues at the α -position during the labelling. Therefore, labelled peptides are obtained by conducting reactions at relatively low temperatures (Table 24).¹⁰⁶ The distribution of the label in the amino acid residues in these peptides was approximately equal but hydrogen at the α -carbon atoms of amino acids proved to be the most reactive in the isotope exchange with tritium. For example, the peptide Met-Gly-His-Phe-Pro-Gly-Pro contained after labelling ($140\text{ }^{\circ}\text{C}$), on average, 1.44 tritium atoms, and 88% of them were in the α -positions of amino acid residues. At $180\text{ }^{\circ}\text{C}$, 4.29 tritium atoms were incorporated in this peptide, and only 76% of tritium occurred in the α -position of the amino acid residues.¹⁰⁶ Thus, the same trend is observed: the higher the reaction temperature, the more uniform the distribution of the label (Table 25).

The influence of the peptide structure on the distribution of the label among amino acid residues was studied using model

Table 24. Molar radioactivity of tritium-labelled peptides ($T = 140\text{ }^{\circ}\text{C}$, labelling was carried out using an additional support or the rhodium complex with the peptide).¹⁰⁶

Peptide	MR /PBq mol ⁻¹
Tyr-D-Ala-Gly-Phe-Leu-Arg	1.68
Thr-Lys-Pro-Arg-Pro-Gly-Pro	1.96
Met-Gly-His-Phe-Pro-Gly-Pro	1.74
Tyr-Ala-Gly-Phe-Tyr-Pro	1.63
Gly-Leu-Leu-Asn-Leu-Lys	1.40
Tyr-Pro-Arg	1.44
Tyr-D-Ala-Gly-Phe-Gly(OH)	1.78
Gly-Asn-NH ₂	1.42
Tyr-Pro-Pro-Gly-Gly-Ser-Lys-Val-Ile-Leu-Phe	2.33
Tyr-Ala-Gly-Phe-Leu	1.67
Tyr-Gly-Gly-Phe-Leu-Arg	1.11
Tyr-Gly-Gly-Phe-Leu	0.89
Met-Glu-His-Phe-Pro-Gly-Pro	1.69

Table 25. Distribution of tritium in the labelled His-Gly-Gly tripeptide at various temperatures.¹⁰⁴

$T/^{\circ}\text{C}$	MR /PBq mol ⁻¹	His	Gly(I)	Gly(II)
135	1.85	$\frac{86}{17.2}$	$\frac{5}{2.5}$	$\frac{9}{4.5}$
150	4.07	$\frac{72}{14.4}$	$\frac{12}{6}$	$\frac{16}{8}$
170	6.30	$\frac{63}{12.6}$	$\frac{16}{8}$	$\frac{21}{10.5}$

Note. The fraction of the label in the given amino acid (%) is indicated above the bar and the fraction of the label in the same amino acid per hydrogen atom (%) is below the bar.

Table 26. Distribution of tritium in labelled tripeptides ($T = 150\text{ }^{\circ}\text{C}$).¹⁰⁴

Peptide	MR /PBq mol ⁻¹	Yield (%)	Label distribution (%)		
			His (or Val)	Gly(I)	Gly(II)
His-Gly-Gly	4.07	40	72	12	16
Gly-His-Gly	2.41	25	62	30	8
Gly-Gly-His	2.59	12	57	29	14
Val-Gly-Gly	2.59	45	72	10	18
Gly-Val-Gly	1.41	30	13	59	28
Gly-Gly-Val	1.74	32	6	79	15

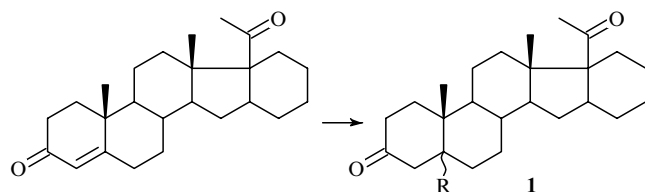
tripeptides.¹⁰⁴ It can be seen from the data listed in Table 26 that at $150\text{ }^{\circ}\text{C}$, the label is inserted non-uniformly. For example, the amounts of tritium in Gly(I) and Gly(II) in the Gly-Gly-Val peptide differ by a factor of ~ 5 . When tritium is introduced in identical amino acid residues, the label is mainly found in terminal amino acids; in the case where both residues are terminal, the label is inserted predominantly into the amino acid residue located at the N-end of the peptide. The patterns of label distribution in a free amino acid molecule and in the same molecule incorporated in a peptide are similar. At $180\text{ }^{\circ}\text{C}$, the molar radioactivity of Val-Gly-Gly reaches 7.70 PBq mol^{-1} . The overall replacement of protium by tritium amounts to 70%. It should be noted that racemisation did not exceed 1%, which corresponds to the accuracy of the experiment.¹⁰⁴

Interesting results have been obtained during the introduction of a tritium label into dalargin (Tyr-D-Ala-Gly-Phe-Leu-Arg), a synthetic analogue of the endogenous opioid peptide [Leu⁵]enkephalin (Tyr-Gly-Gly-Phe-Leu), which is used as a drug in gastroenterology.¹⁰⁷ In conformity with the temperature dependence of the degree of isotope substitution, the isotope label was incorporated in all amino acid fragments of dalargin (a 5% Rh/Al₂O₃: peptide: Al₂O₃ ratio of 2 : 1 : 20). At $140\text{ }^{\circ}\text{C}$, higher reactivity was found for alanine and glycine residues, while at $190\text{ }^{\circ}\text{C}$, the fraction of tritium that entered the aromatic residues of phenylalanine and tyrosine increased. A temperature of $160\text{ }^{\circ}\text{C}$ and storage in an atmosphere of tritium gas for 40 min were found to be the conditions of choice for labelling, the molar radioactivity of the labelled peptide being 1.93 PBq mol^{-1} . This peptide fully retained the biological activity, which was estimated as the ability to bind to the opioid receptors of the rat brain.

During labelling of more complex amino acid sequences, it may happen that one fragment of the molecule shields another fragment from the reaction with active tritium species. In this case, the distribution of the label along the amino acid chain is no longer uniform.¹⁰⁸

(1.85–2.04 PBq mol⁻¹ per bond). In this case, the solid-phase hydrogenation procedure is more efficient than the standard liquid-phase procedure. This is due to the fact that hydrogenation carried out with heating is accompanied by isotope exchange (see Table 29).

For example, hydrogenation of methacrylic acid by treatment with tritium gas on the 5% Pd/C catalyst at 170 °C gave a labelled specimen with a molar radioactivity ~3 times as high as could be expected upon the reduction of the double bond.⁶³ In addition, by using solid-phase hydrogenation, one can increase the yield of the labelled specimen (with respect to the liquid-phase method). This situation is often observed when hydrogenation affords isomeric products as, for example, in the reduction of 16 α ,17 α -cyclohexanopregn-4-ene-3,20-dione.



R = —H (5 β ,16 α ,17 α -cyclohexanopregnane-3,20-dione),
 $\cdots\text{H}$ (5 α ,16 α ,17 α -cyclohexanopregnane-3,20-dione).

The reaction gives rise to saturated steroids, namely, the 5 α - and 5 β ,16 α ,17 α -cyclohexanopregnane-3,20-dione isomers, in a ratio of 1:14. Only several percent of the 5 α -isomer could be isolated from the reaction mixture; preparative amounts of this compound (a 1:3 ratio in the reaction mixture) have been obtained by using solid-phase hydrogenation.¹¹² This difference can be explained by the fact that the liquid-phase hydrogenation proceeds in the active sites of the catalyst, while in the solid-phase process, atoms of the metal catalyst generate activated tritium species, which react with a steroid molecule. Evidently, when the steroid is adsorbed on the catalyst active sites during hydrogenation in solution, the influence of the steric factors is maximum; however, if the active species of tritium attack the double bonds of the substrate molecule adsorbed on a support, the formation of 5 α -isomers is more likely.

The dependence of the 5 α - to 5 β -isomer ratio on the reaction temperature can be followed using the data of Table 30, which presents also the amounts of isomers in the reaction mixture obtained from 1 mg of the substance introduced in the reaction.

For the solid-phase hydrogenation of unsaturated carbon–heteroatom bonds, thorough selection of the labelling conditions is required. For example, the nitrile of glycolic acid was used as the precursor in the synthesis of labelled ethanolamine. This precursor was reduced in the presence of 5% Pt/C, 5% Pd/C, 5% Rh/Al₂O₃ and 5% Rh/CaCO₃.^{113–115} The 5% Rh/C catalyst (Table 31), a temperature of 100 °C and a reaction time of 20 min were found to be the best conditions as regards the synthesis of a highly labelled specimen (1.04–1.48 PBq mol⁻¹). When palladium catalysts are used, the labelled specimen is

Table 30. Ratio (*z*), amounts (*m*₁, *m*₂) and molar radioactivities of the 5 α - and 5 β -isomers of compound **1** in the reaction mixture at various temperatures.

<i>T</i> /°C	<i>z</i>	<i>m</i> ₁ /mg mg ⁻¹	<i>m</i> ₂ /mg mg ⁻¹	MR ^a (rel.u.)
80	1:3	0.16	0.46	1.04
100	1:2.7	0.17	0.45	1.27
110	1:2.1	0.20	0.41	1.49
140	1:1.8	0.15	0.28	2.84
170	1:1.5	0.08	0.13	—

^a The radioactivity of saturated steroids obtained by the liquid-phase method.

Table 31. Relative molar radioactivities of the specimen prepared by the reduction of glycolic acid nitrile (catalyst 5% Rh/C, the catalyst:substance ratio is 5:1) at different reaction temperatures and durations.

<i>T</i> /°C	RMR (%) (see ^a)	τ /min	RMR (%) (see ^b)
20	11	5	26
50	31	10	50
70	55	15	80
90	67	20	100
100	100	30	92
120	85	40	78
140	66	50	57
160	33	60	29
180	13	75	16
190	6	90	11
		120	9
		150	6

^a Reaction time 20 min. ^b Reaction temperature 100 °C.

formed in 10%–20% yield and has a molar radioactivity of 0.15–0.22 PBq mol⁻¹ (see Ref. 114). This rather low yield can be explained by assuming that dehydration, deamination and other reactions take place in parallel on the metal catalysts.^{61, 69}

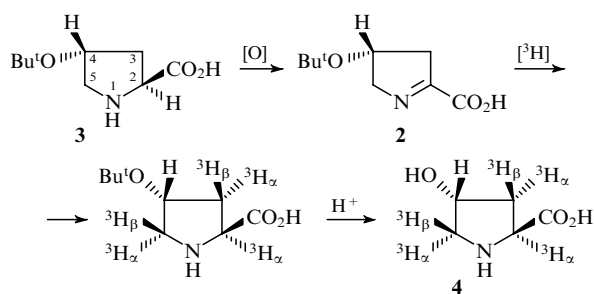
As an example of solid-phase reduction of the keto group, one can consider the synthesis of [2-³H]inositol from *scyllo*-inosose (pentahydroxycyclohexanone) and 2,2,6,6-tetramethyl-4-hydroxypiperidine from 2,2,6,6-tetramethyl-4-oxopiperidine.^{62, 113} To select the optimal conditions for the reduction of *scyllo*-inosose, the 5% Pd/CaCO₃, 5% Rh/Al₂O₃, 5% Pd/BaSO₄, 5% Pt/C and 5% Pd/C catalysts were tested. The best results were attained with the rhodium catalyst (the catalyst: substrate ratio was 10:1) and with heating to 150 °C for 15 min (the molar radioactivity of the labelled specimen was 0.56 PBq mol⁻¹ and the yield was 25%). 2,2,6,6-Tetramethyl-4-oxopiperidine was hydrogenated on 5% Rh/C to give 2,2,6,6-tetramethyl-4-hydroxypiperidine (see Table 29).

The molar radioactivities attained upon labelling in the former and in the latter case differ by a factor of ~9, as the efficiency of isotope exchange depends appreciably on the structure of the compound. In the former case, the keto–enol tautomerism of *scyllo*-inosose is hampered and the label is inserted only *via* ketone hydrogenation. In the latter case, all four α -hydrogen atoms have time to be replaced before the keto group is reduced. This appears to be a weighty reason supporting the formation of ³H⁺ as the activated species in the spillover.

Apart from the reduction of the C $\equiv$ N fragment to C³H₂NH₂ and the C=O fragment to C³(H)OH, data on hydrogenation of C=NOH to C³H₂NH₂ have been reported. For example, reduction of 2,2,6,6-tetramethyl-4-hydroxyiminopiperidine to 2,2,6,6-tetramethyl-4-aminopiperidine has been described;⁶² in this case, the isotope exchange is no less intensive than in the case of reduction of 2,2,6,6-tetramethyl-4-oxopiperidine (see Table 29).

In order to have an apprehension of the mechanism of solid-phase hydrogenation, Zolotarev *et al.* studied¹¹⁶ the reduction of (*R*)-4-*tert*-butoxy-4,5-dihydro-3H-pyrrole-2-carboxylic acid (**2**) prepared from amino acid **3**.

Compound **2** was applied onto alumina, dried and mechanically mixed with 5% Pd/BaSO₄. The mixture was subjected to freeze-drying (at a catalyst:Al₂O₃:substrate ratio of 10:20:1, *T* = 100 °C, τ = 60 min). After the reaction, the *tert*-butyl protection was removed by treating the reaction mixture with hydrochloric acid and the product was purified by the procedure described previously.^{117–119} The yield of (*R*)-4-hydroxy[G-³H]-L-proline (**4**) was 23% and the molar radioactivity was 1.85 PBq mol⁻¹. The isotopomer was isolated in a yield of 4%. The distribution of the label was determined by ³H NMR spectroscopy.



The distribution of the label in proline **4**, obtained by hydrogenation of compound **2** by tritium gas at 100 °C, was as follows:

Position of the label	3 β	3 α	5 α	5 β	2	4
Content of the label (%)	29	20	0	35	16	0

4,5-Dihydro-3H-pyrrole-2-carboxylic acid was used as the reference compound. The distribution of the label in [G-³H]proline (the molar radioactivity was 2.07 PBq mol⁻¹) obtained on hydrogenation of 4,5-dihydro-3H-pyrrole-2-carboxylic acid at 100 °C is given by

Position of the label	3 β	3 α	5	2	4
Content of the label (%)	34	34	6	26	0

Apparently, the first stage of hydrogenation of compound **2** involves the capture of tritium cations by nitrogen and oxygen atoms; as a consequence, the mobility of hydrogen at the third and fifth carbon atoms substantially increases and the carboxy group acquires the ability to occupy the *trans*-position relative to the 4-*tert*-butoxy group. Therefore, hydrogenation of the initial double bond can be accompanied by the addition of tritium into the 2-, 3- and 5-positions. The attack by tritium of the 5-position occurs necessarily from the β -H side; the attack of the 3-position is governed, on the one hand, by shielding of the β -H atom by the carboxy group and, on the other hand, by shielding of the α -H atom by the 4-*tert*-butoxy group. Thus, the contents of tritium in the α - and β -positions at C(3) should be comparable. Indeed, the data presented here on the distribution of the label show that the label is missing from the 5 α -position of proline **4**, while the ratio of the degrees of labelling at C(3) is 29:20 in favour of the 3 β -position. This may be due to the fact that the label in the 2-position of proline **4** appears, in the researchers' opinion,¹¹⁶ upon the intramolecular transfer of tritium from the 3 α -position of the molecule. If hydrogenation of 4,5-dihydro-3H-pyrrole-2-carboxylic acid gives a racemate, no steric restrictions are involved in the labelling of the C(3) atom, and the major portion of tritium is found at the 3-position of the molecule of this amino acid. For the same reason, the content of the label at the 2-position of the proline molecule increases and the probability of tritium insertion into the 5-position decreases ~6-fold.

If the first stage of the solid-phase hydrogenation is the reaction of the substrate with the tritium cations, it is reasonable to assume that the addition of the tritium cations to the molecules of unsaturated amino acid gives two options for the subsequent transformations: (1) capture of an electron to give a radical, which undergoes recombination with atomic tritium; (2) hydrogenation involving tritium gas on the sites arising due to the spillover.⁷⁻¹¹ The observed steric effects may be indicative of a predominant direct participation of tritium gas in the hydrogenation.

As an example, Fig. 3 shows the curves for the time variation of the yield of the labelled amino acid obtained by the reduction of 2-benzoylamino-3,3-dimethylacrylic acid to give *N*-benzoyl[³H]-valine (2.74 PBq mol⁻¹) at different temperatures and different pressures of tritium gas.⁸¹ It can be seen that with an increase in temperature, duration and pressure of tritium gas, the hydrogenation rate increases, but below 100 °C, the reaction does not proceed to completion,⁸¹ although even at 60 °C, isotope equilibration of virtually all the labile hydrogen atoms (attached to nitrogen, oxygen, sulfur and other atoms) takes place as a result of

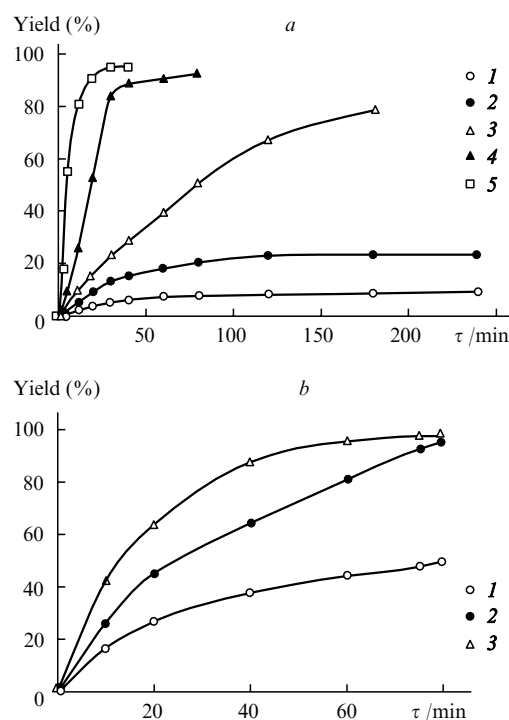


Figure 3. Yield of the labelled product of solid-phase hydrogenation of 2-benzoylamino-3,3-dimethylacrylic acid ($P = 333$ hPa, 5% Pd/BaSO₄ as the catalyst) vs. reaction time at different temperatures (a) and different pressures (b).

a: $T/^{\circ}\text{C}$: (1) 60, (2) 80, (3) 100, (4) 120, (5) 140;
b: P/hPa : (1) 50, (2) 150, (3) 250; $T = 120^{\circ}\text{C}$.

tritium spillover. Apparently, this is due to the fact that at these temperatures, the metal catalyst is rapidly saturated with hydrogen and deactivated (see Section IV).

The activation energy for hydrogenation of 2-benzoylamino-3,3-dimethylacrylic acid (46.09 kJ mol⁻¹) is close to the activation energy for the isotope exchange between valine and tritium gas (50.28 kJ mol⁻¹).^{81, 120} In the researchers' opinion, this attests that both reactions are limited by the same step of tritium inclusion. These values are in good agreement with the well-known activation energy of the solid-phase hydrogenolysis on platinum metals.⁷ It can be asserted that this step is not isotope exchange because the activation energies for the isotope exchange and hydrogenation depend appreciably on the nature of the substrate and differ even for different fragments of the same molecule. The assumption that a process related to the formation of active tritium species and to the spillover of these species to the reaction area is the limiting step seems doubtful. It has been shown⁸¹ that even at 20 °C, the active hydrogen atoms in the 2-benzoylamino-3,3-dimethylacrylic acid molecule are replaced by tritium over a period of 20 min. Therefore, the most plausible assumption is that the activation energies presented above are due to the fact that the tritium cation has to approach a carbon atom of the organic compound for the formation of the transition state.

The solid-phase hydrogenation technique can be used to reduce uridine derivatives. For example, the reduction of 5-hydroxymethyl-2'-deoxyuridine 5'-monophosphate (7% Pd/BaSO₄, $T = 170^{\circ}\text{C}$, $\tau = 30$ min) yielded thymidine 5'-monophosphate with a molar radioactivity of 2.54 PBq mol⁻¹ in 10% yield.¹²¹ It is of interest that the use of hydrogenation to prepare high-labelled purine and pyrimidine compounds gave no advantages over isotope exchange.⁷⁸ For example, the reduction of 5-formyluracil and 5-hydroxymethyluracil to thymine gave labelled preparations with molar radioactivities of 3.15 and 4.07 PBq mol⁻¹, respectively,^{80, 122, 123} while labelled thymine

obtained by isotope exchange had a molar radioactivity of $4.26 \text{ PBq mol}^{-1}$. In the case of reduction of 5-hydroxymethyl-deoxyuridine to thymidine, the molar radioactivity was even lower ($2.82 \text{ PBq mol}^{-1}$).¹²⁴

3. Solid-phase dehalogenation

Catalytic dehalogenation is the best known hydrogenolysis reaction. If tritium gas is used as the reagent, dehalogenation gives rise to tritium-containing compounds.

Usually, aromatic compounds are dehalogenated by a liquid-phase procedure.¹⁰⁵ This affords labelled specimens with a molar radioactivity of $0.7\text{--}0.9 \text{ PBq mol}^{-1}$. However, the liquid-phase approach cannot be used, as a rule, for labelling of saturated halogen-containing compounds under conditions acceptable for work with tritium gas.

The solid-phase catalytic dehalogenation was first employed to introduce a tritium label into uracil.¹ Characteristic features of this reaction as applied to tritium labelling of nucleic acid components have been studied in detail.¹²⁵

The advantages of the solid-phase approach have been demonstrated in relation to the dehalogenation of aliphatic compounds.⁶⁰ 11-Chloroundecanoic acid was chosen as the model compound for working out the conditions for the labelling of aliphatic compounds by dehalogenation. The dependence of the degree of labelling of both 11-chloroundecanoic acid and undecanoic acid formed in the reaction on the nature of the catalyst and the reaction temperature was studied (Fig. 4). The molar radioactivity of 11-chloroundecanoic acid reached $6.30 \text{ PBq mol}^{-1}$, while that of the undecanoic acid formed from it was $4.20 \text{ PBq mol}^{-1}$. For comparison, debromination of 3-bromo-

propionic acid (10% Pd/C, 1 M NaOH, $\tau = 4 \text{ h}$, $P = 905 \text{ hPa}$) furnishes $[3\text{-}^3\text{H}]$ propionic acid with a molar radioactivity of $0.72 \text{ PBq mol}^{-1}$ (see Ref. 126).

It can be seen from the above data that under the optimal conditions (10% Pd/BaSO₄, $T = 180^\circ\text{C}$), the yield of undecanoic acid reached 25%–30%. If the goal was to label the starting compound, the reaction was carried out at 170°C and the yield of the chlorine-containing precursor was 50%–60% (see Fig. 4). It was found that the isotope exchange in halogen-containing saturated acids proceeded much more readily than dehalogenation. Apparently, this is due to the fact that halogens are nucleophiles and can be removed from the organic molecule under these conditions only as hydrogen halides. Therefore, the solid-phase dehalogenation of aliphatic compounds at relatively low temperatures is less probable than isotope exchange. At high temperatures, a radical mechanism of dehalogenation is most likely.

The introduction of a label *via* solid-phase dehalogenation has been studied in detail for bromo-substituted components of nucleic acids (Table 32).^{75, 127}

Table 32. Molar radioactivities of labelled heteroaromatic compounds prepared by solid-phase debromination (5% Pd/C, $T = 100^\circ\text{C}$, $\tau = 120 \text{ min}$; the position of tritium corresponds to the bromine position in the precursor).

Compound	MR /PBq mol ⁻¹	Compound	MR /PBq mol ⁻¹
[5- ³ H]Uracil	0.60	[8- ³ H]Guanosine	0.19
[8- ³ H]Guanine	0.46	5'-monophosphate	
[5- ³ H]Cytidine	0.60	[5- ³ H]Uridine	0.10
[8- ³ H]Guanosine	0.25	5'-monophosphate	
[8- ³ H]Adenosine	0.39	[5- ³ H]Cytidine	0.22
[5- ³ H]Uridine	0.43	5'-monophosphate	
[5- ³ H]2'-Deoxyuridine	0.68	[8- ³ H]2'-Deoxyadenine	0.08
		5'-monophosphate	
[5- ³ H]2'-Deoxycytidine[8- ³ H]	1.22	[8- ³ H]2'-Deoxyguanosine 5'-mono-	0.06
2'-Deoxyadenine	0.61	phosphate	
[8- ³ H]Adenosine	0.18	[5- ³ H]2'-Deoxycytidine	0.06
5'-monophosphate		5'-monophosphate	

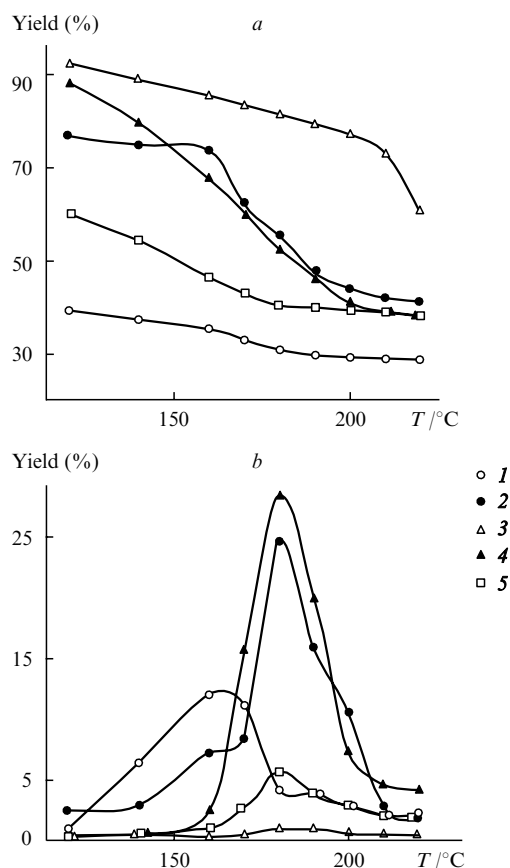


Figure 4. Yield of labelled 11-chloroundecanoic acid (a) and undecanoic acid produced from it (b) vs. temperature and the catalyst nature (the catalyst : acid ratio is 5 : 1, $\tau = 20 \text{ min}$).

(1) 5% Pt/C; (2) 10% Pd/C; (3) 5% Pd/C; (4) 10% Pd/BaSO₄; (5) 5% Rh/C.

It has been shown¹²⁷ that the degree of dehalogenation increases with an increase in the palladium content on carbon or with an increase in the catalyst to substance ratio. This is due to the fact that hydrogen bromide deactivating the catalyst is formed as a side product. When a certain palladium : halogen-containing precursor ratio was reached, the yield increased to 85%–90% and then remained constant. Therefore, the notion of catalytic capacity of the catalyst was introduced for these reactions. This value is defined as the number of moles of the halogen derivative which can be converted into the debrominated compound by a particular amount (weighed portion) of the palladium catalyst. During the study, it was found that these compounds cannot migrate over the support surface; therefore, the catalytic capacity depends on the reaction temperature and the nature of the initial halogen derivative.

Solid-phase dehalogenation of aromatic compounds is less efficient than dehalogenation in solution (Table 33). In the latter case, the experimental procedure is simpler and better reproducible, the reaction products can be more easily purified and often have better radiochemical parameters. Therefore, study of the solid-phase dehalogenation of aromatic compounds makes sense if it is necessary to label a halogen-substituted biologically active compound with retention of its native structure. For example, alprazolam was converted into a labelled preparation with a molar radioactivity of $0.15 \text{ PBq mol}^{-1}$ without loss of chlorine even at 175°C ,¹²⁸ i.e., selective isotope exchange was carried out for an

Table 33. Molar radioactivities of labelled aromatic compounds obtained by debromination in solution (the position of tritium corresponds to the bromine position in the precursor).

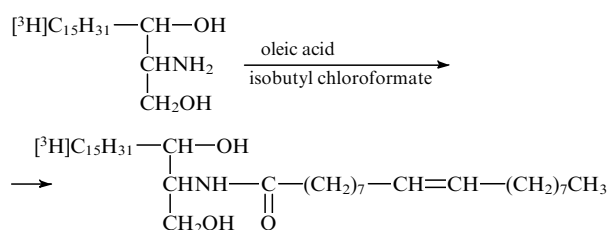
Compound	MR /PBq mol ⁻¹	Compound	MR /PBq mol ⁻¹
[8- ³ H]Adenosine	0.36	[8- ³ H]GMP	0.41
[8- ³ H]Guanosine	0.47	[5- ³ H]Cytidine	0.64
[5- ³ H]Uracil	0.67	[2- ³ H]Adenine	0.93
[5- ³ H]Uridine	0.78	[2,8- ³ H]Adenine	1.85
[5- ³ H]2'-Deoxy- uridine	0.79	[5- ³ H]Cytosine	1.11
[8- ³ H]AMP	0.23	[8- ³ H]ATP	0.63
[5- ³ H]UMP	0.14	[8- ³ H]GTP	0.41
[5- ³ H]CMP	0.04	[5- ³ H]UTP	0.63
		[5- ³ H]CTP	0.78

Note. The following designations are used: UMP is uridine 5'-monophosphate, CMP is cytidine 5'-monophosphate, GMP is guanosine 5'-monophosphate, GTP is guanosine 5'-triphosphate, UTP is uridine 5'-triphosphate, CTP is cytidine 5'-triphosphate.

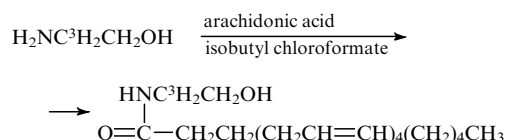
organic molecule containing fragments labile under a tritium gas atmosphere.

4. Preparation of tritium-containing compounds on the basis of reagents labelled by the solid-phase method

In some cases, it proves to be more difficult to introduce a label into a biologically active compound than into one of its fragments. In these cases, the label is introduced into this fragment and then the structure of the molecule is reconstituted. For example, *N*-oleoyldihydrosphingosine with a high molar radioactivity was synthesised in two stages. First, dihydrosphingosine was labelled by a solid-phase procedure;⁶⁹ then the product was condensed with oleic acid by the method of mixed anhydrides.

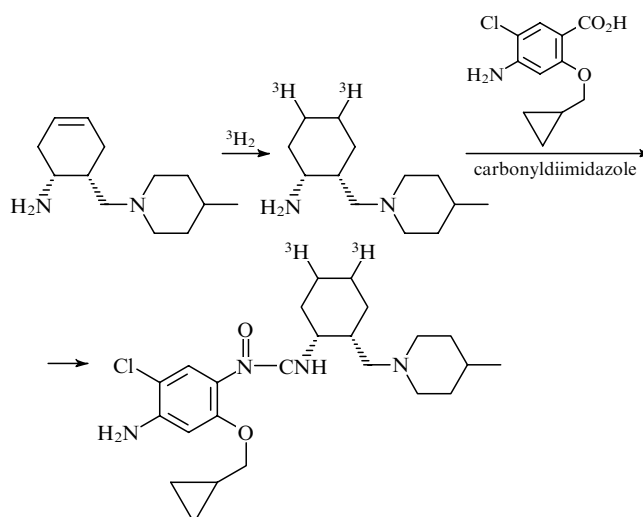


2-Hydroxyethylamides of eicosapolyenoic acids were synthesised in a similar way. Evidently, it is impossible to introduce any significant amounts of tritium into the final compound without affecting the double bonds of polyunsaturated fatty acids. Therefore, solid-phase tritiation of glycolic acid nitrile was used to obtain aminoethanol,¹¹⁴ which was then condensed with a fatty acid by the method of mixed anhydrides.



The unlabelled reagent was taken in a tenfold excess.

The condensing agents used in this type of reactions include carbonyldiimidazole, carbonylditriazole and carbodiimides. For example, carbonyldiimidazole was used to prepare labelled (1*R*,2*R*)-*N*-[2-(4-methylpiperidylmethyl)cyclohexyl]-4-amino-5-chloro-2-cyclopropylmethoxybenzamide.⁷⁴



Acetylation of amines by non-labelled reagents presents no problem. Reactions using acetic anhydride, acetyl chloride, *etc.* give high yields of amides. However, synthesis of labelled analogues of these compounds presents a number of difficulties, which make these procedures unattractive. The main difficulty is high volatility of these substances. Work with such compounds (unlike non-volatile compounds) can be carried out only in a specially equipped laboratory. In addition, extensive use of these reagents is hampered by their high cost. Sodium acetate can be labelled by a direct reaction, as it is non-volatile (m.p. = 324 °C);⁶¹ therefore, this compound makes a convenient reagent for the preparation of labelled amides. The method consists of mixing of solutions of labelled sodium acetate¹²⁹ and amine hydrochloride; this gives labelled acetic acid and sodium chloride. After addition of the condensing agent, the tube is sealed and heated. When the reaction has been completed, the contents of the tube are frozen and refrozen to separate non-volatile products, the residue is dissolved in methanol, and the solution is acidified by hydrochloric acid and concentrated to remove traces of labelled acetic acid. Dicyclohexylcarbodiimide and carbonylditriazole were used as condensing agents. The best results were attained with carbonylditriazole (the yield of the labelled preparation reached 15%).

5. The selectivity problems in the solid-phase hydrogenolysis by tritium

It has been shown above that molecules containing halogen atoms can be labelled using selective isotope exchange. As has already been noted, labelling of alprazolam made it possible to obtain a labelled specimen with a molar radioactivity of 0.15 PBq mol⁻¹ (see Ref. 128).

This Section considers approaches designed for solid-phase labelling either by isotope exchange when the substrate molecules contain readily reducible fragments (for example, nitro groups or double bonds) or by selective dehalogenation and hydrogenation (Fig. 5, Table 34).^{130, 131} The selective hydrogenation can involve

Table 34. Molar radioactivities of labile compounds labelled in the presence of heterogeneous platinum group metal catalysts.¹³¹

Compound	<i>T</i> / °C	MR / PBq mol ⁻¹
9-Nitrocamptothecin	190	0.59
Dimethomorpholine	160	0.24
Thyroxine	180	0.25
Methyl ester of <i>N</i> -nitroarginine	180	0.85
Etomidate	160	0.86
Vitamin K ₁	130	2.3

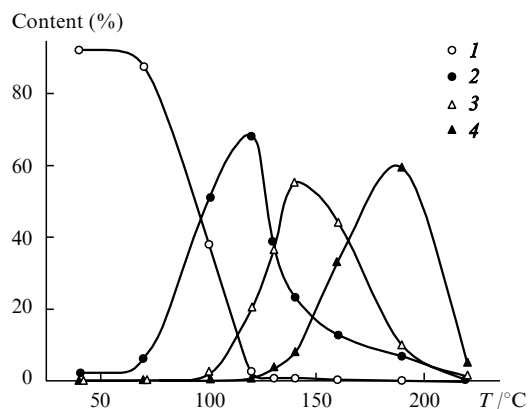
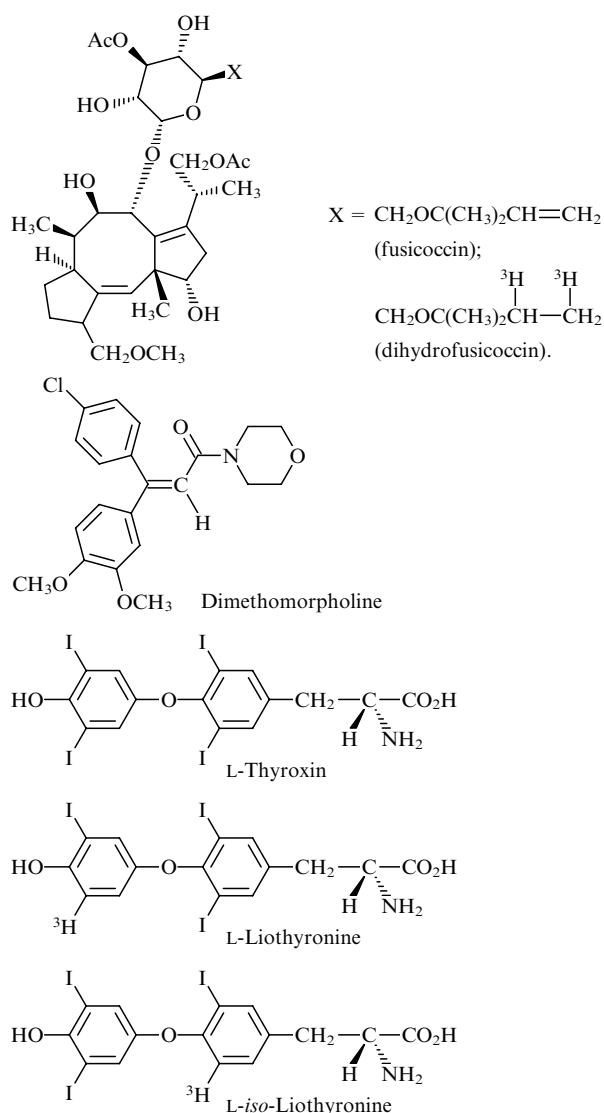


Figure 5. Temperature dependence of the content of hydrogenation products of fusicoccin in the reaction mixture.¹³⁰ (1) Fusicoccin, (2) dihydrofusicoccin (DHF); (3) [³H₄]tetrahydrofusicoccin (THF); (4) [³H₆]hexahydrofusicoccin (HHF).

either hydrogenation of one or several double bonds or hydrogenation of one aromatic fragment in the presence of several other such fragments.



For compounds containing nitro groups, isotope exchange was carried out at temperatures of 180–190 °C and for compounds containing double bonds, at 100–160 °C.

As noted above, stability of a biologically active compound can be increased by using rhodium trichloride, an additional support or a partially deactivated catalyst. For example, in the case of thyroxine and vitamin K₁, palladium catalysts deactivated by lead diacetate were used;¹³⁰ rhodium trichloride was employed for dimethomorpholine⁷³ and an additional support, for etomidate.¹³¹

For selecting the optimal conditions for labelling compounds with double carbon–carbon bonds, a special study has been carried out to establish the temperatures of reduction of double bonds with different degrees of substitution.¹³⁰

Fusicoccin was chosen as the model compound to elucidate the conditions of labelling by selective solid-phase hydrogenation of one double bond,^{132–134} because this compound contains mono-, tri- and tetra-substituted double bonds. Selective solid-phase hydrogenation was studied in the temperature range of 40–220 °C, the reaction time and the pressure of tritium gas being also varied (see Fig. 5, Table 35). The selective hydrogenation of a monosubstituted double bond starts even at 40 °C and proceeds efficiently at 100 °C.

Table 35. Dependence of the content of major hydrogenation products of fusicoccin in the reaction mixture on the pressure of tritium gas and the reaction time ($T = 100$ °C, the Lindlar catalyst: substance ratio is 10:1).¹²⁹

Reaction conditions		Content (%)		
P /hPa	τ /min	fusicoccin	[³ H ₂]DGP	[³ H ₄]TGP
210	20	38	51	2
280	20	32	57	2
350	20	13	60	3
350	60	6	69	4

An increase in the pressure of tritium gas and the reaction time affect to a lesser extent the process selectivity.¹³⁰ If the goal of the experiment is to obtain the highest yield of dihydrofusicoccin, the reaction should be carried out at 130 °C (see Fig. 5).

The results were verified during labelling of vitamin K₁ (Table 36).¹³⁰ The presented data show that trisubstituted double bonds withstood temperatures in the 120–140 °C range; therefore, labelling of vitamin K₁ was carried out at 130 °C (see Table 34).

Table 36. Content of vitamin K₁ in the reaction mixture and degree of isotope exchange at different temperatures of tritium labelling (the Lindlar catalyst: substance ratio is 10:1, $P = 333$ hPa, $\tau = 20$ min).¹³⁰

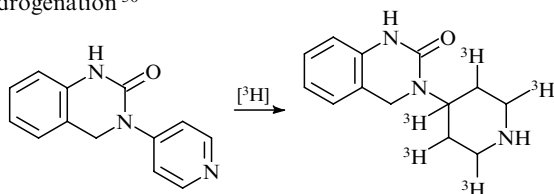
T /°C	Content (%)	RMR (%)	Radiochemical purity (%) (see ^a)
80	99	9	95
100	68	16	64
120	60	52	21
140	16	100	8

^a Radioactivity of the label in the substance divided by the radioactivity of the reaction mixture.

Thyroxine was used as the halogen-containing compound to study the possibility of labelling by selective dehalogenation. At high temperatures (180–200 °C), liothyronine and *iso*-liothyronine could be isolated from the reaction mixture in a pure state. At 180 °C ($\tau = 10$ min), the yields of these compounds were 3.2% and 0.4%, and at 200 °C ($\tau = 5$ min), they were 5.3% and 1.3%, respectively. The molar radioactivity of the dehalogenated products reached 0.7 PBq mol⁻¹ (see Ref. 130).

Research into solid-phase hydrogenation and dehalogenation is usually necessary for studying the stability of a particular labile fragment in the molecule corresponding to a given class of compounds and to carry out solid-phase isotope exchange with retention of the native state of the initial compound as, for example, in the case of labelling of vitamin K₁.

An absolutely different situation occurs in working out the conditions of selective hydrogenation of one aromatic fragment in the presence of other aromatic fragments (for example, the pyridine and benzene rings). Hydrogenation of aromatic compounds in solution is known to occur only at very low pH.^{68,135} However this results in high isotope dilution of the labelled specimen. For example, in the synthesis of cyclohexylmethylamine from benzylamine using the liquid-phase hydrogenation procedure, the molar radioactivity of the labelled preparation was 1.66 PBq mol⁻¹, while the solid-phase hydrogenation procedure gave a specimen with a molar radioactivity of 7.78 PBq mol⁻¹ (see Ref. 68). In this case, the advantage of the solid-phase approach is obvious. Apparently, the nature of the activated tritium species is largely responsible for whether or not the process can, in principle, be selective. If these species are cations, the process selectivity would be high (the pyridine fragment is protonated much more efficiently than the benzene fragment). The aromatic structure of the pyridine fragment is violated and hydrogenation is thus facilitated. Thus in the case of selective hydrogenation⁵⁰



the labelled molecule contained five tritium atoms (6.44 PBq mol⁻¹). The content of this product in the reaction mixture was 7 times as high as the total content of all other substances, *i.e.*, the process was highly selective. This indicates that tritium cations play an active role in the hydrogen spillover. In other words, the specificity of solid-phase reactions may be largely responsible for the relative stability of organic compounds labile under the conditions of hydrogenolysis. Therefore, below we consider the features of solid-phase reactions that influence not only the retention of the native structure of the initial compounds (including chirality) but the distribution of the label in the molecules.

IV. Characteristics of solid-phase hydrogenolysis by tritium

A leading specialist in the synthesis of tritium-labelled organic compounds, Evans, has noted¹³⁶ that labelling methods in which organic compounds are kept under a tritium atmosphere with process initiation by a Tesla discharge or by UV or γ -radiation or gas exposure of a material applied on a heterogeneous catalyst are nothing but various modifications of the Wilzbach method. Many researchers still adhere to this point of view.¹³⁷ However, back in the 1960s, it was found that the label distribution in the aromatic ring obtained using heterogeneous catalysts differs appreciably from that obtained using other procedures (Tables 37, 38).^{138,139}

It can be seen from these data that electrophilic substitution predominates in the replacement of hydrogen in the aromatic ring by tritium using heterogeneous catalysts, whereas in other cases, radical substitution is the prevailing process. A similar tendency has been noted in another publication.¹⁴⁰ For example, upon labelling of a peptide with N-terminal tyrosine supported on a heterogeneous catalyst at 135 °C, the amount of the label inserted in the *ortho*-position relative to the hydroxy group of tyrosine was ~20 times as high as that in the *meta*-position.

Table 37. Distribution of the label (%) in toluene introduced by the Wilzbach method and by its modifications.¹³⁸

Label position	No activating factor (Wilzbach method)	Activation method		
		γ -radiation	Tesla discharge	UV radiation
<i>ortho</i>	56.5	54.7	39.7	49.8
<i>meta</i>	29.3	29.3	40.8	33.5
<i>para</i>	14.2	16.0	19.5	16.7

Table 38. Distribution of the label in benzoic and salicylic acids introduced by the Wilzbach method (I) and by treatment with tritium gas of the acids applied on the heterogeneous catalyst (II).¹³⁹

Acid	Content of the label (%) in the position		
	<i>ortho</i>	<i>meta</i>	<i>para</i>
Benzoic	58.3	21.3	20.4
	5.0	72.5	22.5
Salicylic	39.0 ^a	48.4 ^a	13.6 ^a
	16.9 ^a	31.7 ^a	51.4 ^a

Note. The value indicated above the bar was obtained using method I and that below the bar was obtained using method II. ^a Relative to the hydroxy group.

Thus, the mechanism of reactions between tritium gas and a substance applied on a heterogeneous catalyst differs from that involved in labelling by the Wilzbach method.

Usually, this is related to the processes taking place when catalysts are saturated with hydrogen.^{141–143} According to a view proposed and substantiated on the basis of a study of the valence state of hydrogen in intermetallic hydrides,¹⁴¹ hydride dispersion can be considered as being due to a redox process giving rise to hydride ions H ^{δ^-} , which takes place when the hydrogen concentration (*c_H*) in the solid hydride is higher than a critical concentration *c_{Hcr}*. The *c_{Hcr}* value is determined by the redox potential of the reaction



where MM is the metallic matrix of the catalyst.

According to this model, hydrogen chemisorbed on the active sites of the catalyst surface donates some of its s-electrons to the conduction band of the metal. Therefore, at low *c_H* values, the behaviour of absorbed hydrogen is described satisfactorily by the Ubbelode model,¹⁴² which implies high diffusional mobility of H ^{$\delta+$} and an increase (or, at least no decrease) in the electrical conductivity of the hydride phase with respect to that of the initial metal. The *c_{Hcr}* value corresponds to a concentration of the oxidant (H ^{$\delta+$}) at which these species oxidise the metallic matrix and become electron density acceptors, being converted into bulky and low-mobility H ^{$\delta-$} ions, and thus deplete the conduction band of the metal. It is evident that at higher degrees of filling of voids by H ^{$\delta-$} ions having a relatively great effective volume, the electron deficiency on the metal atoms that form the metal sublattice in the crystal structure of the catalyst should increase, which may restrict the reversible adsorption of hydrogen. This sharply decreases the concentration of activated species (tritium, in the case of preparation of labelled substances) able to enter into exchange reactions, and hence arrests almost completely the isotope exchange. The *c_{Hcr}* value may not be attained for a long period when hydrogen spillover takes place.

The causes of the transfer of activated species from the metal crystallite to the support are not discussed here in detail, as this has been the subject of numerous publications (see, for example, Refs 144–148) which evaluate how this process is affected by adsorp-

tion of molecular hydrogen, extensive rearrangement of the sorbent surface, relaxation of disordered structures and other factors. The migration of a proton over the oxygen-containing surface of the support follows a relay mechanism. The activation energy of this transfer equals 20.1 kJ mol^{-1} (see Ref. 149). Study of spillover over the support surface revealed both electronic and ionic conduction.³⁵ Therefore, the observed process, unlike those involved in the Wilzbach method, can be described more reliably in terms of the 'capacitor model' proposed by Shevchenko *et al.*¹⁵⁰ According to this model, the $^3\text{H}^+$ ions and the electrons formed in the reaction of tritium gas with the catalyst migrate separately over the surface. The support surface acts as a sort of multilayer capacitor. Depending on the experimental conditions, interaction of tritium cations with electrons (discharge of the neighbouring oppositely charged zones) takes place with one or another probability, giving rise to tritium atoms, which rapidly recombine and pass to the gas phase. When the flux of $^3\text{H}^+$ ions and electrons reaches the substrate, isotope exchange, hydrogenation, dehalogenation and other reactions occur efficiently. If the substrate contains easily protonated groups, the degree of labelling should markedly diminish. It is evident that at higher temperatures, the probability of interaction between neighbouring oppositely charged zones would increase; therefore, the contribution of the reactions of atomic tritium to the processes resulting in the formation of the labelled compound would also increase. Thus, if the substrate contains readily protonated groups, the molar radioactivity of the labelled product should markedly increase with temperature rise (the neutral species of atomic tritium would react more efficiently with these compounds). As an example, one can consider the above-mentioned preparation of labelled peptide with N-terminal tyrosine. Thus at 150°C , the degree of labelling of the *ortho*-position relative to the hydroxy group of tyrosine was only 3 times higher than that of the *meta*-position and the molar radioactivity increased 1.9-fold.¹⁴⁰

The distribution of the label in aromatic amino acids is especially useful for elucidation of the nature of the activated tritium species. This can be illustrated using the distribution of the label in aromatic rings of tyrosine and serotonin as examples. The contents (%) of the label in the aromatic rings (the total amount of the label in the ring was taken to be 100%) were as follows:¹⁰⁴

Position	<i>ortho</i>	<i>meta</i>
Tyrosine	78	22
Serotonin	85	15

As noted in the previous Section, the distribution of the label corresponding to that expected in terms of the electrophilic substitution model can serve as strong evidence supporting the assumption that the tritium cation is the activated species involved in the hydrogen spillover.

The published data provide grounds for two conclusions: (1) inclusion of the label follows predominantly the electrophilic substitution mechanism; (2) the lower the reaction temperature, the higher the predominance of electrophilic substitution. The 'capacitor model' concept is useful for explaining the roles of particular factors in the preparation of tritium-labelled specimens and eliminates many contradictions arising in the study of the theoretical aspects of this problem.

For example, the capacitor model can account for the high yields of labelled specimens obtained *via* solid-phase reactions. This is due to the fact that the participation of atomic tritium in the labelling is insignificant, as the radical detachment of hydrogen followed by recombination of the resulting radical is a more intricate process than the mere recombination of atomic tritium.^{151–153}

As noted above, the mechanism of tritium labelling influences the distribution of the label in organic molecules. For instance, a ^3H NMR study (alanine supported on carbon was labelled in the presence of platinum group catalysts) has shown¹⁴⁰ that at 130°C , the rate of tritium inclusion to the third carbon atom is

7.5 times as high as that to the second carbon atom. In the $70–155^\circ\text{C}$ range, the rate constant for isotope exchange changed by two orders of magnitude (the activation energy was equal to 62.8 kJ mol^{-1}). At 30°C , the isotope label was selectively inserted into the methyl group of alanine, whereas, at 190°C , the label was uniformly distributed throughout the alanine molecules. The activation energy of the isotope exchange in the methyl group of alanine was 58.7 kJ mol^{-1} and that for the alanine methine group was $107.7 \text{ kJ mol}^{-1}$. This sharp difference can be explained in the following way. The amino group is readily protonated, which hampers the reaction of $^3\text{H}^+$ with the carbon atom of the methine group of alanine. The charge that appears on nitrogen induces migration of the electron density in the methyl group (hyperconjugation⁴⁵). As a result, the deficit of electron density on the carbon atom at the 2-position is compensated, the methyl-group hydrogen atoms become more active, and the activation energy of isotope exchange at the third carbon atom decreases. At higher temperatures (190°C), radical elimination reactions become more significant. Therefore, the labelling efficiency at the 2-position sharply increases, which is responsible for the different label distribution.

The validity of this approach is confirmed by the distribution of the label in some other amino acids (Table 39). Only in the case of serine and methionine was the C(2) position labelled to a higher degree. Apparently, this is due to the fact that oxygen and sulfur, like amino groups, are easily protonated and the carboxy group located near the amino group makes the isotope exchange at C(2) prevailing.

Table 39. Distribution of the label (%) in amino acids applied on heterogeneous catalysts and treated with tritium gas at 150°C .¹⁰⁴

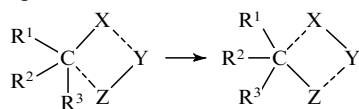
Amino acid	Content of the label at the atoms				
	C(2)	C(3)	C(4)	C(5)	C(6)
Alanine	4	96			
Asparagine	40	60			
Aspartic acid	40	60			
Arginine	19	23	14	44	
Proline	9	6	4	81	
Methionine	75		4	21	
Serine	70	30			
Threonine	18	9	73		
Leucine	4	5	5	86	
Lysine	31	10	12	18	29
Valine	4	4	92		

The possibility of introducing a label into organic substances susceptible to hydrolysis is also largely determined by the mechanism of this process. It is known that liquid-phase reactions proceed in the active sites of the catalyst. These sites adsorb, first of all, unsaturated fragments of molecules and, hence, hydrogenolysis and hydrogenation are the predominant types of reactions. Under solid-phase conditions, labelling is due to reactions of molecules of the substance with activated tritium. Apparently, reduction of the $\text{N}-\text{CHR}-\text{C}_6\text{H}_5$ and $\text{O}-\text{CHR}-\text{C}_6\text{H}_5$ fragments to toluene or its derivatives or reduction of the $-\text{NO}_2$, $=\text{N}-\text{OR}$ groups to amino groups, *etc.*, would be hampered under solid-phase reaction conditions, as nitrogen and oxygen atoms are prone to be protonated and isotope exchange can be carried out selectively without disturbing the native structures of biologically active products. An important feature of solid-phase hydrogenolysis is the retention of the initial structure of compounds including chirality. Now we consider the reasons for this fact.

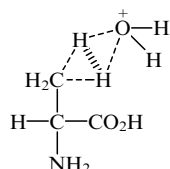
When labelling biologically active compounds, researchers pay considerable attention to the problem of preserving the

optical activity. Only the invariability of the native conformation of compounds can ensure the retention of the initial biological properties of the substrate.

Research into characteristic features of electrophilic substitution in the series of aliphatic compounds⁴⁵ basically ended in the 1960s. Bimolecular (S_E2), monomolecular (S_E1) and intramolecular (S_{EI}) mechanisms of electrophilic substitution were found. Of special interest for our purposes are data concerning the S_{EI} mechanism because it is obvious that upon substitution according to this mechanism, the stereochemical configuration does not change.



The results of calculation of the spatial repulsion forces based on the putative structures of the transition state were consistent with experimental results.⁴⁵ The mechanism of the solid-phase isotope exchange has been studied by quantum-chemical calculations.¹⁵⁴ The water molecule was taken as Y. The results of Dewar AM1 semiempirical calculations of fragments of the potential energy surface for the interaction of alanine carbon atoms with the hydroxonium ion were refined by Hartree–Fock *ab initio* calculations in the 3-21G and 6-31G basis sets using the GAMESS program. According to the results obtained, the activation energy of isotope exchange decreases due to an additional interaction of hydrogen atoms, *i.e.*, this transition state is additionally stabilised by a bond between the exchanging hydrogen ions. In the transition state, tritium attacks the C–H bond from the same side as where the atom being replaced is located, *i.e.*, the S_{EI} mechanism is executed. Thus, if this isotope exchange takes place at a chiral carbon atom, the native configuration of the initial compound will be retained. The transition state involved in the S_{EI} mechanism of electrophilic aliphatic substitution can be represented as follows:¹⁵⁴



Direct evidence for the assumption that the active species of hydrogen react with the substrate without modifying its crystal lattice was obtained in the 1980s.¹⁵⁵ Experiments were carried out with 4-isopropyl-3-methylphenol. This compound is not optically active in solution but it spontaneously forms chiral structures (dextro- and levorotatory crystals) upon crystallisation. The powder obtained from one sort of 4-isopropyl-3-methylphenol crystals was tritiated with 5% Pt/C and kept for 95 min at 80 °C under a hydrogen atmosphere. The reaction product proved to be optically active.

At higher temperatures where the contribution of atomic tritium to the isotope exchange becomes substantial, the absence of racemisation can be explained by the fact that the activation energy for radical elimination reactions is markedly lower than that for the electrophilic isotope exchange (Table 40). Apparently, in this case, the retention of chirality is due to the fact that the rate of recombination of the resulting radicals is incomparable with the rates of radical formation or, all the more, conformational changes.

The possibility of preparing labelled compounds containing trisubstituted unsaturated carbon–carbon bonds depends also on the nature of activated tritium. It is known⁴⁵ that the transfer of $^3H^+$ is the rate-determining step of hydrogenation and that the carbenium ion ($R'-H^3HC-C^+H-CH_2R$) is formed as the intermediate product. This intermediate is reduced to give a saturated compound. Thus, the presence of an easily protonated

Table 40. Kinetic parameters of the radical elimination and addition reactions.¹⁵²

Reaction	E_{c0} /kJ mol ⁻¹	$10^{11}r_c$ /m	$(r^+/r_c)_0$	ΔH /kJ mol ⁻¹
$H^+ + RH \rightarrow H_2 + R^+$	54.6	3.762	0.48	94.5
$H^+ + CH_2=CHX \rightarrow$ $\rightarrow CH_3C^+HX$	101.6	4.563	0.41	227.6
$H^+ + HOR \rightarrow$ $\rightarrow H_2 + RO^+$	38.3	2.812	0.47	33.5
$H^+ + O=CR^1R^2 \rightarrow$ $\rightarrow HOC^+R^1R^2$	102.9	4.401	0.38	149.7

Note. The following designations are used: r_c is the distance equal to the sum of vibration amplitudes of atoms of the reacting bonds in the transition state; r^+ is the parameter characterising the position of the transition state on the section r_c ; the $(r^+/r_c)_0$ ratio characterises the position of the transition state for $\Delta H = 0$.

fragment which has acquired a charge near a C=C bond decreases the probability of protonation of this double bond and thus this bond is additionally strengthened. The formation of carbenium ions during the solid-phase hydrogenation is indirectly confirmed by the possibility of double bond migration ($R'-H^3HC-CH=CHR$). This process is detected most easily if $R = OH$. In this case, migration of the double bond gives an aldehyde stable under the reaction conditions. For example, in hydrogenation of allyl alcohol at room temperature under solid-phase conditions, the yield of aldehyde was $\sim 10\% - 20\%$.¹⁵⁶ Thus, by solid-phase reactions, it is possible to carry out selective isotope exchange and obtain unsaturated labelled preparations.

If the reaction is carried out at a higher temperature, one should bear in mind that double bonds may be reduced by atomic tritium. Comparison of the kinetics of radical addition and elimination reactions has shown that hydrogen elimination always proceeds more easily than hydrogen addition to a double bond. This is due to different geometries of the reaction centre and to stronger repulsion in the non-linear centre, which is formed upon the reaction of activated hydrogen with the double bond (see Table 40).⁴³ Another important parameter is the force constant of the bond being attacked, which is always higher for a multiple bond than for a single bond. Moreover, the activation energy of the addition reaction depends more appreciably on the enthalpy change than the activation energy of elimination. As a result, the major process is recombination of atomic tritium, resulting from coupling of tritium cations with electrons, which increases the stability of unsaturated compounds under these conditions.

Thus, if the organic molecule contains easily protonated fragments, they are the first to react with activated tritium species. If the protonated fragments in the molecule are labile, this may give a series of specific side products. In the labelling of compounds whose melting points are higher than the temperature used to conduct the isotope exchange, the degree of isotope exchange would mainly depend on the efficiency of tritium spillover in the bulk of the organic substance applied on a catalyst. If protonated fragments or charged groups present initially in the molecule prevent electrophilic substitution or tritium spillover to the bulk of the organic compound, the final molar radioactivity of the labelled specimen would substantially diminish.

Indeed, it was noticed long ago¹³⁶ that the exchange of hydrogen isotopes occurs, first of all, in hydroxy, carboxy, amino and other functional groups. When tritium labelling by solid-phase isotope exchange is carried out for amines⁶⁸ (benzylamine, spermine, ethylenediamine and its derivatives) (Table 41), a series of deaminated products are formed; in the case of spermine, it was impossible to isolate the labelled specimen from the reaction mixture.

Table 41. Molar radioactivity and yield of tritium-labelled amines (5% Pd/C, $T = 190\text{ }^{\circ}\text{C}$, $\tau = 15\text{ min}$).^{53,61,74}

Compound	MR /PBq mol ⁻¹	Yield (%)
Ethylenediamine	0.13	50
Piperazine	0.32	23
1,4-Diazabicyclo[2.2.2]octane	0.46	15

In the labelling of high-melting compounds, the physicochemical properties of the starting compound exert a considerable influence on the final molar radioactivity of the labelled compound. For example, whereas in methyl stearate molecules (m.p. = $39\text{ }^{\circ}\text{C}$) hydrogen is replaced almost completely by tritium, in the case of sodium acetate (m.p. = $324\text{ }^{\circ}\text{C}$), according to ^3H NMR spectroscopy,⁶⁸ only some of the molecules occur in the areas where isotope exchange proceeds efficiently.

Analysis of the ^3H NMR spectra of labelled sodium acetate has shown that labelled molecules comprise 74% triply substituted, 24% doubly substituted and 2% monosubstituted isotopomers, *i.e.*, the molar radioactivity should be $\sim 3\text{ PBq mol}^{-1}$. However, in reality, the molar radioactivity of [^3H]CH₃CO₂Na was $1.1\text{--}1.3\text{ PBq mol}^{-1}$. The reason is that the ^3H NMR technique allows one to determine only the ratio of different tritium-containing isotopomers in sodium acetate molecules. The amount of the unlabelled initial substance remaining in the reaction mixture is not detected by ^3H NMR spectroscopy. Therefore, the discrepancy between the results obtained by ^3H NMR and by radioactivity measurements is due to the fact that $\sim 60\%$ of sodium acetate has not entered into the isotope exchange, which markedly decreases the final molar radioactivity of the labelled preparation. Indeed, as shown by micrographic studies,¹⁵⁷ solid-phase hydrogenolysis of another high-melting compound, namely, disodium *trans*-epoxysuccinate (m.p. = $262\text{ }^{\circ}\text{C}$), is not accompanied by a noticeable diffusion of this compound over the surface of the palladium catalyst.

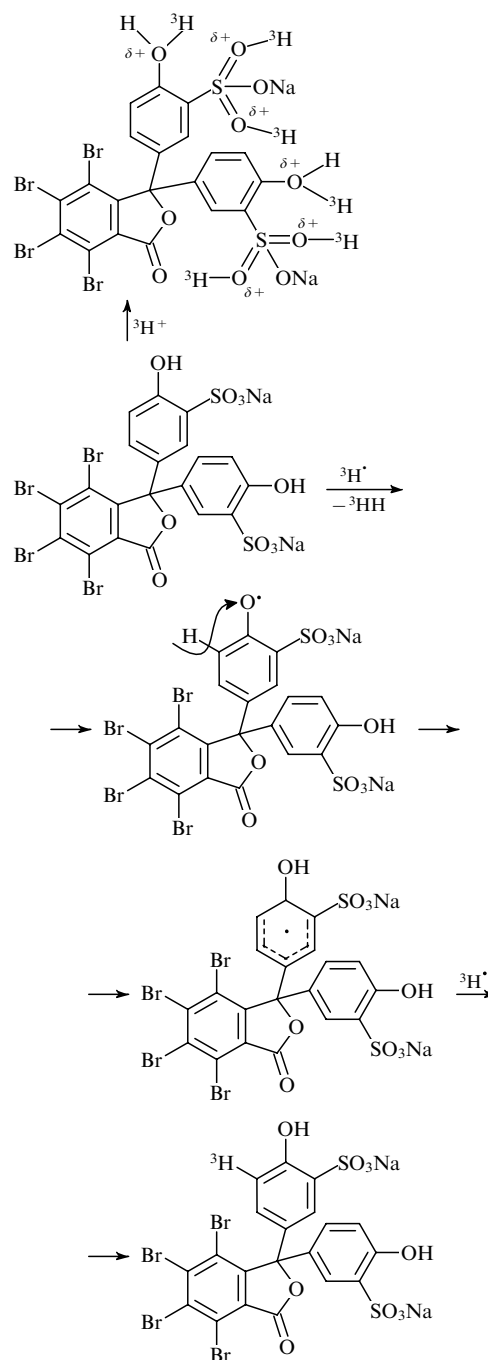
Thus, if the melting point of the compound is comparable with or lower than the temperature at which the isotope exchange is carried out, displacement of substrate molecules relative to one another is possible; each molecule can be subjected to the action of activated tritium with the same probability,⁶⁰ and the effect of the tritium spillover to the bulk of the given substance on the final molar radioactivity of the labelled specimen is moderate. This can be illustrated by the following data on the molar radioactivity obtained upon solid-phase tritium labelling of fatty acids:²⁹

Acid	Stearic	Palmitic	Myristic	Lauric
MR /PBq mol ⁻¹	13.0–13.5	12.5–12.9	12.0–12.1	11.0–11.5

To confirm the statement that solid-phase reactions can involve both tritium cations and atomic tritium whose contributions to the final molar radioactivity of the labelled specimen depend on the nature of the initial compound, it was necessary to choose a model compound that, on the one hand, could serve as a sort of trap for tritium cations and, on the other hand, would be sufficiently thermally stable to ensure favourable conditions for isotope exchange involving atomic tritium.

A series of compounds have been tested,⁵³ but they proved to be either good substrates for tritium cations or insufficiently thermally stable. Sulfobromophthalein satisfied the above-out-

lined conditions to the highest extent.¹⁵⁸ The synthetic route to the tritium-labelled sulfobromophthalein is presented below:



This compound contains easily protonated groups (including sulfo groups), which may give rise to a substantial positive charge; in addition, it withstood heating to $280\text{--}290\text{ }^{\circ}\text{C}$ in the presence of a catalyst in an atmosphere of tritium gas. The label was introduced in the presence of palladium supported on barium sulfate, calcium carbonate, carbon or alumina. The catalyst : substance ratio was 10 : 1 and the temperature range was $150\text{--}290\text{ }^{\circ}\text{C}$. At $150\text{--}180\text{ }^{\circ}\text{C}$, the yield of the specimen was almost quantitative; at $180\text{--}220\text{ }^{\circ}\text{C}$, it gradually decreased to 60%; at $250\text{ }^{\circ}\text{C}$, to 53%; at $270\text{ }^{\circ}\text{C}$, to 46%; and at $285\text{ }^{\circ}\text{C}$, to 34%. Even when the reaction

was carried out at 210 °C for 0.5 h, the molar radioactivity of the labelled specimen did not exceed 0.08 PBq mol⁻¹. Only at temperatures higher than 285 °C did the radioactivity reach 0.5–0.6 PBq mol⁻¹. The fact that the aromatic compound containing four bromine atoms can be isolated in 30%–50% yield after the reaction with tritium gas at these high temperatures attests to the lack of interaction between tritium cations and protonated sulfobromophthalein molecules.

The observed phenomenon supports the view that labelling proceeds in this case by the mechanism of radical elimination of hydrogen with subsequent recombination of the resulting radical. Indeed, the reaction of atomic tritium with the phenolic fragment of the sulfobromophthalein yields the aryloxy radical, which then undergoes recombination with the abstraction of hydrogen from the *ortho*-position. This gives a radical which can be stabilised upon conjugation with the radical centre delocalised over three positions of the benzene ring.⁴⁵ This is followed by the reaction with atomic tritium to give the labelled specimen. It is clear that the spillover of electrically neutral atomic tritium into the bulk of the substrate crystallite would take place even if the molecules of the substance contain easily protonated groups.

Thus, labelling in solid-phase reactions involves both tritium cations and tritium atoms. The molar radioactivity of labelled specimens at relatively low temperatures (usually below 180 °C) is mainly determined by reactions of the organic compound with tritium cations. The degree of isotope exchange depends mainly on the efficiency of tritium spillover to the bulk of the organic compound applied on the catalyst. At higher temperatures, the contribution of atomic tritium in the labelling increases.

V. Conclusion

This review covers the results of synthesis of labelled specimens using solid-phase hydrogenolysis reactions including hydrogenation and isotope exchange with tritium. The regularities of these reactions were studied, in particular, the effects of the nature of the substrate and the catalyst, the pressure of tritium gas, the process duration, temperature, *etc.* on the yield and molar radioactivity of the resulting specimens. Examples of preparation of labelled biologically active compounds are cited.

It was found that at temperatures below 180 °C used most often for solid-phase labelling, the key radiochemical parameters of labelled specimens (yield, molar radioactivity, tritium distribution) are governed by the reaction of ³H⁺ with the substrate. At higher temperatures, the concentration of atomic tritium increases. In this case, especially for substrates containing easily protonated groups, the molar radioactivity of the product should markedly increase (non-charged species of atomic tritium react more efficiently with these compounds).

The service life of the catalyst depends on the time it takes to reach a certain threshold concentration of hydrogen in the crystallites of the metal catalyst, c_{H_2} . The time required to reach this value is dictated by the relationship between the rate of saturation of metal crystallites with tritium gas and the efficiency of its spillover. The efficiency of tritium spillover as applied to the synthesis of labelled organic compounds is determined by the time period tritium exists as a system of cations and electrons solvated on the support surface and in the substrate bulk.

If the goal is to prepare a labelled specimen in a high yield and with the distribution of the label corresponding most closely to that obtained upon electrophilic substitution, the solid-phase reaction should be carried out at the lowest temperature that would ensure the required molar radioactivity. The reaction time is determined by the period of catalyst deactivation. If the aim is to obtain the labelled specimen with the highest possible molar radioactivity, the reaction is carried out in the temperature range in which the required [³H]-labelled compound can be isolated in a yield of at least 5%–10%. The reaction time is usually 5–15 min.

Judging by the data reported in the literature, a promising expedient is to combine various catalysts (palladium–rhodium or

palladium–technetium mixed catalyst), supports (separate application of the catalyst and the substrate followed by mechanical mixing) or substrates (consecutive application of several substrates). These approaches increase the yield of the labelled specimen and in some cases, the synthesis of such substances would be otherwise impossible.

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^e — *Russ. J. Appl. Chem. (Engl. Transl.)*

^f — *Kinet. Catal. (Engl. Transl.)*

Naphthaldehydes

A F Pozharskii

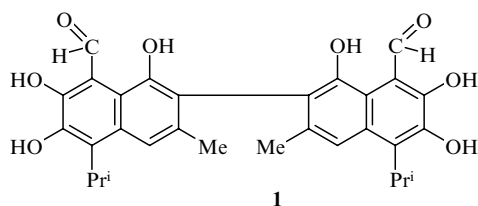
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Abstract. Data on methods for the preparation of naphthaldehydes, their physicochemical properties, structural characteristics and reactivities are generalised. Particular attention is given to procedures for formylation of naphthalenes and *peri*-interactions involving the aldehyde group in the α -position. The bibliography includes 201 references.

I. Introduction

Naphthaldehydes^{1–3} play a very important role in naphthalene chemistry, much as other aldehydes play a significant part in the chemistry of other classes of organic compounds, which is associated primarily with the diversity of reactions involving these compounds. The high reactivity of the formyl group is widely utilised in the synthesis of complex natural compounds containing the naphthalene fragment. In addition, naphthaldehydes and, primarily, α -naphthaldehydes possess specific features, which receive the continuing attention of both synthetic and theoretical chemists. Among these features are, in particular, different manifestations of *peri*-interactions^{4–6} and the possibility of performing *peri*-cyclisation.⁷ Interest in naphthaldehydes has increased substantially after isolation of gossypol (**1**), *viz.*, 2,2'-binaphthyl polyphenol dialdehyde, from cotton seeds. This compound appeared to be the first efficient contraceptive pill for men.⁸



Gossypol also exhibits antitumor and antiviral activity and, in spite of substantial toxicity, is registered in some countries for use as a pharmaceutical. It was established that the toxicity of

gossypol is associated with the presence of aldehyde groups. However, all attempts to replace these groups by other functionalities led only to the disappearance of biological activity (the history of the discovery of gossypol and its chemical and pharmacological properties were surveyed in a review).⁸

The published data on the chemistry of naphthaldehydes are voluminous and scattered throughout various sources. These data have not been generalised, except for outdated information summarised in the monographs,^{9,10} which causes great inconvenience for researchers. This fact gave impetus to the present review. Since it is practically impossible to cite all studies concerning naphthaldehydes, emphasis is given to main trends associated with the synthesis, reactions and physicochemical characteristics of these compounds. Most attention is concentrated on the preparation of naphthaldehydes by direct formylation of naphthalenes or naphthalene carbanions (organometallic compounds), *peri*-interactions, *peri*-cyclisation reactions involving the α -formyl group, characteristic features of the molecular structures of these compounds and their relationship with physicochemical properties and reactivity. Other aspects of the chemistry of naphthaldehydes are considered as necessary.

II. Synthesis of naphthaldehydes

Naphthaldehydes can be prepared according to virtually all procedures generally used in the synthesis of aromatic aldehydes.^{1–3,11} In addition to direct formylation, these methods involve oxidation of methyl-, hydroxymethyl- and halomethyl-substituted naphthalenes, reduction of nitriles and naphthalene-carboxylic acid chlorides, *etc.* Data on these methods published up to the mid-1950s are generalised in the monograph.⁹ Since then, almost all the above-mentioned synthesis methods have been improved primarily due to the use of new reagents. Generally, this enables one to use milder conditions of reactions and enhance their selectivity. The most typical examples are considered below.

1. Formylation of naphthalenes

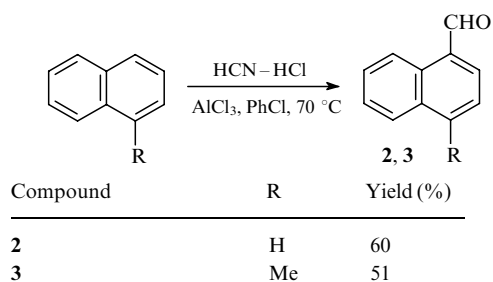
a. Naphthalene and alkynaphthalenes

Gattermann formylation (under the action of a mixture of HCN and HCl in the presence of AlCl_3 , CuCl_2 or other Lewis acids) of naphthalene¹² and α -methylnaphthalene¹³ afforded α -naphthaldehyde (**2**) and its 4-methyl derivative **3**. The modification of this reaction consists in replacing HCN by less toxic $\text{Zn}(\text{CN})_2$ (Adams method)¹⁴ or *sym*-triazine.¹⁵ Thus, the synthesis with the use of *sym*-triazine afforded aldehyde **2** in 57% yield.

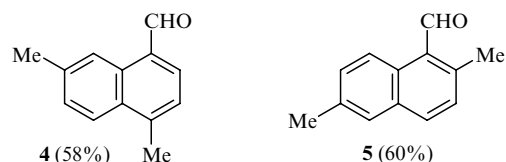
A F Pozharskii Department of Chemistry, Rostov State University, ul. Zorge 7, 344090 Rostov-on-Don, Russian Federation.
Fax (7-863) 224 59 05. Tel. (7-863) 222 39 58.
E-mail: APozharskii@chimfak.rsu.ru

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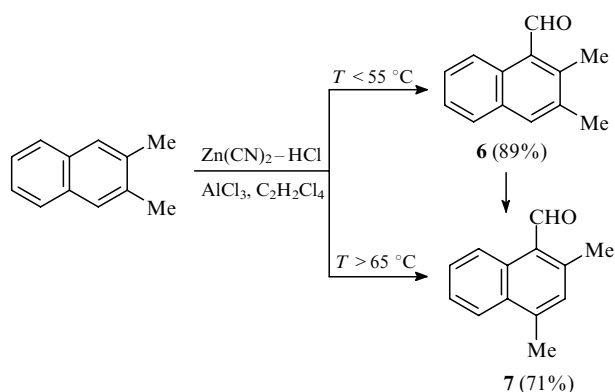
Uspekhi Khimii 72 (5) 498–523 (2002); translated by T N Safonova



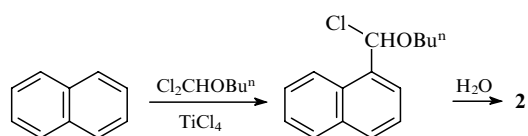
Under the conditions of the Gattermann reaction, 1,6- and 2,6-dimethylnaphthalenes gave aldehydes **4** and **5**, respectively.¹²



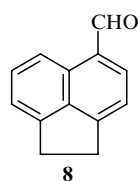
Formylation of 2,3-dimethylnaphthalene should be carried out with thorough control over the reaction temperature. Thus, 'normal' product **6** was generated in good yield only at a temperature below 55 °C, whereas it was transformed into 2,4-dimethyl-1-naphthaldehyde (**7**) at a temperature above 65 °C.^{16, 17}



Naphthalene is readily subjected to formylation by dichloromethyl *n*-butyl ether in the presence of TiCl₄ (Rieche method).¹⁸ Apparently, this procedure is among the simplest approaches to α -naphthaldehyde **2** (79% yield).



Naphthalene does not react with the milder formylating Vilsmeier reagent^{19, 20} (a mixture of POCl₃ with *N,N*-dimethylformamide or other formamide derivatives, for example, with *N*-methylformanilide). However, the reaction of acenaphthene performed under these conditions afforded acenaphthene-5-carbaldehyde (**8**) (81% yield).^{21, 22}

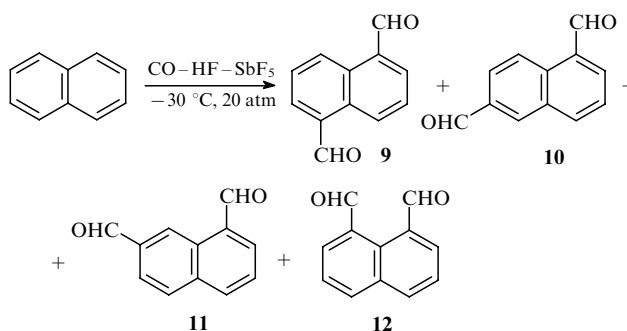


Recently, a convenient procedure was proposed for the preparation of aldehyde **8** by microwave irradiation of a mixture of acenaphthene and the Vilsmeier complex on a support (DMF-POCl₃-SiO₂, 300 W, 2 min, 89% yield).²³ Naphthalene, like acenaphthene, is formylated by the modified Vilsmeier complex in which phosphorus oxychloride is replaced by trifluorome-

thanesulfonic anhydride.²⁰ The reaction proceeded under very severe conditions (130 °C, 48 h) to give aldehydes **2** and **8** in 50% and 90% yields, respectively.

Under standard conditions of the Gattermann-Koch reaction (CO-HCl, AlCl₃), naphthalene does not undergo formylation.²⁴ However, aldehyde **2** was prepared with the use of the CO-HF-BF₃ system under high pressure.²⁵ It was demonstrated that formyl fluoride served as the true formylating agent in this reaction.²⁶ In the presence of BF₃, the latter compound reacted (CS₂, 0–10 °C, 3–5 h) with naphthalene to form a mixture of α - and β -naphthaldehydes in 20% and 67% yields, respectively. Considering the traditionally higher reactivity of the α positions in naphthalene compared to the β positions, the formation of β -naphthaldehyde as the major product under such mild conditions seems to be surprising. However, this fact was not commented in the study²⁶ and the review.²⁷

The modified Gattermann-Koch reaction with the use of the stronger Lewis catalyst SbF₅ instead of BF₃ can lead to diformylation of naphthalene.²⁸ This reaction afforded a mixture of 1,5- (**9**), 1,6- (**10**), 1,7- (**11**) and 1,8-diformylnaphthalenes (**12**) in a total yield of 80% in a ratio of **9**:**10**:**11**:**12** = 51:6:27:16. It should be noted that the positions of substituents in formylation products of naphthalene differ substantially from those in nitration products. It is known that nitration gives rise to 1,8- and 1,5-dinitronaphthalenes in a ratio of ~7:3.⁹ By contrast, 1,5-dialdehyde prevails among diformylation products, the second highest yield was observed for the 1,7-isomer. Apparently, the first step of this reaction affords β -naphthaldehyde in a noticeable amount and further formylation of the latter at the free α positions of the unsubstituted ring gives dialdehydes **10** and **11**.



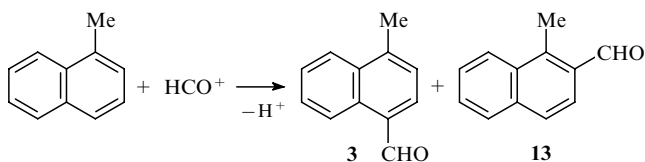
When studying Gattermann-Koch (CO-HF-SbF₅) and Friedel-Crafts (HCOF-HF-SbF₅) formylation of α -methyl-naphthalene, Tanaka and co-workers^{29, 30} found that the rate and regioselectivity of the Gattermann-Koch reaction depend on the SbF₅: α -methyl-naphthalene molar ratio (Table 1). The authors attributed this fact to a superposition of two mechanisms

Table 1. Results of Gattermann-Koch (GK) and Friedel-Crafts (FC) formylation of α -methyl-naphthalene.³⁰

Molar ratio SbF ₅ : α -methyl-naphthalene	Reagent	Temperature /°C	Time /h	Product ratio 3 : 13	Reaction type
1:1	CO	0	2	100:0	GK
1.25:1.00	CO	0	0.15	68:32	ditto
1.25:1.00	CO	-40	2	64:36	"
1:1	HCOF	0	1	93:7	FC
1.25:1.00	HCOF	0	1	94:6	ditto
1.25:1.00	HCOF	-40	1	94:6	"
2:1	HCOF	-40	1	94:6	"

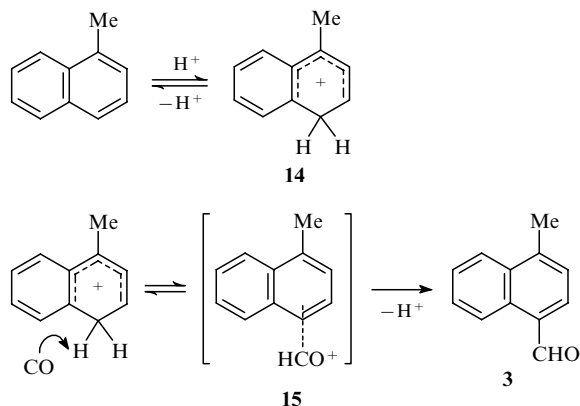
Note. Reaction conditions: 10 mmol of 1-methylnaphthalene, 500 mmol of HF; CO pressure was 20 atm (GK reaction); 80 mmol of HCOF (FC reaction).

of electrophilic substitution, *viz.*, conventional and non-conventional (intracomplex). In the course of formylation by a conventional mechanism, the electrophilic species (HCO^+), which is generated through the reaction of the reagent acting as a protoelectrophile (CO or HCOF) with protic (HF) or Lewis (SbF_5) acid, attacks the aromatic substrate at the *ortho* or *para* positions with respect to the methyl group to form the corresponding σ -complexes, which give aldehydes **3** and **13**.



In the naphthalene series, σ -complexes corresponding to α substitution are more stable than σ -complexes corresponding to β substitution. Hence, *para* isomer **3** is generally produced in higher yield than *ortho* isomer **13**.

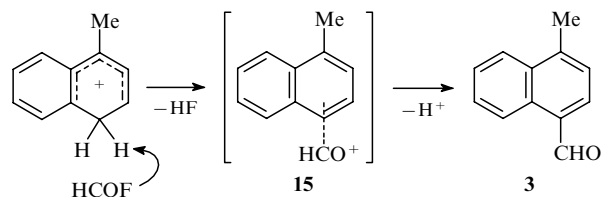
The first step of formylation according to an alternative mechanism involves protonation of the substrate giving rise exclusively to methylnaphthenium cation **14**. The latter donates a proton to the protoelectrophile (CO) thus transforming it into the active electrophile. If the electrophile and substrate in the *para*-oriented π -complex **15** thus produced have no time to move apart, their interaction gives rise to the *para*- σ -complex and finally (after proton elimination) to *para*-aldehyde **3**.



If the substrate and electrophile in complex **15** are separated, the reaction mechanism consists of the usual electrophilic attack.

The highest regioselectivity of the Gattermann–Koch reaction is observed at the SbF_5 : α -methylnaphthalene molar ratio of 1:1. Since the HF – SbF_5 system acts as a superacid, this reagent ratio allows the substrate to be completely protonated to give methylnaphthenium cation **14**. As a result, the reaction proceeds by an intracomplex mechanism to give *para* isomer **3** as the only product. In the presence of a larger amount of SbF_5 and, consequently, a larger amount of the superacid, carbon monoxide molecules are also subjected to protonation to give the HCO^+ cations. Since the reaction of the latter with cation **14** is unlikely, the contribution of the conventional mechanism of formylation increases and, as a consequence, the yield of *ortho* isomer **13** increases.

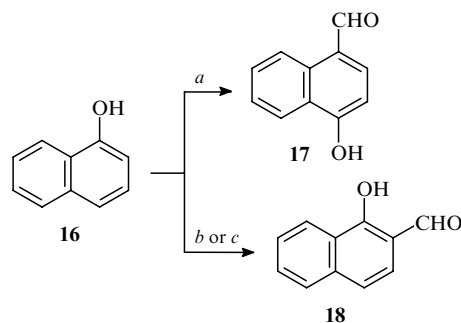
Since the basicity of formyl fluoride is lower than that of carbon monoxide, the dependence of the Friedel–Crafts reaction on the amount of SbF_5 is less pronounced and the constancy of the *para/ortho* regioselectivity most likely indicates that the reaction proceeds predominantly by the intracomplex mechanism.



Formylation of naphthalene and its 1- and 2-methyl derivatives was also performed with the use of triformamide $\text{N}(\text{CHO})_3$ in the presence of AlCl_3 . However, these reactions afforded aldehydes **2** and **3** and 2-methyl-1-naphthaldehyde in low yields (18%–30%).³¹

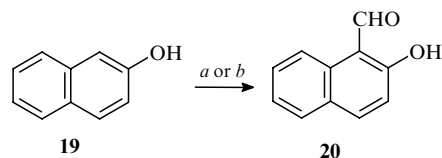
b. Naphthols and alkoxy- and alkylthionaphthalenes

Depending on the nature of the formylating agent, α -naphthol (**16**) is formylated at either *ortho* or *para* position with respect to the hydroxy group. For example, the reaction of compound **16** with the HCN – AlCl_3 system (Gattermann reaction) afforded 4-hydroxy-1-naphthaldehyde (**17**) in high yield,^{14, 32, 33} whereas the Reimer–Tiemann reaction (70–80 °C, CHCl_3 – NaOH) gave rise to its *ortho* isomer **18** in ~40% yield.³⁴ Apparently, one of the best methods for the synthesis of the latter compound involves the reaction of α -naphthol with orthoformic ester in the presence of AlCl_3 producing aldehyde **18** in almost quantitative yield.³⁵ The reaction of α -naphthol with α, α -dichlorodimethyl ether in the presence of TiCl_4 (Rieche method) afforded a mixture of aldehydes **17** and **18** in 68% and 10% yields, respectively.³⁵



(a) HCN – AlCl_3 (>90%); (b) CHCl_3 – NaOH (38%–48%); (c) $\text{HC}(\text{OEt})_3$ – AlCl_3 (97%).

Formylation of β -naphthol (**19**) gave rise to 2-hydroxy-1-naphthaldehyde (**20**) regardless of the method used. The Gattermann reaction with the use of the HCN – ZnCl_2 system³³ or the $\text{Zn}(\text{CN})_2$ – HCl system¹⁴ produced aldehyde **20** in virtually quantitative yield. However, even in spite of lower yields, this hydroxy aldehyde is much more convenient to prepare by the Duff³⁶ (with the use of urotopine and acetic acid), Rieche,³⁵ Vilsmeier³⁷ and, particularly, Reimer–Tiemann reactions.³⁸

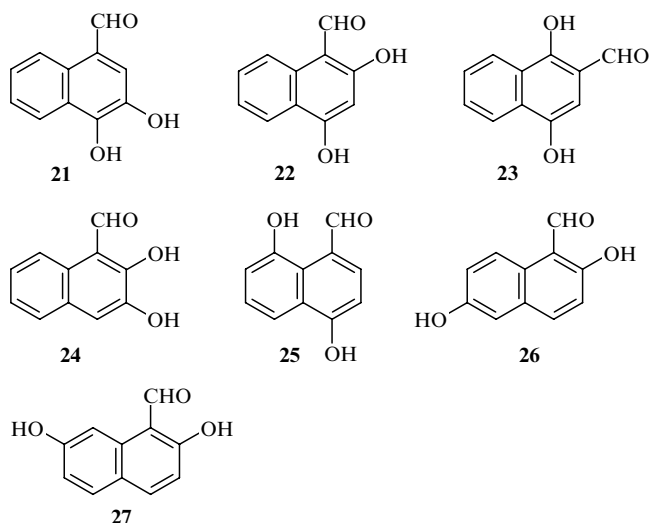


(a) $(\text{CH}_2)_6\text{N}_4$ – AcOH (76%); (b) CHCl_3 – NaOH (40%).

Recently, the $(\text{CH}_2\text{O})_n$ – MgCl_2 – Et_3N system in acetonitrile was proposed for *ortho*-formylation of phenols.³⁹ In this reaction, β -naphthol gave aldehyde **20** (72%) and 1-methoxymethyl-2-naphthol (9%).

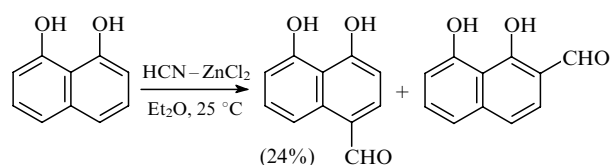
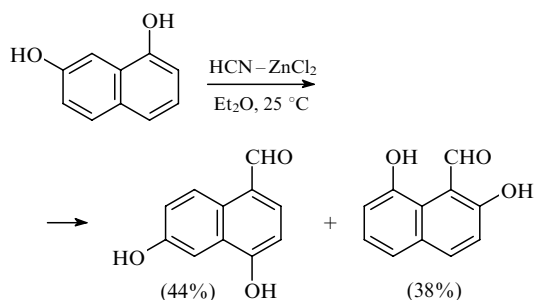
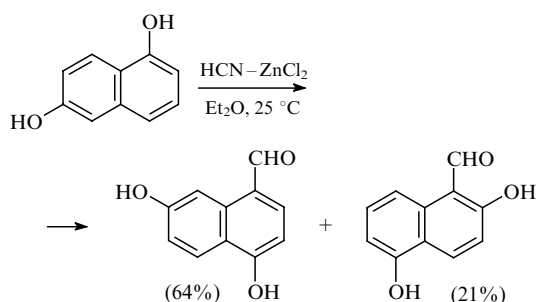
Gattermann formylation (HCN – ZnCl_2 , ether, 20 °C) of 1,2-dihydroxy-, 1,3-dihydroxy-, 1,4-dihydroxy-, 2,3-dihydroxy-, 1,5-dihydroxy-, 2,6-dihydroxy- and 2,7-dihydroxynaphthalenes

afforded aldehydes **21**–**27**, respectively, as the only products.^{40, 41} Aldehyde **25** can also be synthesised by Rieche formylation of 1,5-dihydroxynaphthalene. However, the latter reaction is accompanied by the formation of impurities, which are difficult to separate.⁴²



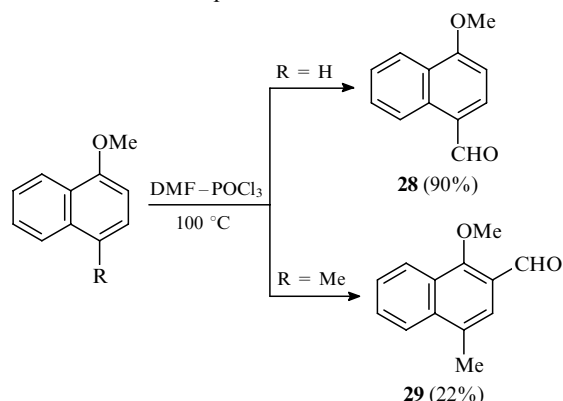
Compound	Yield (%)	Ref.
21	21	40
22	42	40
23	13	40
24	62	40
25	not given	40, 41
26	<i>ditto</i>	40, 41
27	70	40
27	100	41

Unlike the above-mentioned dihydroxy derivatives of naphthalene, Gattermann formylation of 1,6-, 1,7- and 1,8-dihydroxynaphthalenes afforded two isomeric aldehydes in all cases.⁴⁰

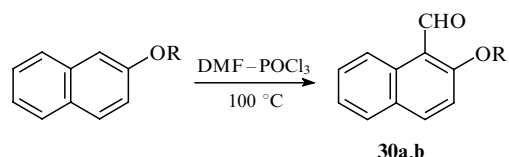


3-Hydroxy-2-naphthoic acid is subjected to Vilsmeier formylation at position 4.¹⁹

Formylation of alkoxy-naphthalenes proceeds much as that of naphthols, although there are some exceptions. For example, Gattermann⁴³ or Vilsmeier⁴⁴ formylation of 1-methoxynaphthalene gave 4-methoxy-1-naphthaldehyde (**28**) in nearly quantitative yield (the reaction with the use of triformamide as the formylating agent, aldehyde **28** was prepared in only 42% yield).³¹ If position 4 is occupied by the methyl group, the aldehyde group is added at the α position with respect to the more electron-donating methoxy substituent to form compound **29**.

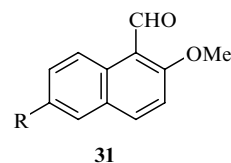


2-Alkoxy-naphthalenes were smoothly formylated at position 1 to give aldehydes **30a,b** in good yields.^{45–47}

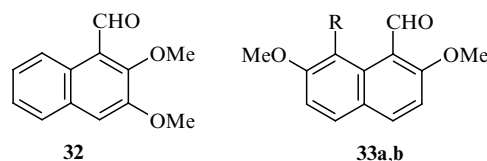


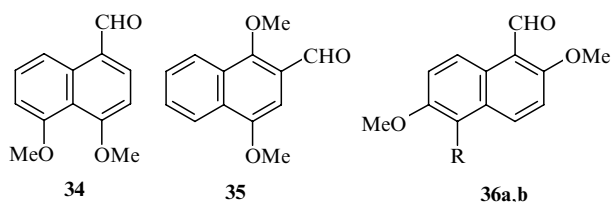
Compound	R	Yield (%)	Ref.
a	Me	90	45, 46
b	Et	74–84	46, 47

Under the same conditions, 6-alkyl-2-methoxynaphthalenes produced aldehydes **31**.^{48–50}



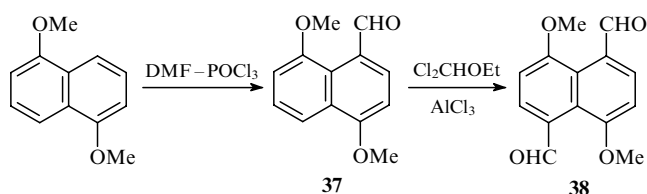
Vilsmeier formylation of dimethoxynaphthalenes giving rise to aldehydes **32–36** was carried out in the studies.^{44, 51–55}



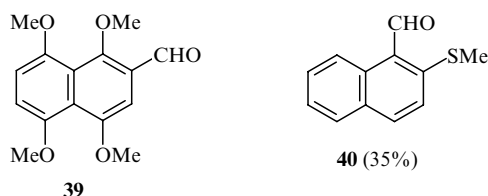


Compound	R	Yield (%)	Ref.
32	—	23	51
33a	H	82	44
33b	Me	82	44
34	—	23	52
34	—	88	53
35	—	42	54
35	—	88	55
36a	H	80	44
36b	Me	40	54

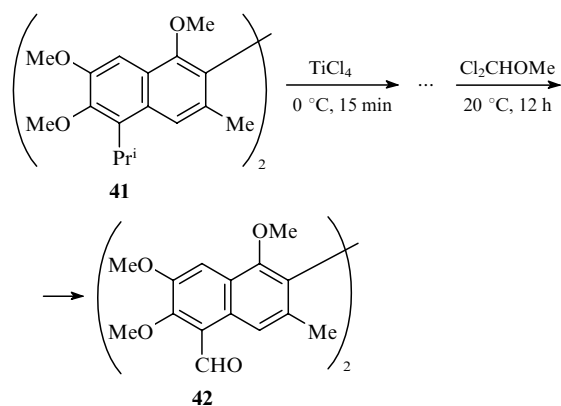
The Vilsmeier reaction of 1,5-dimethoxynaphthalene afforded 4,8-dimethoxy-1-naphthaldehyde (**37**) with a small impurity of dialdehyde **38**.⁵⁶ It was demonstrated⁴² that the latter can also be synthesised by Rieche formylation of monoaldehyde **37** (93% yield).



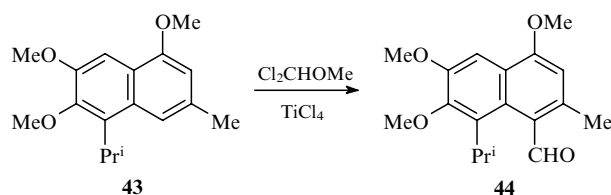
Vilsmeier formylation of 1,4,5,8-tetramethoxynaphthalene gave aldehyde **39** in quantitative yield. The latter was used as the starting compound in the synthesis of natural compounds.^{57–59} Formylation of 2-methylthionaphthalene produced aldehyde **40**, which is one of a few known sulfur-containing naphthaldehydes.⁶⁰



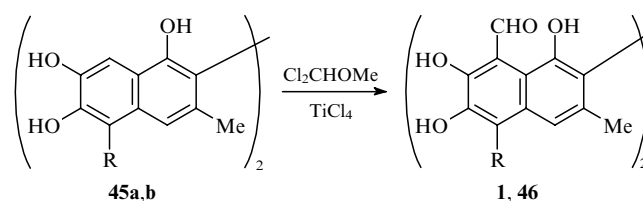
A rare example of *ipso*-formylation with the substitution of the isopropyl group was observed in attempting to subject 2,2'-binaphthyl derivative **41** to the Rieche reaction in the presence of TiCl_4 . Dialdehyde **42** was obtained in 79% yield.⁶¹



Interestingly, the reaction of monomeric substrate **43** performed under analogous conditions afforded 'normal' formylation product **44** in quantitative yield.⁶²



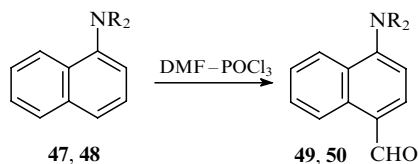
Formylation of compounds **45a** (apogossypol) and **45b** giving rise to gossypol **1**^{61,63} and its ethyl analogue **46**, respectively,⁶¹ follows another pathway compared to the above-mentioned reactions involving polymethoxy derivatives **41** and **43**. Apparently, the hydroxy groups, which can form hydrogen bonds with an electrophile, efficiently stabilise the transition state corresponding to aldehydes **1** and **46**.



R = Pr^i (**45a**, **1**), Et (**45b**, **46**).

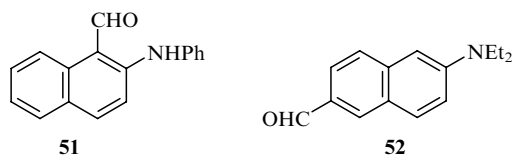
c. Aminonaphthalenes and aminonaphthols

Aminonaphthalenes exhibit much higher reactivity in formylation compared to naphthols and alkoxy-naphthalenes. However, the orientation effects in both series of compounds are virtually identical. For example, the Vilsmeier reactions of 1-dimethylamino- (**47**)^{64,65} and 1-diethylaminonaphthalenes (**48**)⁶⁶ afforded the corresponding 4-dialkylamino-1-naphthaldehydes **49** and **50**.



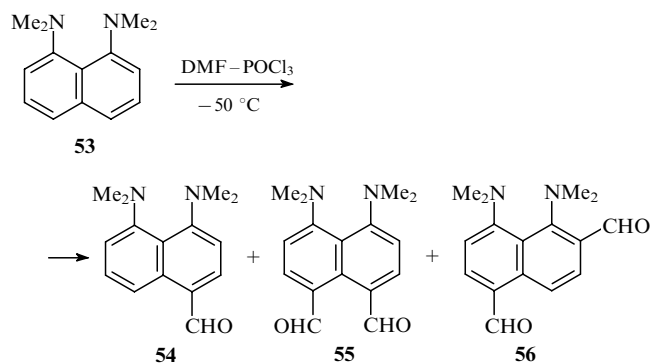
R = Me (**47**, **49**), Et (**48**, **50**).

2-Anilinonaphthalene was formylated at position 1 to give aldehyde **51** (48% yield).⁶⁷ 2-Diethylaminonaphthalene was formylated at the *amphi* position with respect to the NEt_2 group to form aldehyde **52**.⁶⁶

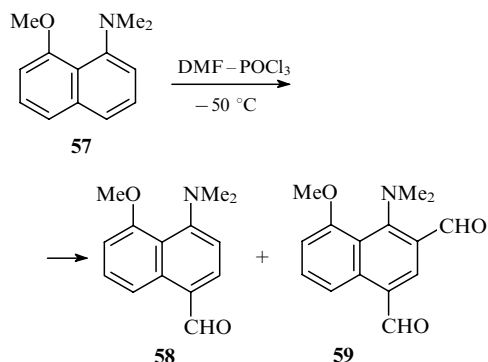


1,8-Bis(dimethylamino)naphthalene (**53**) known under the name of 'proton sponge' exhibits high reactivity with respect to formylating agents. This diamine reacts with the Vilsmeier reagent (DMF-POCl_3) already at $-50\text{ }^\circ\text{C}$.⁶⁸ The results of this reaction depend substantially on the diamine **53**: Vilsmeier reagent molar ratio. Apparently, the proton abstracted upon formylation is bound by a highly basic ($\text{p}K_a$ 12.1) compound **53** to form a cation, which is not involved in formylation. Hence, 2 equiv. of diamine **53** per equivalent of the DMF-POCl_3 mixture should be used for the preparation of monoaldehyde **54**. As a result, more than 50% of the starting compound is regenerated and aldehyde **54** is produced in 70% yield with respect to bis(dimethylamino)naphthalene **53** consumed. In the reaction of diamine **53** with the Vilsmeier reagent taken in a ratio of 1:1, the yield of monoaldehyde **54** decreased to 16.5%, *peri*-dialdehyde **55** was produced as the main reaction product (50%), and unsymmetrical dialdehyde **56** was generated as an impurity (all yields are given with respect to

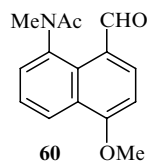
compound **53** consumed). Diamine **53** was also subjected to formylation by chloral in pyridine, but aldehyde **54** was obtained in a yield of no higher than 7%.⁶⁸ Unlike compound **53**, its tetraethyl analogue is difficult to formylate and 4,5-bis(diethylamino)-1-naphthaldehyde was isolated in only 13% yield.⁶⁹ Apparently, due to strong steric hindrances in the 4,5-bis(diethylamino)-1-naphthaldehyde molecule, the electron-donating effect of two *peri*-NEt₂ groups with respect to the naphthalene system is much weaker than that in the 'proton sponge.'



1-Methoxy-8-dimethylaminonaphthalene **57** exhibits reactivity as high as that of diamine **53**.⁷⁰ This compound readily reacts with the Vilsmeier reagent at $-50\text{ }^{\circ}\text{C}$ to form monoaldehyde **58** in 85% yield with an insignificant (2.5%) impurity of dialdehyde **59** (the yields are given with respect to amine **57** consumed in the reaction, about one-half of the latter being involved in the formation of inert cations and regenerated). The formation of compound **59** is the first example of the introduction of two aldehyde groups into the same ring of the naphthalene system. Interestingly, the yield of dialdehyde increased substantially when the reaction was performed at $-10\text{ }^{\circ}\text{C}$ and the **58**:**59** product ratio was 3 : 1.



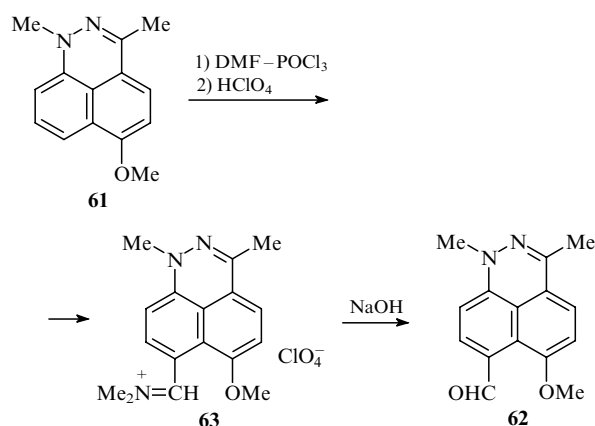
In 1-methoxy-5-(*N*-methylacetamido)naphthalene, the methoxy group exhibits a stronger activating effect in contrast to compound **57**. Formylation (Rieche method) afforded aldehyde **60** as the only product (yield 60%).⁷¹



d. Naphthalene-based heterocyclic systems

Formylation of *peri*-fused heterocyclic systems based on naphthalene was carried out in a series of studies. These systems are of interest because the heterocycle in these compounds serves as a special kind of substituent exerting a substantial effect on the

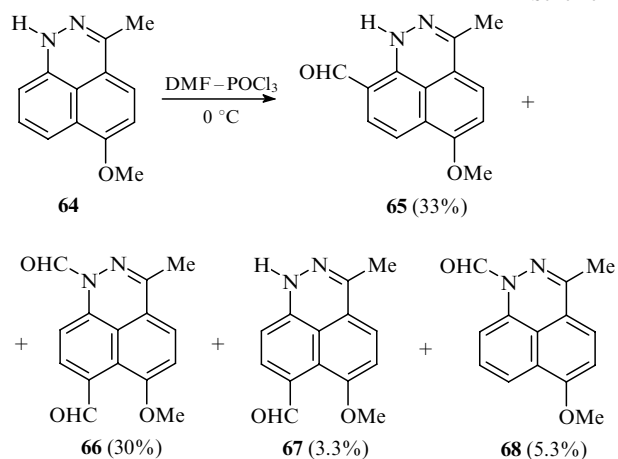
degree of activation of the naphthalene system with respect to the electrophilic substitution as well as on the orientation effects. It was demonstrated⁷² that 6-methoxy-1,3-dimethyl-1*H*-1,2-diazaphenylene (**61**) rapidly reacted with the Vilsmeier reagent even at $0\text{ }^{\circ}\text{C}$ to give 7-carbaldehyde **62** as the only product (87% yield). In this experiment, intermediate immonium salt **63** was isolated as a perchlorate. The ease of formylation results from π -excessiveness of the heterocycle in diazaphenylene **61**, which formally contains 7 π electrons. The partial shift of the excessive Hückel electron from the heterocycle in molecule **61** induces substantial negative π -charges in the *ortho* and *para* positions of the naphthalene fragment.



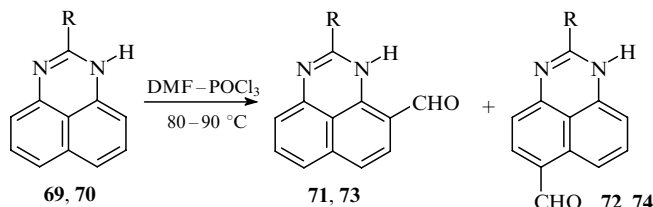
Formylation of 1,2-diazaphenylene **64** containing the unsubstituted NH group proceeds less selectively. In this reaction, the sterically non-hindered *ortho* position and the pyrrole nitrogen atom are subjected to electrophilic attack along with the *para* position with respect to the NH group. The reaction afforded aldehyde **65** and dialdehyde **66** as the major products. In addition, formyl derivatives **67** and **68** were isolated in low yields (Scheme 1).

Since heterocyclic 1,2-diazaphenolens are characterised by very low basicity ($\text{p}K_{\text{a}} < 3$), they are present in reaction mixtures predominantly as bases, which, evidently, undergo formylation. A different situation occurs in the case of much more basic ($\text{p}K_{\text{a}} > 5.5$) 1,3-diazaphenolens (perimidines). Perimidine (**69**) and 2-methylperimidine (**70**) are very difficult to formylate. A large excess of the Vilsmeier reagent and prolonged heating at $80\text{--}90\text{ }^{\circ}\text{C}$ are required for the latter reactions to proceed. However, the yields of 4(9)- (**71**) and 6(7)-formylperimidines (**72**) produced under these conditions were also no higher than 10%. Aldehydes **73** and **74** derived from 2-methylperimidine were

Scheme 1

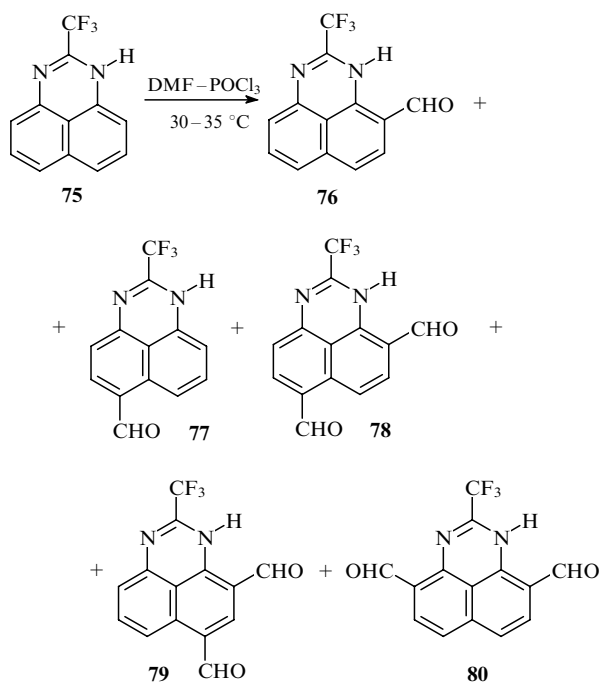


prepared in only 1%–2% yields.⁷³ Since the 1,3-dimethylperimidinium cation does not undergo formylation at all, it can be concluded that perimidines **69** and **70** are virtually completely protonated under the conditions of the Vilsmeier reaction and the reaction proceeds through formation of the free base, which is present in the reaction mixture in a low equilibrium concentration.



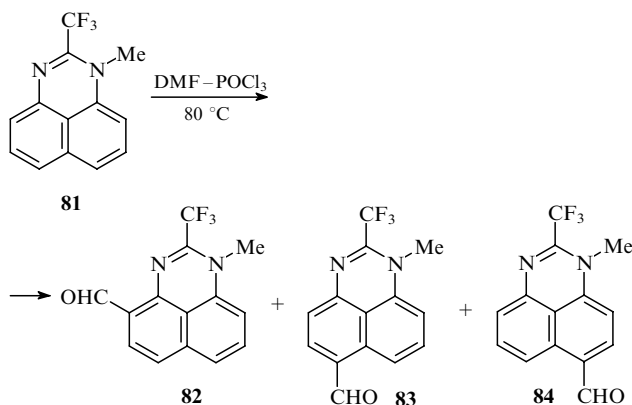
R = H (**69**, **71**, **72**), Me (**70**, **73**, **74**).

An important role of the basicity of the substrate is evidenced by the fact that 2-trifluoromethylperimidine (**75**) of low basicity is readily subjected to formylation.⁷⁴ This reaction afforded 4(9)-carbaldehyde **76** (yield 42%) and 6(7)-carbaldehyde **77** (22%) as the major products along with small amounts of dialdehydes **78**–**80**. It should be noted that formation of the latter product is the only example of diformylation of the naphthalene ring at two β positions.

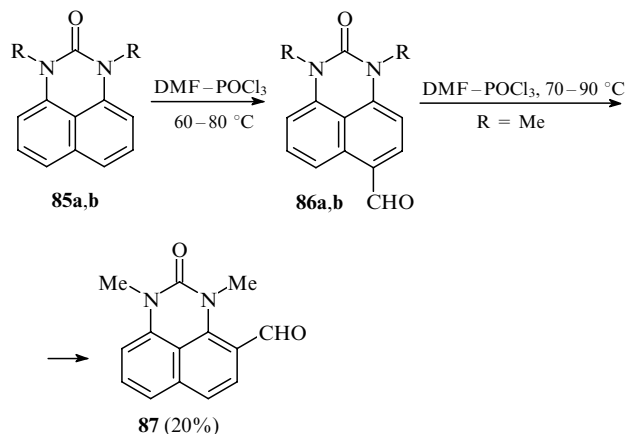


It should be noted that 1-methyl-2-trifluoromethylperimidine (**81**) is much more difficult to formylate than its non-methylated analogue **75**.⁷⁴ For example, the reaction of compound **81** proceeded at a noticeable rate only at 80 °C, and the total yield of aldehydes **82**–**84** was 46% after 3.5 h, whereas formylation of perimidine **75** was completed within 2.5 h even at 35 °C. In

addition, perimidines containing the unsubstituted NH group were formylated predominantly at positions 4(9), whereas an analogous reaction of *N*-methylated derivative **81** gave rise predominantly to 6- and 7-carbaldehydes (product ratio **82**:**83**:**84** = 22:20:58). It can be hypothesised that the NH group in molecule **75** is efficiently involved in stabilisation of the transition complex corresponding to *ortho*-formylation (this is, to a large extent, true also for 1,2-diazaphenylene **64** and other analogous compounds).

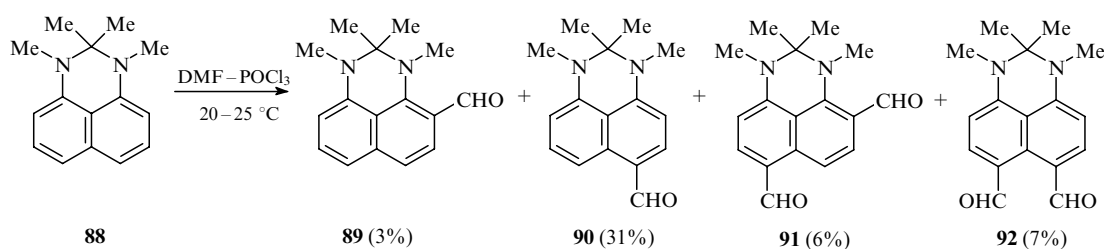


1,3-Dialkylperimidones **85a,b**, which are less basic than 2-trifluoromethylperimidines, were smoothly formylated at position 6 to form aldehydes **86a,b** in 85% yield.⁷⁴ In attempting to perform further formylation, compound **86a** underwent isomerisation to 4-carbaldehyde **87**. The fact that the second formyl group is difficult to introduce can be attributed to the lower π -donating ability of the heterocycle in perimidones due to the electron-withdrawing effect of the carbonyl group. This is also evidenced by the fact that formylation requires high temperature.



85, 86: R = Me (**a**), Et (**b**).

The electronic structure of 1,2,2,3-tetramethyl-2,3-dihydroperimidine (**88**) is more similar to that of 1,8-bis(dimethylamino)-naphthalene (**53**) rather than to that of perimidines **69** and **70**. Being in addition a weak base, compound **88** is readily formylated (Scheme 2) to give monoaldehydes **89** and **90** and dialdehydes **91**



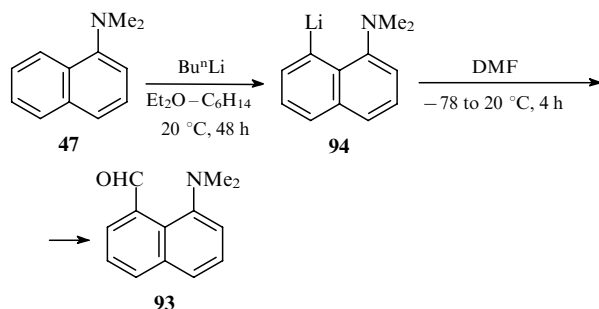
Scheme 2

and **92**.⁷⁴ These results are very similar to those observed upon formylation of 'proton sponge' **53**, with the only difference that the formation of mono-*ortho*-aldehyde was not observed in the latter case.

2. Organometallic syntheses

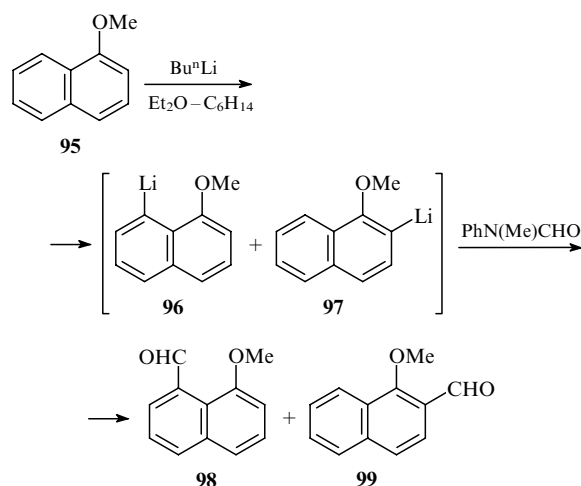
Not all aldehydes of the naphthalene series can be prepared by electrophilic formylation of naphthalenes. One of the typical limitations concerns compounds in which the CHO group and an electron-donating substituent are present in different benzene rings. In such cases, the problem can be solved by performing formylation of organometallic compounds of the naphthalene series with the use of DMF, *N*-methylformanilide or *N*-formylpiperidine. These organometallic compounds are synthesised by either direct metallation of the corresponding naphthalenes or replacement of the halogen atom by metal.

Direct metallation of C–H bonds in naphthalenes generally gives good results for molecules containing a group with a lone electron pair. Due to preliminary coordination with a metallating reagent, this group directs metallation and subsequent formylation at the *ortho* or *peri* position. A characteristic example is 1-dimethylaminonaphthalene (**47**) from which 8-dimethylamino-1-naphthaldehyde (**93**) was prepared as the only product (67% yield) according to the following scheme.^{75,76}

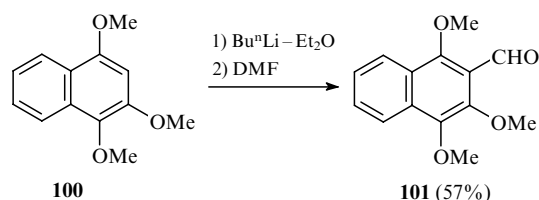


Apparently, metallation at position 8 (rather than at position 2) of the naphthalene system can be explained as follows. Due to steric hindrances, the NMe_2 group is twisted so that the lone electron pair of the nitrogen atom is oriented toward the *peri*-proton. Consequently, after coordination of this pair to the lithium ion, the Bu^- anion appears to be adjacent to the hydrogen atom at position 8, which is eliminated first to form 8-lithium derivative **94**.

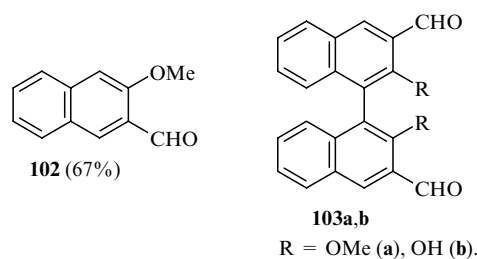
In the case of 1-methoxynaphthalene (**95**) in which the MeO group is conformationally more labile, the situation is not so unambiguous. This compound is lithiated by *n*-butyllithium at both positions 8 and 2, the contribution of *ortho*-metallation being much higher. Treatment of the resulting mixture of lithium derivatives **96** and **97** with *N*-methylformanilide afforded 8-methoxy-1-naphthaldehyde (**98**) in only 9% yield and 1-methoxy-2-naphthaldehyde (**99**) in 38% yield.^{77,78} Nevertheless, in spite of such a low yield, this procedure for the preparation of *peri*-aldehyde **98** is preferable to alternative multistep syntheses. It was demonstrated that metallation of compound **95** depends substantially on the nature of both the metallating agent and solvent.⁷⁹ Thus, the addition of tetramethylethylenediamine completely shifted the reaction toward *ortho*-metallation, whereas the use of *tert*-butyllithium instead of *n*-butyllithium led to the predominant formation of *peri*-metallation product **96**.⁷⁹ (The latter observation is consistent with the data on the reaction of *tert*-butyllithium with 1,4-dimethoxynaphthalene.⁸⁰) Treatment of 8- and 2-lithium derivatives thus prepared with dimethylformamide afforded *peri*- and *ortho*-naphthaldehydes **98** and **99** in a ratio of 2 : 1.



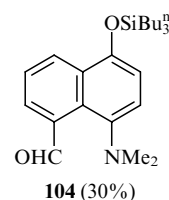
Neither of the two accessible *peri* positions was subjected to metallation upon treatment of 1,2,4-trimethoxynaphthalene (**100**) with *n*-butyllithium. The reaction proceeded at position 3 with high selectivity due, apparently, to its activation simultaneously by two methoxy groups. Treatment of the 3-lithium derivative with dimethylformamide gave aldehyde **101** as the only product.⁵⁵



Interestingly, 2-methoxynaphthalene was also metallated at position 3 rather than at position 1. Subsequent formylation afforded aldehyde **102**.⁷⁷ Analogously, dialdehyde **103a** was generated from 2,2'-dimethoxy-1,1'-binaphthyl. Demethylation of **103a** with BCl_3 gave rise to dialdehyde **103b**.⁸¹

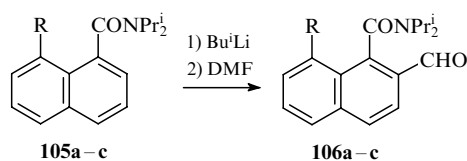


The dimethylamino group exerts a stronger orienting action in the course of metallation compared to the alkoxy group. Treatment of 4-dimethylamino-1-tributylsilyloxynaphthalene with *tert*-butyllithium followed by the addition of DMF produced aldehyde **104** as the only product.⁸⁰



The carbamoyl group possesses an even higher metal-orienting ability than the NMe_2 , CH_2NMe_2 or OMe groups. This is

evidenced by the transformation of compounds **105a–c** into aldehydes **106a–c**.⁸²



R = NMe₂ (a), CH₂NMe₂ (b), OMe (c).

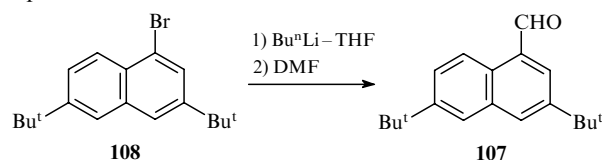
If metallation of C–H bonds in naphthalenes is either hindered or does not provide the required reaction pathway, naphthaldehydes are synthesised with replacement of the halogen atom by metal followed by formylation. For example, treatment of α -naphthylmagnesium bromide with dimethylformamide, *N*-formylpiperidine, *N*-formylmorpholine or 2-(*N*-formyl-*N*-methyl)aminopyridine afforded α -naphthaldehyde **2** in good yields (Table 2). For this purpose, 1-tributylstannyl naphthalene was also used. The latter was transformed into α -naphthaldehyde under the action of α,α -dichlorodimethyl ether in the presence of anhydrous AlCl₃. Analogously, β -naphthaldehyde was generated from 2-tributylstannyl naphthalene.⁸⁷ The reaction of 6-methoxy-2-naphthylmagnesium bromide with DMF gave 6-methoxy-2-naphthaldehyde in 80% yield.⁸⁸

Table 2. Organometallic syntheses of α -naphthaldehyde.

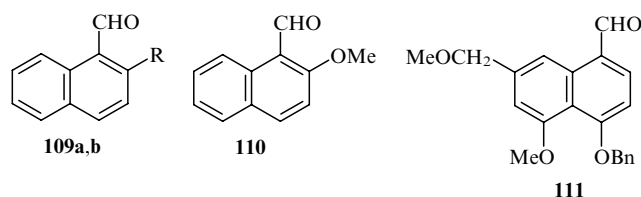
M	Formylating agent ^a	Reaction conditions	Yield (%)	Ref.
MgBr	DMF	Et ₂ O, 0–20 °C	87	83
MgBr	NFP	Et ₂ O, 0 °C	94	84
MgBr	NFM	Et ₂ O, 0 °C	92	85
MgBr	NMFAP	THF, 0 °C	76	86
SnBu ₃	Cl ₂ CHOMe	AlCl ₃ , –78 to 20 °C	80	87

Note. The following notations are used: NFP is *N*-formylpiperidine, NFM is *N*-formylmorpholine, NMFAP is 2-(*N*-methyl-*N*-formyl)aminopyridine.

Lithiated naphthalenes, which are generated upon treatment of bromonaphthalenes with butyllithium, have found wide use in the synthesis of naphthaldehydes. The synthesis of 3,6-di-*tert*-butyl-1-naphthaldehyde (**107**) from bromide **108**⁸⁹ is a typical example.



Aldehydes **49**,⁹⁰ **109a,b**⁹¹ and **110**^{91,92} were prepared analogously. In these reactions, DMF or *N*-formylpiperidine generally serve as the formylating agents. However, the synthesis of aldehyde **111** was carried out with the use of *N*-methoxy-*N*-methylformamide.⁹³



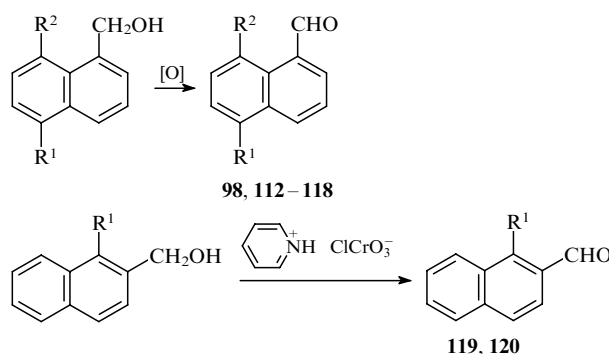
109: R = CH₂OH (a), CH(OMe)₂ (b).

3. Oxidation of alcohols and alkyl naphthalenes

Various oxidising agents are presently used for the preparation of aldehydes from alcohols. These oxidising agents provide good yields, high selectivity and rather mild reaction conditions preventing further oxidation of aldehydes to carboxylic acids. In addition to a traditional oxidising agent (manganese dioxide), *N*-chlorosuccinimide, pyridinium chlorochromate, pyridinium dichromate, methylammonium chlorochromate deposited on silica gel,⁹⁴ the DMSO–oxalyl chloride–Et₃N system (Swern oxidation) and some other reagents also meet these requirements. Examples of their use in the synthesis of substituted α -naphthaldehydes are given in Table 3.

Catalytic procedures were developed for oxidation of alcohols of the naphthalene series to aldehydes. Thus, good results were obtained in oxidation of 1-hydroxymethylnaphthalene by molecular oxygen in the presence of heterogeneous catalysts based on transition metal salts (Ru, Co).⁹⁹ Bis(pentafluorophenyl)borinic acid (C₆F₅)₂BOH–Bu^tCHO–MgSO₄ was proposed as an efficient catalyst for homogeneous Oppenauer oxidation of the same alcohol to 1-naphthaldehyde.¹⁰⁰

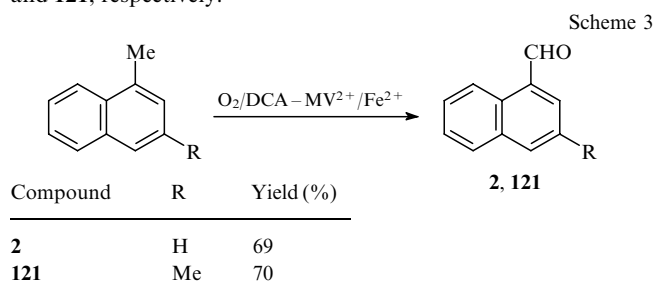
Table 3. Synthesis of selected naphthaldehydes by oxidation of alcohols.



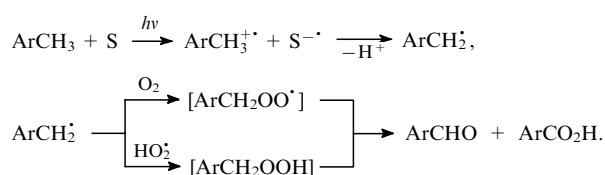
Aldehyde	R ¹	R ²	Oxidant [O] ^a	Yield (%)	Ref.
98	H	MeO	MnO ₂	88	95
112	H	Br	NCS	85	96
113	H	I	NCS	70	96
114	Cl	Cl	NCS	78	96
115	Cl	Me	PDC	83	97
116	Br	Me	PDC	88	97
117	PhS	Me	DMSO–OxCl–Et ₃ N	88	97
118	PhSO ₂	Me	DMSO–OxCl–Et ₃ N	78	97
1 (<i>S</i> -gossypol)	–	–	DMSO–OxCl–Pr ₂ NEt	81	63
119	Br	–	PCC	79	91
120	OMe	–	PCC	–	98

Note. The following notations are used: NCS is *N*-chlorosuccinimide; PDC is pyridinium dichromate; PCC is pyridinium chlorochromate; DMSO is dimethyl sulfoxide; OxCl is oxalyl chloride.

Many studies, including patents,^{100–103} were devoted to the synthesis of naphthaldehydes by catalytic oxidation of methyl-naphthalenes. Scheme 3 gives an insight into the mechanism of these transformations. This scheme shows photochemical oxidation of 1-methyl- and 1,3-dimethylnaphthalenes to aldehydes **2** and **121**, respectively.

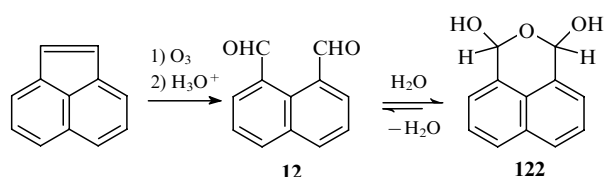


The reaction proceeds by the following mechanism:

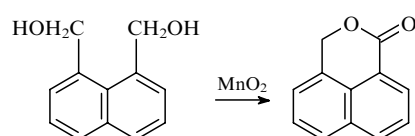


The process is carried out in the presence of 9,10-dicyanoanthracene (DCA) serving as a sensitising agent (S), methyl viologen (MV^{2+}) and divalent iron ions.¹⁰⁴ These reactions often afford naphthalenecarboxylic acid as a by-product. However, this drawback can be remedied by using modern reagents, such as *o*-iodoxybenzoic acid, as an oxidising agent.¹⁰⁵

Vinylnaphthalenes¹⁰⁶ and acenaphthylene were also proposed as the starting compounds for the preparation of naphthaldehydes. Ozonolysis of acenaphthylene afforded 1,8-diformylnaphthalene (**12**) in 73% yield.¹⁰⁷ Due, apparently, to Coulombic repulsions between two closely spaced carbonyl groups, this dialdehyde is very readily hydrated and transformed into cyclic hydrate **122** under normal conditions. The latter exists as two stereoisomers with melting points (T_m) of 140.0–141.5 °C and 106–107 °C (its *cis-meso* form is shown below). Upon sublimation in hard vacuum, this hydrate loses the water molecule and is transformed into non-hydrated form **12** ($T_m = 124$ –125 °C).¹⁰⁸



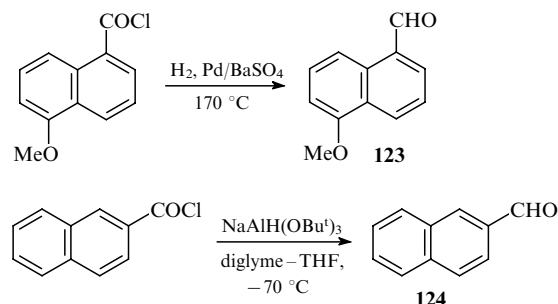
Interestingly, an attempt to prepare dialdehyde **12** by oxidation of 1,8-dihydroxymethylnaphthalene with manganese dioxide¹⁰⁸ led only to the formation of naphthopyranone.



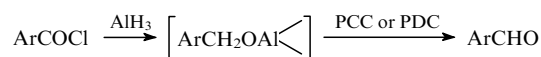
4. Syntheses from naphthalenecarboxylic acid derivatives

First data on syntheses of naphthaldehydes by reduction of naphthalenecarboxylic acid derivatives date back to the beginning of the 20th century. For example, 5-methoxy-1-naphthaldehyde (**123**) was prepared by the Rosenmund reaction.¹⁰⁹ Since that time, new more efficient reagents for reducing carboxylic acid chlorides were found. In our opinion, sodium tris(*tert*-butoxy)-

aluminium hydride (STBA) is a reagent of choice. This reagent allows one to perform the reaction at low temperature and prepare 1- and 2-naphthaldehydes (in particular, aldehyde **124**) in nearly quantitative yields.¹¹⁰ The lithium analogue of STBA can also be used, for example, in the synthesis of dialdehyde **103b**.¹¹¹ However, the reactions with the use of the latter reagent generally afford aldehydes in lower yields.¹¹⁰

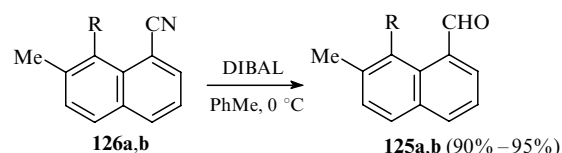


Recently, Korean chemists have developed an original procedure for the redox transformation of aroyl chlorides into aldehydes.¹¹² First, the reaction of aroyl chloride with aluminium chloride was carried out to obtain the corresponding aluminium alkoxide, which was immediately oxidised with pyridinium chlorochromate or pyridinium dichromate to prepare aldehyde. This method made it possible to synthesise 1- and 2-naphthaldehydes in virtually quantitative yields.



This approach was also extended to the synthesis of aldehydes from carboxylic acids,¹¹³ esters¹¹⁴ and directly from primary alcohols.¹¹⁵

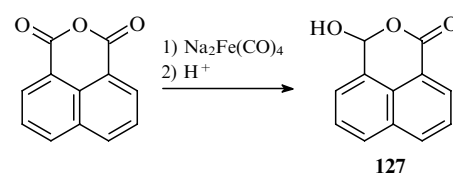
Reduction of acid nitriles is yet another procedure widely used for the preparation of naphthaldehydes. The list¹¹⁶ of reducing reagents used for this purpose consists of more than ten compounds, including tin dichloride and a number of complex hydrides. For example, the use of lithium diisobutylaluminium hydride (DIBAL) as the reducing agent gave good results in the synthesis of aldehydes **125a,b** from nitriles **126a,b**.^{117, 118}

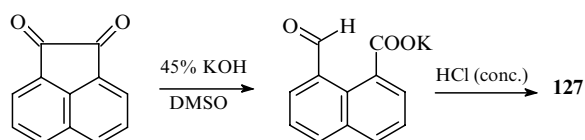


R = H (a), Br (b).

In recent years, high requirements have been imposed upon the selectivity of the process. For instance, potassium 9-(pentan-2-yl)-9-boratabicyclo[3.3.1]nonane¹¹⁹ and lithium tris(diethylamino)aluminium hydride¹¹⁶ were proposed as reagents for reduction of aryl cyanides in the presence of aliphatic acid nitriles. These reducing reagents were also successfully used for the synthesis of naphthaldehydes.

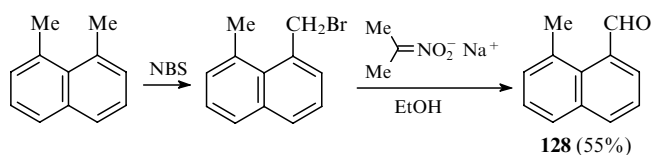
Reduction of 1,8-naphthalic anhydride in the presence of the $\text{Na}_2\text{Fe}(\text{CO})_4$ complex¹²⁰ or treatment of acenaphthenequinone with alkali in DMSO¹²¹ afforded 8-formylnaphthalene-1-carboxylic acid (existing in cyclic form **127**) in good yields.



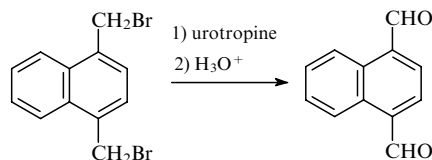


5. Syntheses based on halomethylnaphthalenes

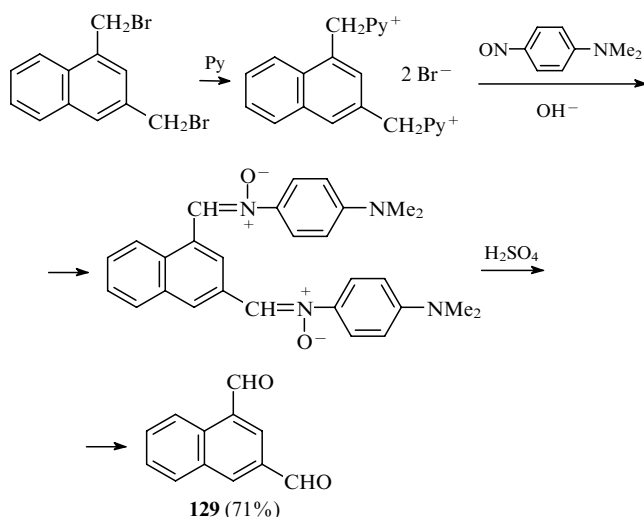
The use of bromomethyl- and dibromomethylnaphthalenes in the synthesis of naphthaldehydes seems to be very attractive because they are readily accessible reagents prepared by free-radical bromination of methylnaphthalenes with *N*-bromosuccinimide (NBS). For example, 8-methyl-1-naphthaldehyde (**128**) was synthesised in two steps from commercial 1,8-dimethylnaphthalene. The bromomethyl group was oxidised with 2-nitropropane.¹²²



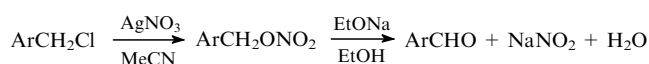
1,4-Naphthodialdehyde was prepared from 1,4-bis(bromomethyl)naphthalene by the Sommelet reaction.¹²³



Isomeric 1,3-, 1,5-, 1,6-, 1,7-, 2,6- and 2,7-dialdehydes as well as 1,3,5-, 1,3,6-, 1,3,7- and 1,4,6-trialdehydes of the naphthalene series were synthesised according to the Kröhnke method.¹²³ This method involves the preliminary transformation of halomethyl derivatives of naphthalene into pyridinium salts and then into nitrones, which are subjected to acid hydrolysis, as exemplified by the synthesis of 1,3-naphthodialdehyde (**129**).

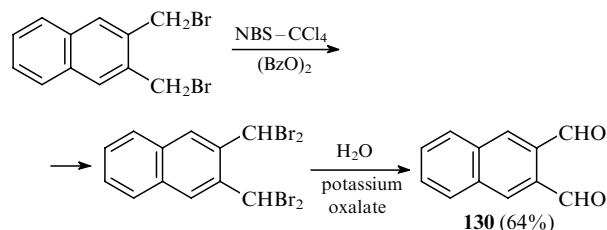


Kochergin and co-workers¹²⁴ developed a procedure for the preparation of aromatic aldehydes, including naphthaldehydes, based on transformations of chloromethylarenes into nitrates and decomposition of the latter under the action of sodium ethoxide.



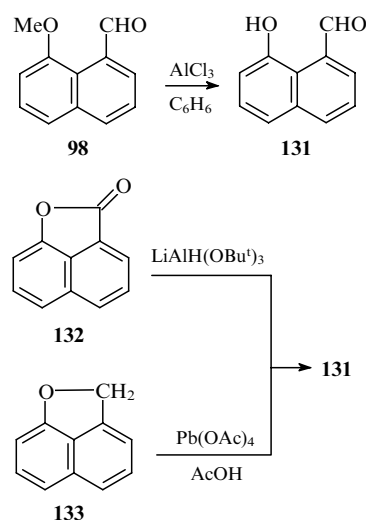
In some cases, naphthaldehydes were synthesised with the use of dibromomethylnaphthalenes as the starting compounds, which

were subjected to hydrolysis. In particular, this method was used for the preparation of *peri*-dialdehyde **12**,¹⁰⁸ 1,1'-binaphthyl-2,2'-dicarbaldehyde¹¹¹ and naphthalene-2,3-dicarbaldehyde (**130**).¹²⁵

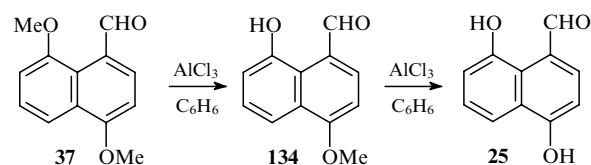


6. Functionalisation of substituents in naphthaldehydes

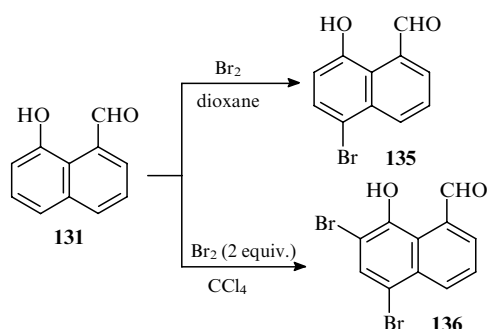
Functionalisation of substituents in naphthaldehyde molecules as well as the introduction of new groups (for example, by electrophilic substitution) is used when target compounds are difficult to prepare according to other methods. For example, demethylation of 8-methoxy-1-naphthaldehyde (**98**) with aluminium chloride afforded aldehyde **131**,^{77,95} which is a very valuable reagent from the preparative standpoint. This compound can also be synthesised by reduction of naphtholactone **132** with lithium tri(*tert*-butoxy)aluminium hydride (75% yield)¹²⁶ or by oxidation of 2*H*-naphtho[1,8-*b*,*c*]furan (**133**) with lead tetraacetate (30% yield).^{95,127} However, the latter reaction is complicated by the formation of by-products. Compound **133** and its 2- and 4-methoxy derivatives are slowly transformed into *peri*-hydroxynaphthaldehydes even in air.^{95,127}



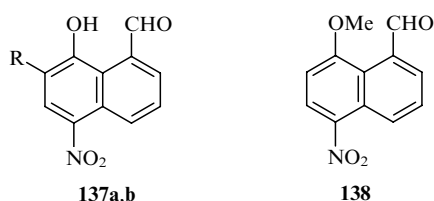
Heating of 4,8-dimethoxy-1-naphthaldehyde **37** with 1 equiv. of anhydrous AlCl_3 in benzene⁴² or with BBr_3 in dichloromethane⁵⁶ led to selective demethylation of the methoxy group at position 8 to give *peri*-hydroxyaldehyde **134** in good yield. The reaction with the use of 2 equiv. of AlCl_3 afforded dinaphthol **25**.⁴² This method was used also for the synthesis of hemigossypol and its analogues from methoxy precursors⁸ (see also the transformation **103a** $\rightarrow$ **103b**).⁸¹



Bromination of aldehyde **131** produced its bromo derivatives **135** and **136**.¹²⁸

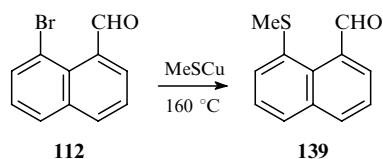


Nitration of aldehyde **131** with nitric acid ($\rho = 1.35 \text{ g cm}^{-3}$) afforded nitro derivatives **137a,b**.¹²⁸ Analogously, the reaction of *peri*-methoxynaphthaldehyde **98** gave rise to 8-methoxy-5-nitro-1-naphthaldehyde (**138**), whose treatment with aqueous alkali produced 8-hydroxy-5-nitro-1-naphthaldehyde (**137b**).¹²⁸



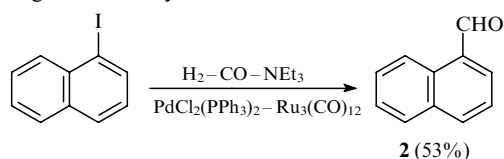
R = NO_2 (a), H (b).

The synthesis of 8-methylthio-1-naphthaldehyde (**139**) from bromide **112** (72% yield)⁹⁶ provides an example of functionalisation based on the nucleophilic substitution.



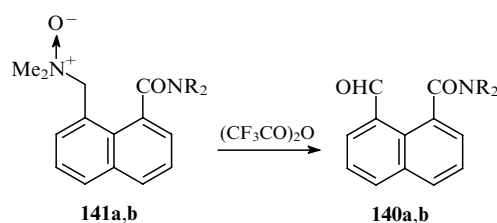
7. Other methods

The synthesis of aldehydes based on formylation of radical anions of polycyclic arenes was described. Thus, the reactions of sodium naphthalenide with ethyl formate or *N,N*-dibutylformamide afforded naphthaldehyde **2** in 55% yield.¹²⁹ Aromatic aldehydes can also be synthesised by formylation of aryl iodides under homogeneous catalysis conditions.¹³⁰



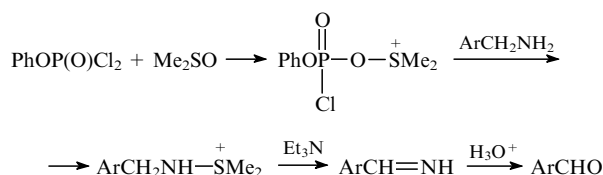
In some cases, naphthaldehydes are synthesised by the Poldovski reaction in spite of the fact that the products are generally

obtained in low yields. The preparation of 8-formyl-1-naphthamides **140a,b** from *N*-oxides **141a,b**⁸² provides a typical example.



Compounds 140, 141	R	Yield 140 (%)
a	Et	19
b	Pr ⁱ	40

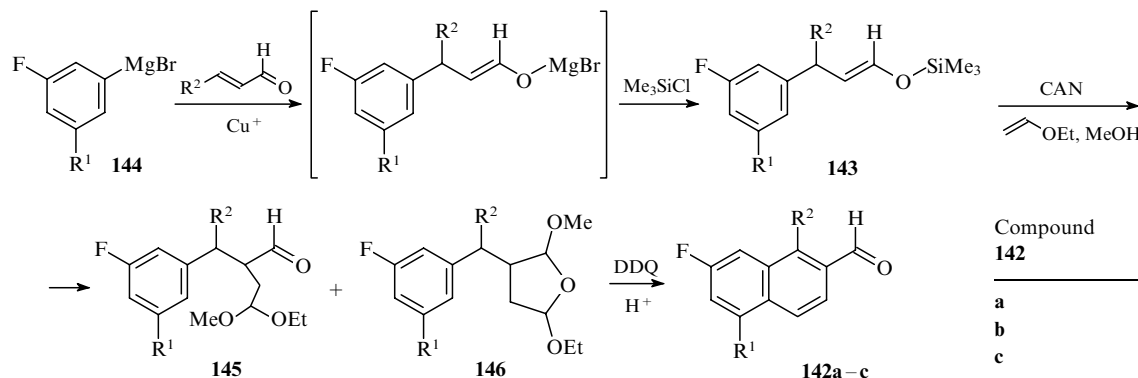
Treatment of benzylamines with phenyl dichlorophosphate and DMSO followed by the successive addition of triethylamine and oxalic acid made it possible to prepare both aromatic ketones and aldehydes.¹³¹ For example, 1-aminomethylnaphthalene was transformed under these conditions into α -naphthaldehyde in 78% yield. This reaction is a modification of the Pfizner–Moffat oxidation and involves preliminary activation with DMSO.



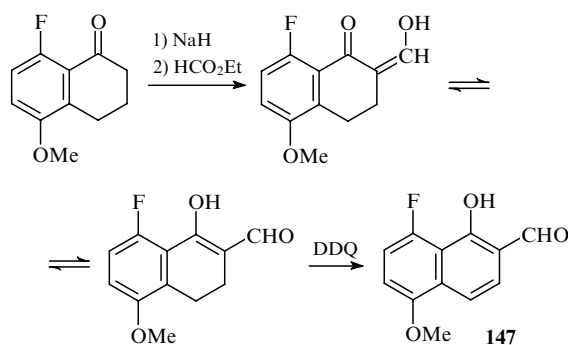
In several studies, naphthaldehydes were prepared by cyclisation. Recently, Italian chemists have developed a procedure for the synthesis of fluorinated 2-naphthaldehydes **142a–c** based on oxidative annelation of the benzene ring to *O*-trimethylsilyl 2-benzylvinyl ethers **143** (Scheme 4).¹³² In addition to the organometallic synthesis of the ethers (**144** $\rightarrow$ **143**), the procedure involves carbon–carbon chain growth through the addition of ethyl vinyl ether to compounds **143** and acid-oxidative cyclisation of isomeric acetals **145** and **146** under the action of dichlorodicyanobenzoquinone (DDQ). The former reaction requires the use of cerium ammonium nitrate (CAN) and proceeds, most likely, by a radical mechanism. Aldehydes **142** were prepared in satisfactory total yield ($\sim 40\%$) with respect to the starting fluorophenylmagnesium bromide.

Tetralones were proposed as the starting compounds for the synthesis of substituted 1-hydroxy-2-naphthaldehydes, in particular, of compound **147**. Tetralones are subjected to successive formylation (through the formation of enolates) and aromatisation under the action of DDQ.¹³³

Scheme 4



Compound 142	R ¹	R ²
a	H	Me
b	F	H
c	F	Me



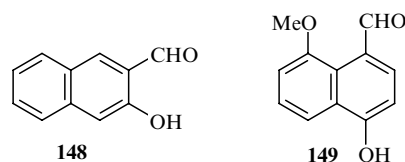
III. Structures and physicochemical properties of naphthaldehydes

In this section, attention is focused on such physicochemical properties that allow one to obtain information on the conformation of the aldehyde group and the character of its electronic interactions with the core and other substituents.

1. Infrared, ultraviolet and mass spectra

Based on the stretching absorption band of the C=O bond ($\nu_{\text{C=O}}$) as the characteristic band in the IR spectra of unsubstituted α - and β -naphthaldehydes **124** (1700 cm^{-1} in CCl_4), it can be seen from Table 4 that the low-frequency shift of this band ($\Delta\nu_{\text{C=O}}$) is favoured by the involvement of the aldehyde group in intramolecular hydrogen bonding, different electronic interactions of this group with other substituents and steric factors. For example, $\Delta\nu_{\text{C=O}}$ in the spectra of *o*-hydroxynaphthaldehydes **18** and **20** is -50 cm^{-1} due, apparently, to intramolecular hydrogen bonding. In the spectrum of 3-hydroxy-2-naphthaldehyde (**148**), this shift is smaller ($\Delta\nu_{\text{C=O}} = -32\text{ cm}^{-1}$). Apparently, the intramolecular hydrogen bond in the latter compound is weaker due to the larger C(β)–C(β) bond length and, consequently, to the larger distance between the CHO group in position 2 and the OH group in position 3 of the naphthalene ring. Interactions between the

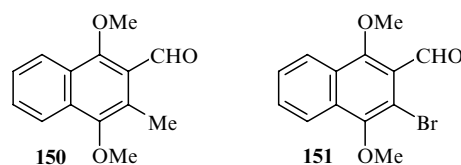
substituents in *peri*-hydroxynaphthaldehyde **131** are of particular interest. Formally, the OH and CHO groups are not conjugated and the intramolecular hydrogen bond cannot be as strong as those in aldehydes **18** and **20** because the seven-membered chelate ring rather than the six-membered ring is closed in **131**. Actually, $\Delta\nu_{\text{C=O}}$ in the IR spectrum (in CHCl_3) of compound **131** (-30 cm^{-1}) is even smaller than that in the spectrum of aldehyde **148**. In a solution of compound **131** in THF, the hydrogen bridge is, apparently, partially broken and the IR spectrum has two $\nu_{\text{C=O}}$ bands one of which (at 1660 cm^{-1}) can be assigned to the form containing an intramolecular hydrogen bond and another band (at 1680 cm^{-1}) can be attributed to the form without an intramolecular hydrogen bond.



A record decrease in $\nu_{\text{C=O}}$ (to 1610 cm^{-1}) is observed in the IR spectra of gossypol **1** and its analogue **46**.^{61,135} This fact suggests that the aldehyde group in compounds **1** and **46** is chelated with the *o*-OH group rather than with the *peri*-OH group (*cf.* ^1H NMR spectra and results of X-ray diffraction analysis discussed in Sections III.2 and III.6). In the IR spectrum of aldehyde **149**, $\Delta\nu_{\text{C=O}}$ is -60 cm^{-1} .

A decrease in the frequency of absorption of the carbonyl group due to its conjugation with the electron-donating substituents is smaller than one would expect (see, for example, Table 4, compounds **2**, **49** and **54**). A small value of $\Delta\nu_{\text{C=O}}$ for *peri*-dialdehyde **55** prepared from the 'proton sponge' is particularly surprising, the more so that other physicochemical characteristics of this compound, in particular, the dipole moments (see below), are indicative of very strong conjugation in its molecule.

Substituents facilitating the twist of the CHO group with respect to the plane of the naphthalene system cause a decrease in conjugation as a result of which $\nu_{\text{C=O}}$ increases [see Table 4, aldehyde **35** and its 3-methyl- (**150**) and 3-bromo derivatives (**151**)].



α -Naphthaldehyde **2** and *peri*-dialdehyde **12** are colourless compounds, and the long-wavelength absorption band in their UV spectra is observed at 300 nm (Table 5). However, the presence of even one electron-donating substituent in the *para* position with respect to the formyl group causes a strong bathochromic shift of this band and the corresponding compounds become coloured. Aldehydes **49** and **54–56** containing the NMe_2 groups are typical examples. The conjugation is particularly pronounced in *peri*-dialdehyde **55**, which occurs as dark-orange crystals with metallic lustre. α -Naphthaldehyde derivatives containing substituents with the lone electron pair (OH, OMe, NAlk_2) in position 8 are also yellow or orange in colour. The fact that aldehyde **93** is coloured was attributed to *peri*-interactions between the substituents (see Section III.6) resulting in an increase in the energy of the highest occupied molecular orbital (HOMO) involving the lone electron pair of the O or N atoms of the electron-donating group.⁷⁶ In our opinion, an alternative explanation can be put forward, according to which the electron-donating (NMe_2) and electron-withdrawing (CHO) substituents are independently conjugated with the π -system of the ring, which facilitates an increase in the energy of the HOMO and a decrease in the energy of the lowest unoccupied molecular orbital

Table 4. Position of the $\nu_{\text{C=O}}$ band in the IR spectra of selected naphthaldehydes.

Compound	Position of CHO groups	Other substituents	Solvent	$\nu_{\text{C=O}}/\text{cm}^{-1}$	Ref.
2	1	—	CCl_4	1700	134
2	1	—	see ^a	1691	87
124	2	—	CCl_4	1702	134
124	2	—	see ^a	1690	87
20	1	2-OH	CCl_4	1649; 1638 ^b	134
18	2	1-OH	CCl_4	1651; 1637 ^b	134
148	2	3-OH	CCl_4	1668	134
131	1	8-OH	CHCl_3	1670	95
131	1	8-OH	THF	1680; 1660	95
134	1	8-OH, 4-OMe	see ^c	1650	56
12	1, 8	—	see ^a	1672	108
49	1	4- NMe_2	CCl_4	1685	65
93	1	8- NMe_2	CHCl_3	1660	76
54	1	4,5-(NMe_2) ₂	CCl_4	1685	68
55	1, 8	4,5-(NMe_2) ₂	CHCl_3	1665; 1635	68
56	1, 6	4,5-(NMe_2) ₂	CCl_4	1670; 1635	68
149	1	4-OH, 8-OMe	see ^c	1640	56
35	2	1,4-(OMe) ₂	see ^a	1675	55
150	2	1,4-(OMe) ₂ , 3-Me	see ^a	1680	55
151	2	1,4-(OMe) ₂ , 3-Br	see ^a	1693	55

^a In KBr pellets. ^b The assignment of this peak to the aldehyde group is doubtful. ^c Data on the solvent were not reported in the study.⁵⁶

Table 5. Position of the long-wavelength band in the UV spectra of selected naphthaldehydes.

Compound	Position of CHO groups	Other substituents	Solvent	λ_{max} /nm (log ϵ)	Colour	Ref.
2	1	—	MeOH	312 (3.39); 328, sh ^a (3.36)	colourless	136
12	1, 8	—	dioxane	296 (3.80)	<i>ditto</i>	108
49	1	4-NMe ₂	MeOH	369 (3.75)	pale-yellow	136
54	1	4,5-(NMe ₂) ₂	MeOH	407 (3.74)	yellow	136
55	1, 8	4,5-(NMe ₂) ₂	MeOH	449 (3.52)	dark-orange	136
56	1, 6	4,5-(NMe ₂) ₂	MeOH	403 (3.67)	yellow	136
131	1	8-OH	cyclohexane	394 (3.52)	orange	95
131	1	8-OH	H ₂ O–MeOH, 3 : 1	350 (3.45)	<i>ditto</i>	95

^a Shoulder.

(LUMO). A narrowing of the energy gap between these orbitals leads to a shift of the absorption band to the visible region. To study this problem in more detail, it would be of interest to record the UV spectra of 5-methoxy- and 5-dimethylamino-1-naphthaldehydes.

It should be noted that UV spectra played a large role in the determination of the structure of gossypol yellow in colour ($\lambda_{\text{max}} = 277, 289$ and 364 nm).¹³⁷

Mass-spectrometric data for naphthaldehydes are scarce. Mezheritskii and co-workers⁴² studied the fragmentation pathways of 4,8-dihydroxy-1,5-naphthodialdehyde in detail. In the mass spectrum of this compound, the molecular ion peak is most intense (100%). The character of fragmentation led the authors of the cited study⁴² to the conclusion that both cyclic and acyclic forms of this dialdehyde are present in the gas phase, and decomposition of each form follows its own pathway. In particular, the fragmentation of the molecular ion of the dialdehyde form begins with elimination of the $\cdot\text{CHO}$ radical followed by liberation of two CO molecules. By contrast, the intensity of the molecular ion peak in the mass spectrum of 8-dimethylamino-1-naphthaldehyde is 60%, whereas the $[\text{M}^{+\cdot} - \text{CO}]$ peak is most intense.⁷⁶

The electron affinities (*EA*) of 1- and 2-naphthaldehydes, which were measured by high-pressure pulse mass spectrometry, are 0.68 and 0.64 eV, respectively (for comparison, *EA* of naphthalene, 1-nitronaphthalene and 2-nitronaphthalene are -1.12 , $+1.23$ and $+1.18$ eV, respectively; the negative electron affinity of naphthalene reflects the instability of its radical anion).¹³⁸

2. NMR spectra

The most useful information on conformations of the formyl group, which can be obtained from ^1H NMR spectra of naphthaldehydes, involves chemical shifts of the protons of the CHO group and also of the nearest-neighbourhood protons, primarily, of *peri*-H. The chemical shifts of the proton of the CHO group for selected naphthaldehydes, which do not contain intramolecular hydrogen bonds, are given in Table 6.

If a molecule contains no bulky substituents adjacent to the formyl group, the latter can be located virtually in the ring plane (see Section III.6). In this case, the signal for the proton of the CHO group is generally observed at δ 10 (see Table 6). If the aldehyde group is twisted with respect to the naphthalene system, its proton is in the region of the diamagnetic component of the ring current and the corresponding signal shifts downfield. In addition, the chemical shift of the proton of the formyl group depends substantially on the anisotropic effect of the adjacent group, particularly, if it contains the lone electron pair. These phenomena can be observed in the ^1H NMR spectra of 8-substituted naphthaldehydes in which the chemical shifts of the proton of the CHO group reach 11 ppm and can be even higher (see Table 6). The rotation of the CHO group can be caused by both steric factors and electronic interactions between the substituents. For example, if a substituent in position 8 of the naphthalene system contains an

Table 6. Chemical shifts of the proton of the CHO group (δ_{CHO}) in the ^1H NMR spectra of selected naphthaldehydes.

Compound	Position of the CHO group	Other substituents	Solvent	δ_{CHO}	Ref.
2	1	—	CCl ₄	10.24	86
2	1	—	CDCl ₃	10.10, 10.38	87, 139
124	2	—	CDCl ₃	9.99, 10.12	87, 139
30a	1	2-OMe	CDCl ₃	10.85	139
49	1	4-NMe ₂	CDCl ₃	10.14	65
54	1	4,5-(NMe ₂) ₂	CCl ₄	9.96	68
55	1, 8	4,5-(NMe ₂) ₂	CDCl ₃	9.78 ^a	68
56	1, 6	4,5-(NMe ₂) ₂	CDCl ₃	10.18 ^a	68
93	1	8-NMe ₂	CDCl ₃	10.65	75
128	1	8-Me	CDCl ₃	10.81	122
112	1	8-Br	CDCl ₃	11.32	96
139	1	8-SMe	CDCl ₃	11.10	96
28	1	4-OMe	CDCl ₃	10.12	140
149	1	4-OH, 8-OMe	DMSO- <i>d</i> ₆	11.12	56
35	2	1,4-(OMe) ₂	CDCl ₃	10.86	55
150	2	1,4-(OMe) ₂ , 3-Me	CDCl ₃	11.03	55
151	2	1,4-(OMe) ₂ , 3-Br	CDCl ₃	10.86	55

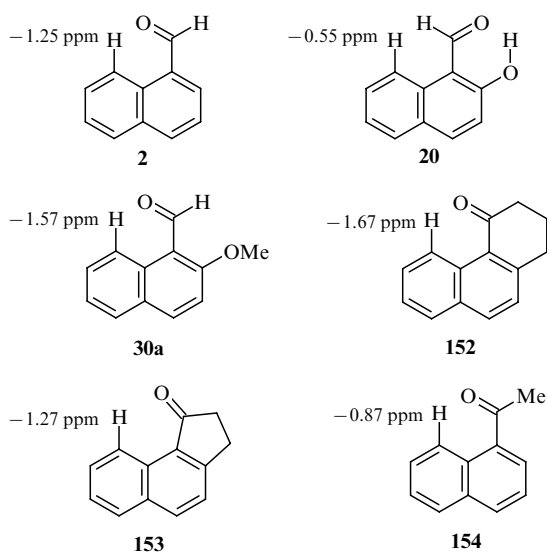
^a 2H.

atom with the lone electron pair (NMe₂, OMe, SMe), the latter tends to attack nucleophilically the carbonyl carbon atom, which requires rotation of the CHO group with respect to the ring plane by a large angle τ (see Section III.6). Apparently, when τ is close to 90° , the signal for the proton of the CHO group is observed at $\delta \sim 11.0$. The arrangement of the ring and formyl group in a single plane is apparently characterised by the chemical shift $\delta_{\text{CHO}} \sim 9.8$.

It is known that the carbonyl group possesses a substantial anisotropic effect. The protons located in the magnetic cone in the vicinity of the oxygen atom are subjected to strong deshielding and their signal shifts substantially downfield. This effect influences also the protons adjacent to the carbonyl carbon atom (however, to a much lesser degree). α -Naphthaldehyde **2** and its 2-hydroxy derivative **20** are characteristic examples. Taking into account the presence of an intramolecular hydrogen bond in compound **20**, the orientation of the CHO group is beyond question. Hence, a substantially larger downfield shift of the signal for the H(8) proton in the ^1H NMR spectra of α -naphthaldehyde indicates that its carbonyl group is directed toward the *peri*-proton (*Z* conformation). The occupancy of the *Z* conforma-

tion in 2-methoxy-1-naphthaldehyde (**30a**) is even higher due, apparently, to the supporting effect of the methoxy group.

According to estimates made in the studies^{141, 142} based, in particular, on a comparison of the chemical shifts of the signal for the H(8) proton in the spectra of α -naphthaldehyde (δ 9.23) and model compound **152** (δ 9.51), the CHO group in molecule **2** is non-coplanar with the ring (the corresponding angle is 22°). Judging from the data for cyclic ketones **152** and **153**, the formyl group in molecule **154** containing the even bulkier acetyl group should be even more non-coplanar. For a series of carbonyl derivatives of naphthalene,¹³⁹ the diamagnetic shifts of the signal for the proton at the *peri* position with respect to the aldehyde group (relative to the corresponding signal in the ^1H NMR spectrum of naphthalene) under the influence of the anisotropic effect of the C=O group are shown below.



Data on deshielding of the *ortho*- and *peri*-protons in naphthaldehydes containing the NMe_2 groups in their cores are presented in Table 7. The downfield shifts of the signals for the *peri*- and *ortho*-protons in the ^1H NMR spectra of dimethylaminonaphthaldehydes relative to the corresponding signals for compounds **47** (for **49**) and **53** (for **54–56**) are shown below.^{65, 68} (The atomic numbering scheme for the hydrogen atoms in compounds **47** and **53** used here and in Table 7 is arbitrary.)

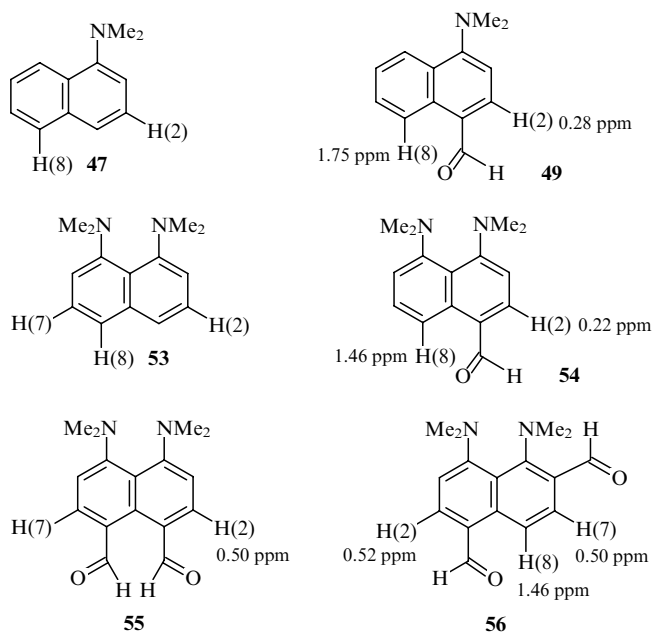


Table 7. Chemical shifts (δ) of the protons experienced the anisotropic effect of the carbonyl group in the ^1H NMR spectra (in CDCl_3) of dimethylaminonaphthaldehydes.^{65, 68}

Compound	δ		
	H(2)	H(7)	H(8)
47	7.50	—	7.60
53	7.33	—	7.39
49	7.78	—	9.35
54	7.55	—	8.85
55	7.83	7.83	—
56	7.83	7.85	8.85

Conclusions about the orientations of the groups in dialdehydes **55** and **56** were made based on the results of X-ray diffraction analysis (see Section III.6). The degree of deshielding of the H(8) proton in monoaldehyde **54** is equal to that in dialdehyde **56**. This indicates that the carbonyl oxygen atom in molecule **54** is also directed toward the *peri*-proton. The same is true for monoaldehyde **49** in which the deshielding of the *peri*-proton is even more substantial. It should be noted that weak deshielding of the *ortho*-protons is observed even if the carbonyl oxygen atom is oriented toward these protons, the more so that this deshielding is, undoubtedly, associated with the electron-withdrawing ability of the CHO group.

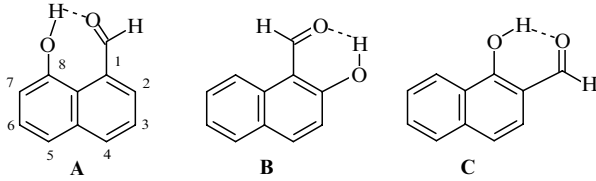
Analysis of the ^1H NMR (see Ref. 142) and ^{13}C NMR (see Ref. 92) spectra and the nuclear Overhauser effect in combination with theoretical MM2 calculations¹⁴³ demonstrated that the occupancy of the *Z* conformation in α -naphthaldehyde is, on the average, 80%–90% regardless of the conditions, whereas the *E* conformer is more favourable for β -naphthaldehyde to the same extent (Table 8). It was believed¹⁴⁴ that both conformers are stabilised through a more efficient conjugation between the *trans*-arranged C=O group and the $\text{C}(1)=\text{C}(2)$ bond characterised by a higher multiplicity. In addition, a weak intramolecular hydrogen bond can occur between the carbonyl oxygen atom and the H(8) proton in 1-naphthaldehyde.¹⁴⁵

The free activation energies of rotation of the CHO group in α - and β -naphthaldehydes determined by dynamic ^{13}C NMR spectroscopy are 26.8 and 34.4 kJ mol^{-1} , respectively. The introduction of the methoxy substituent at position 4 of molecule **2** and at

Table 8. Content of the *Z* form in α - and β -naphthaldehydes.

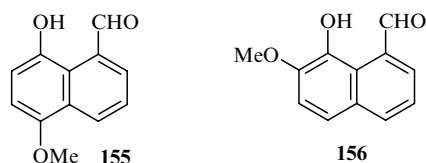
Position of the CHO group	Content of the <i>Z</i> form (%)	Conditions	Ref.
1	77	CDCl_3 , 25°C	142
1	85	CDCl_3 , 25°C	143
1	90	freon, -134°C	92
2	14	CDCl_3 , 25°C	142
2	12	CDCl_3 , 25°C	143
2	20	freon, -108°C	92

Table 9. Chemical shifts (δ) of the protons of the CHO and OH groups in the ^1H NMR spectra of hydroxynaphthaldehydes containing an intramolecular hydrogen bond.

						
Compound	Type of aldehyde	Substituents	Solvent	δ_{CHO}	δ_{OH}	Ref.
131	A	—	CDCl_3	9.76	11.60	95
131	A	—	THF-d_6	10.39	10.72	95
134	A	4-OMe	CDCl_3	11.16	12.06	56
134	A	4-OMe	DMSO-d_6	10.66	9.5	56
155	A	5-OMe	CDCl_3	9.87	10.97	127
156	A	7-OMe	CDCl_3	10.08	10.75	127
135	A	5-Br	CDCl_3	9.84	11.65	128
136	A	5,7-Br ₂	CDCl_3	9.93	12.07	128
137b	A	5-NO ₂	CDCl_3	9.87	10.97	128
20	B	—	CDCl_3	10.78	13.15	139
157	A, B	2,3,8-(OH) ₃ , 4-Pr ⁱ , 6-Me (hemigossypol)	CDCl_3	11.50	14.95	146
1	A, B	2,3,8-(OH) ₃ , 4-Pr ⁱ , 6-Me [(S)-gossypol]	CDCl_3	11.11	15.11	63
18	C	—	CDCl_3	—	12.61	147

position 6 of molecule **124** increases the rotation barrier by 4.6 and 2.9 kJ mol^{-1} , respectively.⁹²

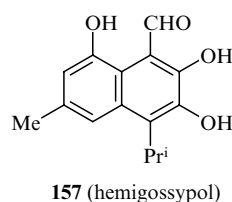
The ^1H NMR spectra of naphthaldehydes in which the CHO group is involved in intramolecular hydrogen bonding have some characteristic features. Among these compounds are *peri*- and *ortho*-hydroxynaphthaldehydes (Table 9). Evidently, the formyl group in 8-hydroxy-1-naphthaldehyde (**131**) is virtually coplanar with its aromatic core, and the carbonyl oxygen atom is directed toward the hydroxy substituent. This is evidenced primarily by the chemical shift of the proton of CHO (δ 9.76) and the position of the signal of OH (δ 11.60) characteristic of the hydroxy group involved in intramolecular hydrogen bonding. Analogous patterns are observed in the spectra of 5-methoxy (**155**), 7-methoxy (**156**), 5-bromo (**135**), 5,7-dibromo (**136**) and 5-nitro derivatives (**137b**) of *peri*-hydroxyaldehyde.



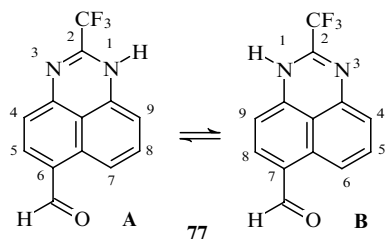
The spectrum of 8-hydroxy-4-methoxy-1-naphthaldehyde (**134**) differs substantially from those mentioned above. The unexpectedly large (δ 11.16) chemical shift of the proton of CHO in the spectrum of this compound can be attributed only to a sharp change in the conformation of the formyl group (for example, to its substantial rotation about the $\text{C}_{\text{Ar}}-\text{CHO}$ bond) necessary for the nucleophilic attack of the hydroxy group on the carbonyl carbon atom (see Section III.6) or its transformation into the *E* form. In the latter case, the proton of the CHO group is located in the diamagnetic field of simultaneously two benzene rings and its signal should be shifted substantially downfield, as was observed for the α -protons of naphthalene (δ 7.81) compared to the β -protons (δ 7.46). However, the role of the 4-methoxy group remains unclear.

As a result of the transformation into the *E* form, the signal for the proton of the CHO group in 2-hydroxy-1-naphthaldehyde (**20**) also undergoes a substantial diatropic shift (δ 10.78). The presence of an intramolecular hydrogen bond in this compound leads

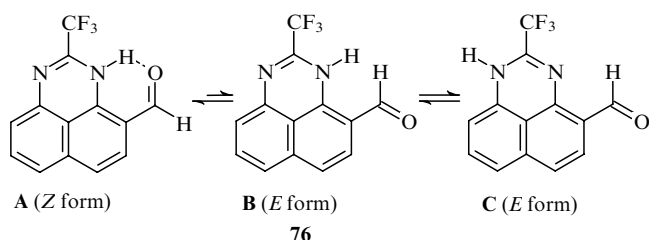
to closure of the more stable six-membered ring, as evidenced by the position of the signal for the proton of OH in the ^1H NMR spectrum of aldehyde **20** (δ 13.15) compared to that in the spectrum of aldehyde **131** (δ 11.60) containing the seven-membered chelate ring. In this connection, gossypol (**1**) and hemigossypol (**157**) are of interest. In these compounds, intramolecular hydrogen bonds can occur between the 1-CHO and OH groups both in positions 2 and 8. The data from Table 9 provide unambiguous evidence in favour of the former type of hydrogen bonding, *i.e.*, in favour of the six-membered ring closure and *E* conformation of the aldehyde functional group in molecules **1** and **157**. The record chemical shift of the proton of CHO in the spectrum of hemigossypol suggests that the aldehyde proton in this compound is, presumably, also involved in intramolecular hydrogen bonding with the oxygen atom of the OH group in position 8 (the assumption that the formyl group can act as an H donor in hydrogen bonding has been made recently in the study¹⁴⁸).



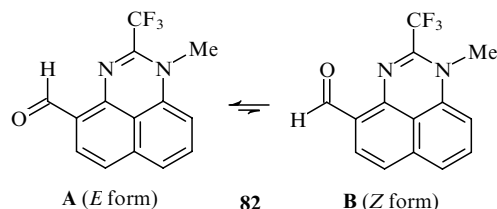
On the whole, the same is true for the signals of the formyl group in the NMR spectra of aldehydes based on naphthalene-containing heterocyclic systems, but there are some specific features associated with annular tautomerism and the presence of heteroatoms. Thus, the ^1H NMR spectrum of 6(7)-formyl-2-trifluoromethylperimidin (**77**) in CDCl_3 has signals of both annular tautomers **A** and **B**, the aldehyde group occurring in the *Z* form in both tautomers.^{149, 150} This is evidenced by a substantial deshielding of the adjacent *peri*-proton whose signal is observed at δ 8.77 and 8.82 for the tautomers **A** and **B**, respectively. The signals for the aldehyde proton are observed at δ 10.04 and 9.97, respectively. This is characteristic of the *Z* conformation of the CHO group, which is virtually coplanar with the naphthalene core (see Section III.6).



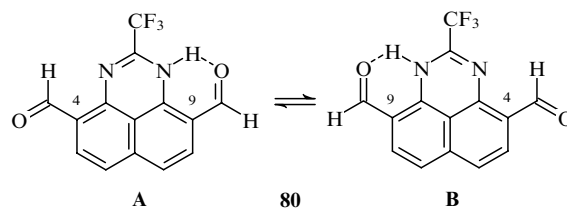
Due to the formation of a strong intramolecular hydrogen bond between the proton of the NH group and the oxygen atom of the formyl group, perimidine-4(9)-carbaldehydes, in particular, compound **76**, occur in non-polar solvents and in the solid state exclusively in the chelated 9-CHO-form **A**.⁷³ However, in polar media, for example, in DMSO, the solvent competes with the aldehyde group for the proton of the NH group, an intramolecular hydrogen bond is partially cleaved and different conformers and tautomers, including the forms **B** and **C**, can either coexist or undergo rapid interconversions. For example, the ¹H NMR spectrum of aldehyde **76** in DMSO-*d*₆ at 25 °C has two signals for the proton of CHO at δ 9.90 and 10.45 with the intensity ratio of ~1 : 3. The former signal belongs, apparently, to the chelated 9-CHO group and the latter signal can be assigned to the 4-CHO group in the tautomer **C**. Upon heating, both peaks coalesce into one signal at δ 10.20, whereas the peak of the proton of NH disappears, which is indicative of the rapid interconversion of the tautomers



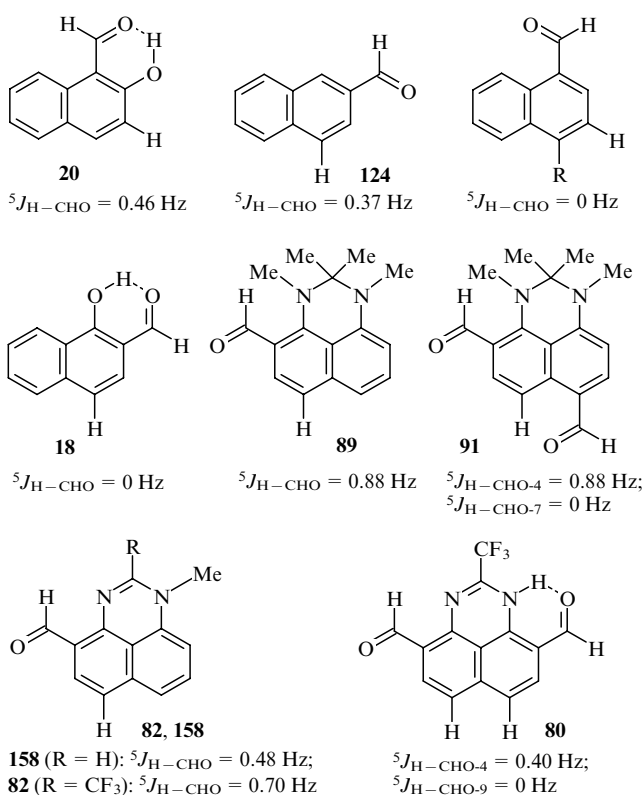
The spectra of 1-*R*-4-formylperimidines, for example, of compound **82**, have a signal for the proton of the CHO group at abnormally low field ($\delta_{\text{CHO}} \sim 10.8$). Since the aldehyde group in these compounds does not experience steric hindrances and its non-coplanarity with the ring is unlikely, this position of the signal indicates that compounds of type **82** adopt the *E* conformation **A** in which the hydrogen atom of the formyl group is deshielded by the adjacent nitrogen atom of the pyridine type. In addition, the *Z* conformation **B** can be destabilised due to repulsion between the lone electron pairs of the oxygen and nitrogen atoms.



Interesting conformational transitions were observed for 2-trifluoromethylperimidine-4,9-dicarbaldehyde (**80**).⁷³ Judging from the ¹H NMR spectrum in CDCl₃, under these conditions the CHO group in position 9 is fixed in the *Z* conformation (δ_{CHO} 9.93), whereas the 4-formyl substituent occurs in the *E* conformation (δ_{CHO} 10.83). In DMSO-*d*₆, the spectral pattern changes sharply. This spectrum has only two two-proton doublets corresponding to aromatic protons and one singlet of two equivalent CHO groups. Symmetrisation of the spectrum indicates that the polar solvent easily cleaves the intramolecular hydrogen bond resulting in rapid prototropism between the degenerate tautomers **A** and **B**.



The conformers of naphthaldehydes can be reliably identified based on the long-range spin–spin coupling constants between the formyl proton and the *meta*-proton of the ring, $^5J_{\text{H-CHO}}$,^{73, 142} whose values are given below. Generally, these constants are not observed in the spectra of the *Z* forms, but are pronounced in the spectra of the *E* conformations. Their values are generally in the range of 0.4–0.9 Hz. It can be readily seen that the necessary condition for the manifestation of the constants $^5J_{\text{H-CHO}}$ is the *trans*-arrangement of the coupling hydrogen atoms with respect to the C_{Ar}–CHO bond.



In principle, the conformations of naphthaldehydes can also be established based on analysis of the ¹³C NMR spectra. For example, it was noted that the ¹³C signal of the *ortho*-carbon atom in the *cis* position with respect to the carbonyl carbon atom shifts downfield, on the average, by ~8 ppm compared to the signal for another *ortho*-carbon atom.⁹² (The detailed data on the ¹³C NMR spectra of naphthaldehydes were reported in the studies.^{63, 140, 144, 151, 152}) The ¹⁷O NMR spectrum of 4-methoxy-1-naphthaldehyde was studied.¹⁴⁰ This spectrum has a signal for the carbonyl oxygen atom at δ 552.3 and a signal for the oxygen atom of the methoxy group at δ 66.0.

The above-considered data lead to the following important conclusion. Naphthalenes have four types of formyl groups, which are subjected to different action of the diamagnetic component of the ring current. These groups correspond to the *E* and *Z* conformations of α - and β -naphthaldehydes. Each group in the planar form is characterised by different chemical shifts of the proton of the formyl group. The proton of CHO in the *E* form of α -naphthaldehyde is characterised by the most substantial deshielding, whereas the chemical shifts for the remaining three forms are much smaller and differ only slightly from each other. In

substituted naphthaldehydes, the situation is complicated because the chemical shifts of the proton of the CHO group are influenced by steric and electronic factors.

3. Dipole moments

To estimate the polarity and degree of conjugation between the CHO and NMe₂ groups in aldehydes **49**, **54** and **55**, their dipole moments were measured (Table 10). A comparison of the dipole moments of α -naphthaldehyde (**2**), 1-dimethylaminonaphthalene (**47**) and 4-dimethylamino-1-naphthaldehyde (**49**) demonstrated that the additional dipole π moment (μ_{π}^{π}) in compound **49** induced by the so-called 'through-conjugation' is 0.35 D, which is almost three times smaller than that in 4-dimethylaminobenzaldehyde ($\mu_{\pi}^{\pi} \approx 1$ D). Presumably, this is a consequence of steric hindrances to the planar arrangement of the CHO and NMe₂ groups, on the one hand, and the naphthalene π -system, on the other, caused by the *peri*-protons. However, the situation sharply changes on going to 4,5-bis(dimethylamino)-1-naphthalene-1,8-dialdehyde (**54**) and, particularly, to 4,5-bis(dimethylamino)-1,8-naphthodialdehyde (**55**). The unexpectedly large dipole moments of these compounds indicate that the conjugation between the CHO and NMe₂ groups becomes at least as efficient as that in 4-dimethylaminobenzaldehyde. The additional π moments in monoaldehyde **54** and *peri*-dialdehyde **55** are ~ 1.4 and 2.3 D, respectively. This is consistent with the X-ray diffraction data for dialdehyde **55**. These data are indicative of a sharp increase in the distance between the NMe₂ groups compared to the corresponding distance in 'proton sponge' **53**, which is favourable for the strong through-conjugation. Considering the dipole moment (9.21 D), *peri*-dialdehyde **55** is similar to ionic substances. Actually, unlike most of 'proton sponge' derivatives, dialdehyde **55** is noticeably water-soluble, has a rather high melting point (162–164 °C) and exhibits metallic lustre. Strong conjugation decreases the positive charges on the carbon atoms of the formyl groups, pushes them apart and is favourable for stabilisation of the molecule. This is a fundamental difference between *peri*-dialdehyde **55** and dialdehyde **12**, which exists as a cyclic hydrate **122** under ordinary conditions.

Table 10. Dipole moments (μ) of selected naphthaldehydes and model compounds.¹³⁶

Compound	μ /D	Compound	μ /D
2	2.87	53	1.19
47	1.19	54	5.44
49	4.41	55	9.21

The Kerr constants and dipole moments of 1- and 2-naphthaldehydes **2** and **124** were determined and compared with those of 1- and 2-acetylnaphthalenes.¹⁵³ The Kerr constants for aldehyde **2** indicate that the CHO group is rotated with respect to the plane of the naphthalene system by 15°. However, these data do not allow one to make a conclusion as to which conformation (*Z* or *E*) is more favourable. The Kerr constants for aldehyde **124** are consistent with the planar *E* form.

Quantum-chemical calculations in the π approximation of dipole moments of two planar conformers of α - and β -naphthaldehydes and a comparison of these values with the experimental values μ did not lead to reliable conclusions about which form is favourable because of the similarity of the experimental and theoretical values.^{154, 155} The dipole moment of 2-naphthaldehyde (**124**) in CCl₄ (3.26 D) is smaller than that of its 1 : 1 complex with phenol (4.6 D).¹⁵⁶

4. Basicity

Like other carbonyl compounds, naphthaldehydes belong to bases and can be protonated by strong acids at the oxygen atom of the carbonyl group. The ionisation constants (pK_a) of 1- and 2-naphthaldehydes determined by spectrophotometry in aqueous

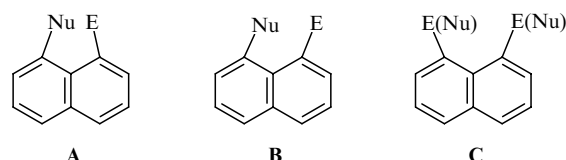
H₂SO₄ are -6.34 and -6.68 , respectively.¹⁵⁷ Therefore, both these aldehydes are somewhat more basic than benzaldehyde ($pK_a -6.99$) but less basic than 1- and 2-acetylnaphthalenes ($pK_a -5.86$ and -6.04 , respectively). The basicities of aromatic aldehydes, including naphthaldehydes, can also be measured by IR and ¹H NMR spectroscopy.¹⁵⁸

5. Electrochemical reduction

Electroreduction of 1- and 2-naphthaldehydes in DMF and acetonitrile was studied by cyclic voltammetry.¹⁵⁹ Radical anions were generated as primary reduction products, which rapidly disappeared due to subsequent dimerisation. It was found that the reactivity of the radical anions decreases in the series benzaldehyde > 2-naphthaldehyde > 1-naphthaldehyde.

6. Results of X-ray diffraction studies

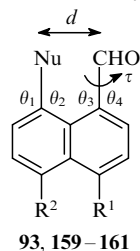
The structural data for the crystal structures of more than 20 derivatives of 1- and 2-naphthaldehydes, including gossypol (**1**) and its numerous crystal solvates, are available in the Cambridge Structural Database (April 2002). These data were used primarily for studying the conformational effects and *peri*-interactions involving the α -formyl group. There are three main types of displacements of the *peri*-substituents.



If one substituent is an electrophile (among which is the CHO group), whereas another substituent is a nucleophile, their interaction can cause these substituents to either approach each other (type **A**) or incline in the same direction (type **B**). If both substituents are either electrophiles or nucleophiles, they are pushed apart (type **C**). The type of interaction in each particular case can be judged from the distance (d) between the atoms of the substituents directly bound to the naphthalene ring and from the angles (θ) between the C–Nu and C–E bonds, on the one hand, and the adjoining bonds of the naphthalene ring, on the other (Table 11). It is very important to take into account the angle of rotation (τ) of the aldehyde group with respect to the ring plane.

The interaction of type **A** leads finally to the formation of covalent bonds. For naphthaldehydes existing in the aldehyde rather than cyclic form, such interactions have not been observed so far. All interactions of the CHO group with nucleophilic substituents in position 8 belong to type **B** (see Table 11). The type **B** displacement is most pronounced in 8-dimethylamino-1-naphthaldehyde (**93**). This is evidenced by the bond angles $\theta_1 - \theta_4$ and a shortened distance between the nitrogen atom and the carbon atom of the carbonyl group. Although both substituents in molecule **93** are inclined in the same direction, the angle of inclination of the NMe₂ group is larger than that of the CHO group due to which the distance between these substituents decreases. In addition, noteworthy is the large angle τ , which is a prerequisite to the attack of the lone electron pair of the amine nitrogen atom on the carbonyl carbon atom. One can conclude that this is the initial phase of the nucleophile–electrophile interaction and covalent binding.^{5, 6}

In spite of the fact that both *peri*-substituents in 8-methoxy-1-naphthaldehydes **159** and **160** are also inclined in the same direction, the distances between these substituents are substantially larger and the angle of rotation of the formyl group with respect to the ring plane is too small to provide the necessary trajectory of attack of the methoxy oxygen atom on the carbonyl carbon atom. It is believed that the leaning effect in molecules **159** and **160** is associated with weak Coulombic attraction between the oxygen atom of the OMe group and the hydrogen atom of the aldehyde group. Apparently, it is this interaction that is responsible for the *E* conformation of the CHO group in both aldehydes.

Table 11. Geometric parameters characterising *peri*-interactions between the formyl and nucleophilic (Nu) groups in 8-substituted 1-naphthaldehydes.

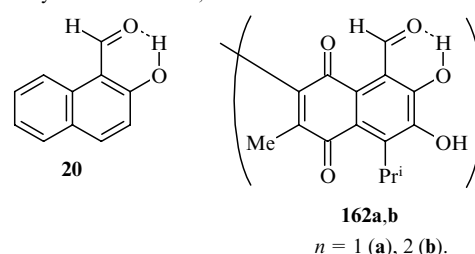
Compound	Nu	R ¹	R ²	<i>d</i> / Å	τ / deg	θ_1 / deg	θ_2 / deg	θ_3 / deg	θ_4 / deg	Ref.
93	NMe ₂	H	H	2.489	65.8	124.3	116.0	122.2	118.5	160
159	OMe	OMe	OTs	2.628	23.9	123.4	115.1	126.4	114.9	5
160	OMe	H	OTs	2.644	32.9	123.5	115.3	124.7	115.8	5
161	OCOPh	OMe	H	2.823	12.8	117.6	118.8	125.5	115.9	5

In molecule **161**, the benzyloxy group is too bulky and the nucleophilicity of the oxygen atom of the ester group is too small to be attracted to the formyl group. That is the reason why this aldehyde is characterised by a large distance (*d*) between the *peri*-substituents, and the plane of the aldehyde group is nearly coplanar with the ring plane. As a consequence, the arrangement of the *peri*-substituents in this compound corresponds to type C. This structural type is even more pronounced in *peri*-dialdehyde **55** based on a 'proton sponge'.¹³⁶ The distance between the carbonyl carbon atoms (2.99 Å) in its molecule is much larger than the distance between the carbon atoms of the methyl groups in 1,8-dimethylnaphthalene (2.56 Å). Both aldehyde groups in molecule **55** exist in the sterically less strained *E* conformation and the angles of their rotation with respect to the plane of the naphthalene ring are relatively small ($\tau = 20.1^\circ$ and -27.3°). All these geometric features are favourable for conjugation between the CHO and NMe₂ groups in this *peri*-dialdehyde.

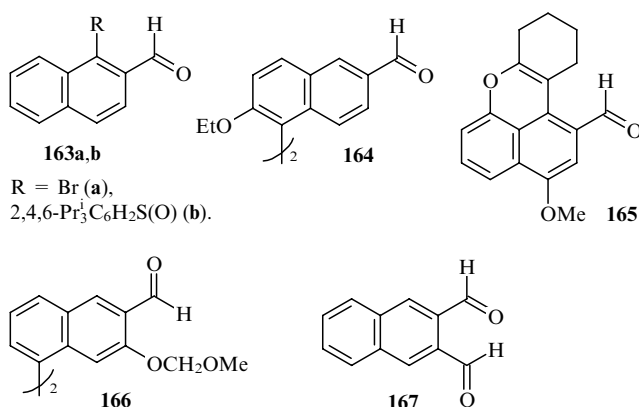
According to the results of X-ray diffraction analysis, the conformations of the *para*- and *ortho*-aldehyde groups in the 2,5-diformyl derivative of 'proton sponge' **56** are virtually identical with those in 1- and 2-naphthaldehydes, respectively. The former group occurs in the *Z* conformation and is located virtually in the plane of the ring ($\tau = 6.8^\circ$). The latter group occurs in the *E* conformation and the angle of its rotation ($\tau = 32.9^\circ$) is substantially larger due to the presence of the adjacent NMe₂ group.¹³⁶ The *Z* form is typical also of the CHO group in trifluoromethyl-perimidine-6(7)-carbaldehyde (**77**).¹⁴⁹ Hence, it can be concluded that if there are no substituents adjacent to the α -formyl group in the naphthalene ring, the oxygen atom of this group is always directed toward the *peri*-proton.

X-Ray diffraction studies, as well as ¹H NMR spectra, demonstrated that an intramolecular hydrogen bond involving the β -hydroxy group in 2-hydroxy-1-naphthaldehyde (**20**),¹⁶¹ hemigossypolone (**162a**),¹⁶² gossypolone (**162b**)¹⁶² and gossypol (**1**)^{163–166} stabilises the CHO group in the *E* conformation not only in solution but also in crystals. The geometric parameters of this intramolecular hydrogen bond are given in Table 12.

X-Ray diffraction studies of dialdehyde **56** and compounds **148**,¹⁶⁷ **163a**,¹⁶⁸ **163b**,¹⁶⁹ **164**¹⁷⁰ and **165**¹⁷¹ showed that the β -formyl group tends to adopt the *E* conformation not only in solution (see Table 8) but in the crystalline state as well. The exception is binaphthyl dialdehyde **166** for which the *Z* form was observed.¹⁷² Apparently, this is attributed to destabilisation of the *Z* conformer due to Coulombic repulsion between the oxygen carbon atom and the oxygen atoms of the substituent in position 3. Evidently, one CHO group in naphthalene-2,3-dicarbaldehyde (**167**) occurs in the *E* conformation, whereas another CHO group exists in the *Z* form for the same reason.¹⁷³

Table 12. Geometric parameters of an intramolecular hydrogen bond in naphthaldehyde derivatives **20**, **162a** and **162b**.

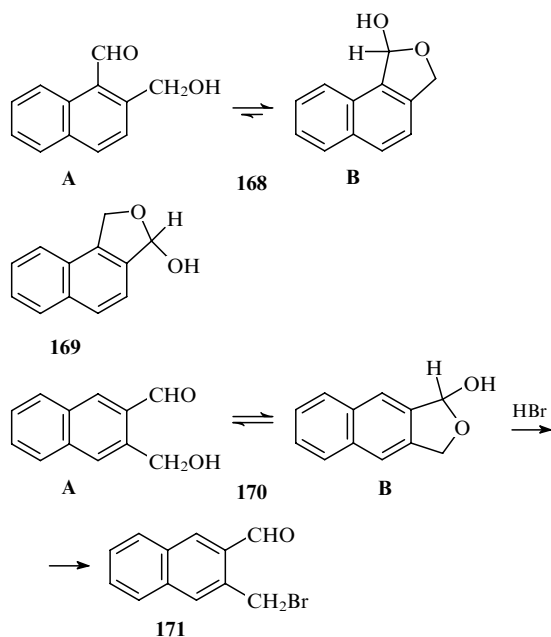
Compound	<i>d</i> / Å			Angle O–H...O / deg	Ref.
	O...O	O–H	H...O		
20	2.567	1.070	1.59	148.9	161
162a	2.55	0.73	1.89	150.4	162
162b	2.54	1.03	1.71	134.7	162



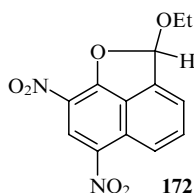
7. Ring-chain tautomerism

If a naphthaldehyde molecule has the OH-, NH- or SH-containing substituent adjacent to the aldehyde group, ring-chain tautomerism can take place due to the intramolecular nucleophilic addition of the O, N or S atoms of this substituent to the carbonyl group. 1,8-Naphthaldehydic acid existing under ordinary conditions in the naphthopyran form **127** serves as an example. Analogously, 2-hydroxymethyl-1-naphthaldehyde (**168**) occurs in the cyclic form **B** both in solution and in the solid state, whereas 1-hydroxymethyl-2-naphthaldehyde exists in form **169**.⁹¹ Crystalline 3-hydroxymethyl-2-naphthaldehyde (**170**) also occurs in the cyclic form **B** (the $\nu_{C=O}$ band is absent in the IR spectrum), but its tautomers **A** and **B** in CDCl₃ co-exist in equilibrium, in which the

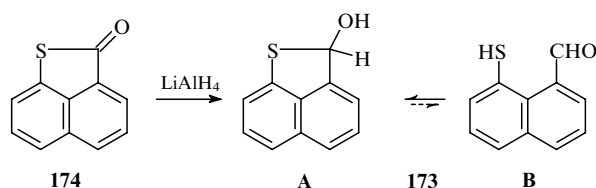
acyclic form **A** prevails (77%). It is this form of aldehyde **170** that is involved in reactions as evidenced by the formation of 3-bromomethyl derivative **171** upon treatment of compound **170** with hydrobromic acid.⁹¹



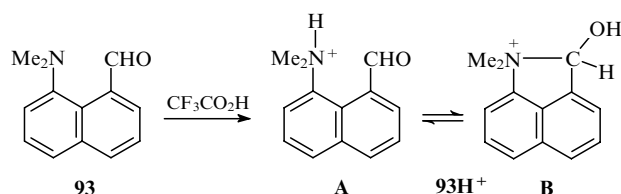
8-Hydroxy-1-naphthaldehyde (**131**) and its derivatives with electron-donating substituents in the naphthalene core are not prone to conversion into the cyclic form in neutral or acidic media although the presence of small amounts of this form in solutions cannot be ruled out.⁷ Heating of 8-hydroxy-5,7-dinitro-1-naphthaldehyde in ethanol afforded cyclic acetal **172**.¹²⁸



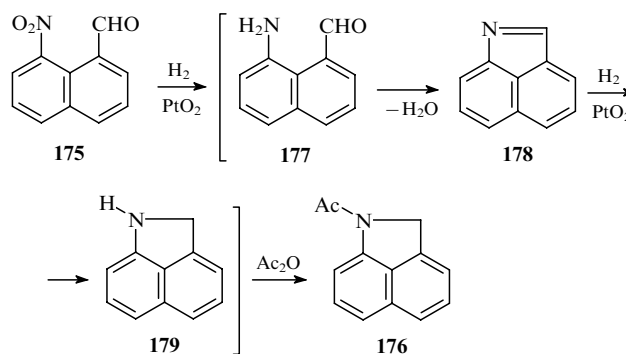
Unstable 8-mercapto-1-naphthaldehyde (**173**) prepared by reduction of 2-oxo-2*H*-naphtho[1,8-*b,c*]thiophene (**174**) with lithium aluminium hydride or diborane exists exclusively in the cyclic form **A**.¹⁷⁴



As mentioned above (see Section III.6), there are pronounced attractions between the substituents in 8-dimethylamino-1-naphthaldehyde (**93**). Treatment of this aldehyde with acids led to its partial cyclisation, both forms of hydrate **93H⁺** (**A** and **B**) being clearly seen in the ¹H NMR spectrum.⁷⁶



Catalytic reduction of 8-nitro-1-naphthaldehyde (**175**) followed by treatment of the reaction mixture with acetic anhydride afforded 1-acetyl-1,2-dihydrobenzo[*c,d*]indole (**176**).¹⁷⁵ Apparently, the initially formed *peri*-aminonaphthaldehyde **177** immediately underwent cyclisation to give compound **178**, which was subjected to further hydrogenation to form unstable benzoin-doline **179**. The latter can be isolated only as the more stable acetylated derivative **176**.

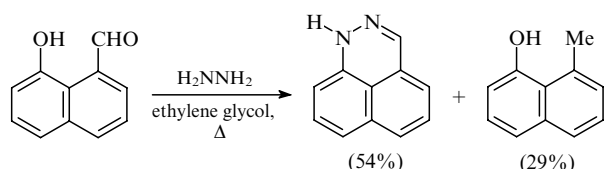


IV. Reactions

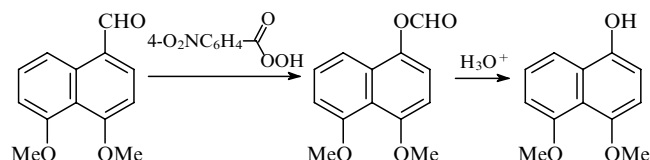
Naphthaldehydes are involved in all reactions typical of aromatic aldehydes. In addition, *peri*-substituted α -naphthaldehydes undergo specific transformations, primarily, cyclisations, due to the presence of closely spaced *peri*-substituents. For this series of compounds, the formation of thiosemicarbazones,⁴⁴ 2,4-dinitrophenylhydrazones,⁶⁸ oximes (which are then transformed into nitriles)^{68, 176, 177} and azomethines,⁶⁸ including polydentate ligands based on 1,1'-binaphthyl dialdehydes of type **103a,b**,^{81, 111, 178, 179} was described. Reduction of naphthaldehydes with complex metal hydrides afforded primary alcohols.^{65, 69, 70, 180} These reactions with the use of lithium tritide and lithium trimethoxyborotritide gave rise to tritium-labelled alcohols.¹⁸¹ Reduction of 2-naphthaldehyde with the TiCl₄–Bu₄N⁺I[–] system afforded 1,2-binaphthylethanediol.¹⁸² Procedures were developed for the enantioselective addition of diethylzinc¹⁸³ and other organometallic compounds¹⁸⁴ to 2-naphthaldehyde with the participation of chiral catalysts or auxiliary groups involved in the substrate. For other naphthaldehydes, analogous reactions were documented.^{58, 185} Naphthaldehydes gave condensation products with compounds containing the active methylene group, *viz.*, diethyl malonate ester,^{122, 186} malononitrile,^{186–188} esters of cyanoacetic¹⁸⁶ and other carboxylic acids,⁸⁹ benzyl cyanides,^{52, 187} γ -picoline,⁹⁸ barbituric acid,¹⁸⁹ trinitrotoluene,⁶⁰ *etc.*

The transformation of 4,8-difluoro-1-naphthaldehyde into the corresponding naphthalenecarboxylic acid under the action of KMnO₄ or the Jones reagent¹¹⁸ can serve as an example of oxidation of naphthaldehydes. The Angeli's salt (sodium tri-oxodinitrate, Na₂N₂O₃) can be used as an oxidising agent. In the latter case, the reaction proceeds by a very complex mechanism involving [2 + 2]-cycloaddition between the N=N bond of the oxidising agent and the C=O group of the aldehyde.¹⁹⁰ Milder reagents can oxidise other groups, the aldehyde group remaining intact. For example, gossypol was converted into gossypolone **162b** (47%–69% yield) under the action of an aqueous solution of FeCl₃.¹⁹¹

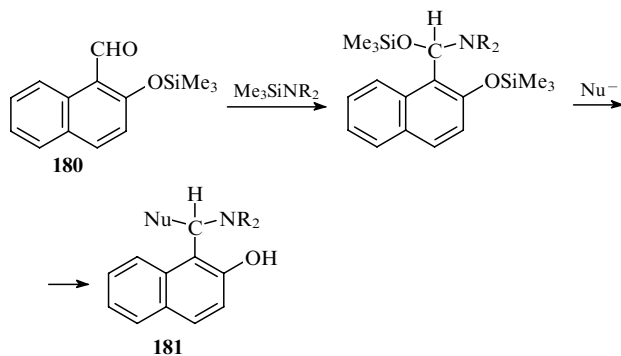
Attempts to prepare hydrazones by treating naphthaldehydes with hydrazine were often unsuccessful and led to the formation of the corresponding azines.^{68, 192} Nevertheless, the *in situ* formation of hydrazones was used for the conversion of naphthaldehydes into methylnaphthalenes (Kishner–Wolff reaction)^{44, 52} and *peri*-heterocyclic compounds.¹⁷⁶



p-Toluenesulfonylhydrazones of α -naphthaldehydes were synthesised and then treated with alkali to prepare naphthyldiazomethanes.^{96,97} Naphthaldehydes are involved in the Baeyer–Villiger reaction accompanied by the replacement of the formyl group by the hydroxy group.⁵³ Examples of such transformations were given in the Refs 55, 56, 117.

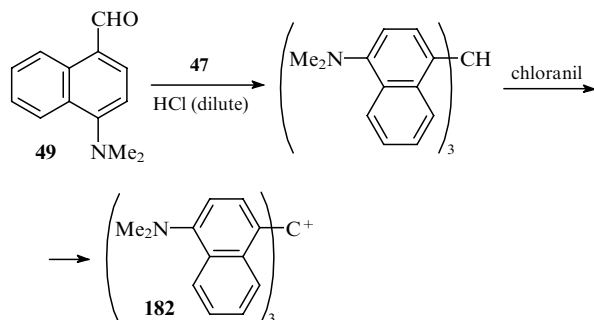


The tandem reactions of 2-trimethylsilyloxy-1-naphthaldehyde (**180**) with various trimethylsilyldialkylamines and nucleophiles afforded naphthols **181**.¹⁹³

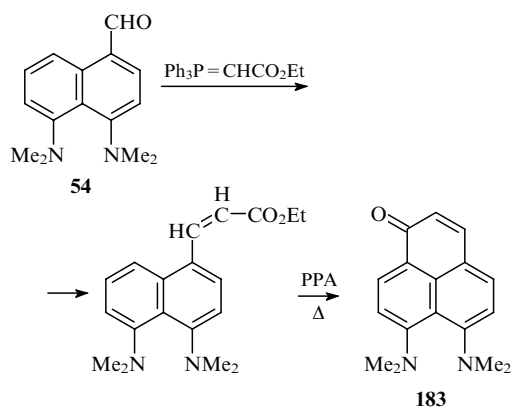


$\text{Nu} = \text{Me}, \text{CH}_2\text{CO}_2\text{Et}, \text{CH}_2\text{CH}=\text{CH}_2, \text{AlkC}\equiv\text{C}; \text{R} = \text{Alk}.$

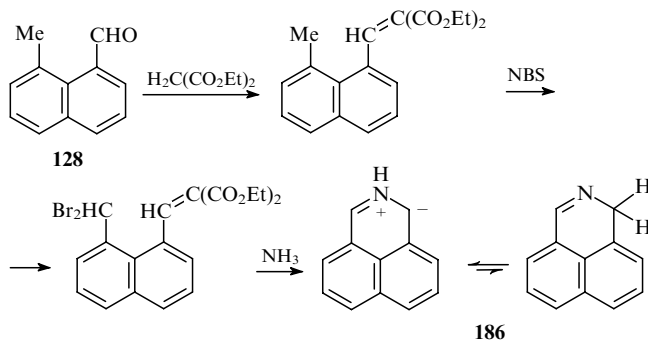
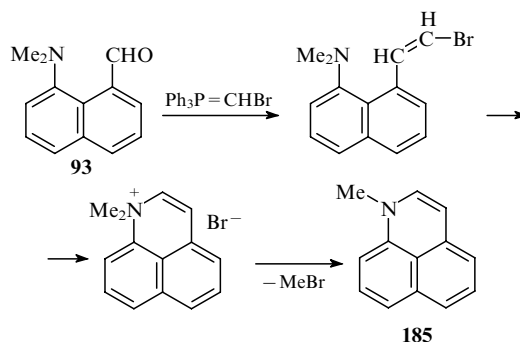
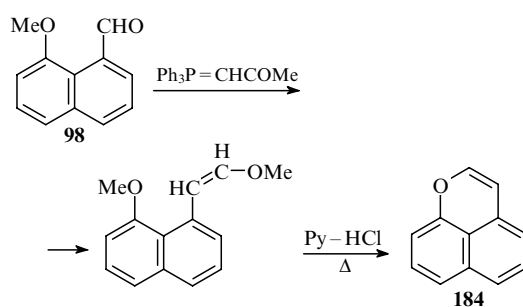
Under the conditions of acid catalysis, naphthaldehydes react with aromatic CH-nucleophiles, for example, with arylamines. This reaction was used, in particular, for the preparation of the dye Victoria Blue (**182**) from 4-dimethylamino-1-naphthaldehyde (**49**) and 1-dimethylaminonaphthalene (**47**).⁹⁰



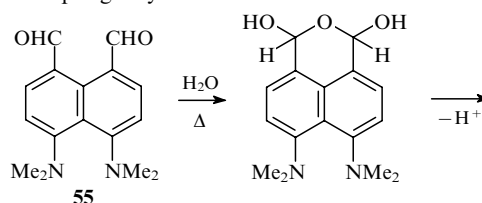
The Wittig^{75,77,78,107,160,194} and Wittig–Horner reactions^{133,195} of naphthaldehydes were studied in detail. These reactions afford alkenes, which are generally used for subsequent cyclisations, including the synthesis of natural compounds,¹⁹⁶ biologically active substances¹³³ and synthetic precursors of fullerene.¹⁹⁷ The syntheses of 6,7-bis(dimethylamino)phenalene (**183**),¹⁸⁶ naphtho[1,8-*b,c*]pyran (**184**)⁷⁸ (a modification of this synthesis was described in the study¹⁹⁸), 1-methylbenzo[*d,e*]quinoline (**185**)¹⁶⁰ and benzo[*d,e*]isoquinoline (**186**)¹²² provide only a few examples of such transformations. An analogous approach was used for the synthesis of linear and angular naphthofurans and benzocoumarins.⁷⁷

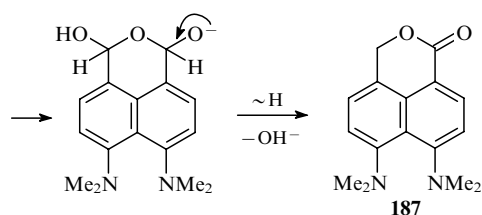


PPA is polyphosphoric acid.



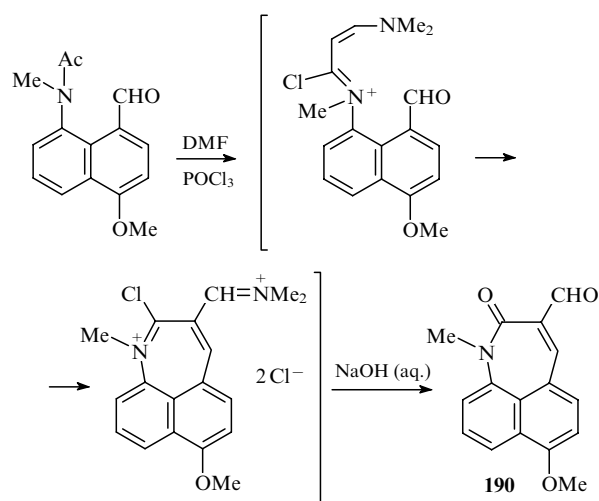
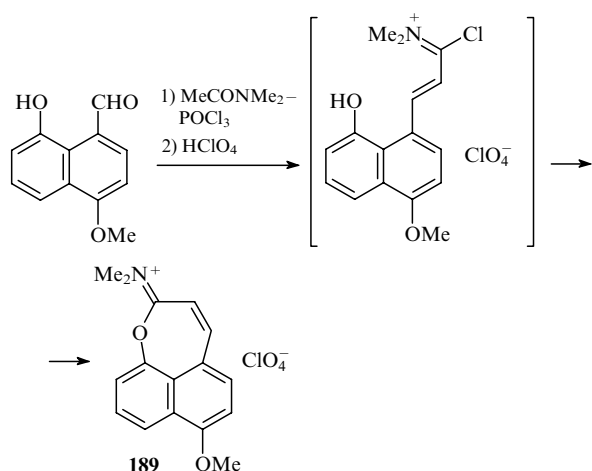
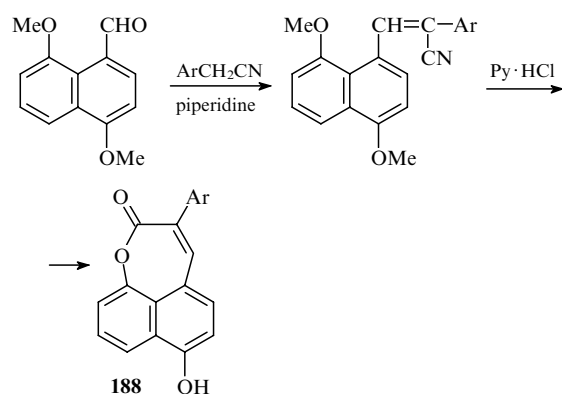
peri-Dialdehyde **55** derived from the ‘proton sponge’ underwent the intramolecular Cannizzaro reaction upon refluxing in water to form 6,7-bis(dimethylamino)naphtho[1,8-*c,d*]pyran-1-one (**187**).⁶⁸ Interestingly, this process, unlike the classical procedure, does not require the use of alkali. Apparently, the necessary alkalinity of the medium is provided by the high alkalinity of the ‘proton sponge’ by itself.





Naphthalene-1,8-dicarbaldehyde is also involved in the analogous reaction with the only difference that the latter reaction does require alkali.¹⁹⁹

Buu-Hoi *et al.*¹⁸⁷ and then Mezheritskii and co-workers^{7, 71, 200} demonstrated that the seven-membered heterocycles can be built up based on *peri*-hydroxy- and *peri*-aminonaphthaldehydes to form naphtho[1,8-*b,c*]oxepine and naphtho[1,8-*b,c*]azepine derivatives **188**–**190**.



In some studies, heterocyclisation was carried out with the use of 2-hydroxy-1-naphthaldehydes.^{188, 201}

* * *

The data surveyed in the present review provide evidence that naphthaldehydes play a very important role in the chemistry of naphthalene. These compounds serve as important starting reagents for the preparation of complex organic compounds, including biologically active and natural substances. Substituted naphthaldehydes are used for studying the effects of *peri*-interactions, in particular, these compounds model the transition state of the nucleophilic addition to the carbonyl group. This gives insight into the action of enzymes in living organisms. Studies of direct formylation of naphthalene derivatives are not only of great preparative importance but also provide a better understanding of the factors responsible for the reactivity of polynuclear arenes. Undoubtedly, these lines of investigation will be extensively developed in the coming years.

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The photorefractive effect in polymeric systems

A V Vannikov, A D Grishina

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Abstract. The review concerns the photorefractive effect in polymeric systems, which involves the creation, upon a primary photochemical reaction, of a phase grating shifted in space relative to the fringe pattern. The interaction of interfering laser beams accompanied by energy transfer from one beam to the other as well as salient features of the refractive index modulation in polymeric systems with low and high glass transition temperatures are considered. Particular attention is given to the photorefractive polymers with high glass transition temperatures containing nanocrystalline J-aggregates of cyanine dyes, which are characterised by high third-order nonlinear electric susceptibilities and induce modulation of the refractive index due to the Kerr electro-optic effect. The prospects for application of polymeric photorefractive materials are outlined. The bibliography includes 113 references.

I. Introduction

The photorefractive (PR) effect is induced by two interfering laser beams (a pump beam and a signal beam) and consists in reversible creation of a phase grating, which is shifted in space relative to the bright fringes. As a consequence, the pump beam reflected from the grating travels parallel to and is in phase with the signal beam. After passing the PR system the intensity of the signal beam is amplified at the attenuation of the reflected pump beam. The reflected signal beam is out of phase with the pump beam; therefore, the intensity of the latter decreases.

The photorefractive effect arises in polymeric media possessing specific properties. First, they must exhibit photoelectric sensitivity and provide the possibility of photogeneration of charge carriers of both signs in bright regions of the interference pattern as a result of a primary photochemical reaction and subsequent charge separation and transport. In most polymeric systems electrons are trapped by deep traps near the generation sites in bright regions of the interference pattern, while holes drift in the applied electric field E_0 towards the dark regions of the

interference pattern until trapping. As a result, a periodic space-charge field E_{sc} is induced, which is shifted in space relative to the fringe pattern. Second, polymeric systems must contain some compounds (chromophores) possessing second- or third-order nonlinear optical properties and/or anisotropy of the linear polarisability (e.g., dipole molecules of organic compounds with electron-donor and electron-acceptor substituents). The orientational or electronic polarisation of chromophores in the periodic field E_{sc} is responsible for periodic modulation of the refractive index, i.e., creation of a phase grating whose maxima coincide with those of the periodic field E_{sc} and, hence, are shifted in space relative to the interference fringes.

Photorefraction was first observed in inorganic crystals LiNbO_3 and LiTaO_3 in 1966.¹ In 1990, the phenomenon was reported for organic crystals² and in 1991 for polymeric composites.^{3,4} Recently, interest in photorefraction in the polymeric materials has increased due to the possibility of using them as highly efficient active optical elements for data transmission and controlling coherent radiation in various electro-optical and optical communication devices. Pioneering attempts to employ photorefractive polymeric materials for writing holograms of moving objects were due to the high writing and erasing speed of such materials. Polymeric systems are also of considerable interest because their spectral properties can be smoothly varied by changing the structure of polymers and polymeric composites. There is a great potential of doping such systems; in addition, they are cheap, readily processable and allow fabrication of parts of any shape and size which are compatible with modern micro-electronic and optoelectronic devices, etc.

Recently, various types of photorefractive polymeric materials have been designed. These are polymers in which functional groups (namely, sensitisers responsible for the photoelectric sensitivity, charge transport sites and nonlinear optical chromophores) are constituents of the main polymer chain or bound to it as side substituents; 'guest–host' composites (functionally doped polymers possessing the charge transport properties); and polymer layers modified in one or another manner (e.g., photochemically). Often, bifunctional polymeric systems are prepared, in which the same chain fragment or dopant simultaneously exhibits the properties of sensitiser and a chromophore or a charge transport site.

In preparing the manuscript the authors of this review focussed on the most interesting, from their viewpoint, results rather than comprehensive consideration of numerous available studies on the title problem.

A V Vannikov, A D Grishina A N Frumkin Institute of Electrochemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119071 Moscow, Russian Federation. Fax (7-095) 952 08 46. Tel. 952 31 22. E-mail: van@elchem.ac.ru

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II. Nature of the photorefractive effect in polymers

The most informative method for studying the PR effect is the two-beam method (Fig. 1). It involves splitting of a laser beam into two beams, which reflect from mirrors and then intersect inside a polymer layer. Each beam is characterised by the

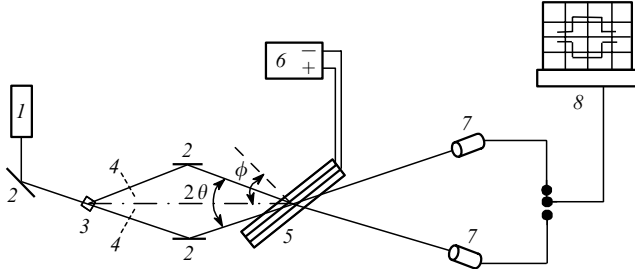


Figure 1. A scheme for measuring the PR effect.

Laser (1), reflecting mirrors (2), beam splitter (3), shutters for beams 1 and 2 (4), sample (5), constant voltage source (6), photodiodes (7), computer (8); 2θ is the angle between beam 1 and beam 2; ϕ is the angle between the z axis (bisectrix of the 2θ angle) and the normal to the surface of the sample.

amplitude, $E_{1,2}(\omega)$, or intensity, $I_{1,2} \sim E_{1,2}^2$, of the electric component of the electromagnetic field. Interference causes a periodic distribution of the light intensity (I) in space

$$\frac{I}{I_1 + I_2} = 1 + 2 \frac{(I_1 I_2)^{0.5}}{I_1 + I_2} \cos\left(\frac{2\pi x}{\Lambda}\right). \quad (1)$$

Here x is the coordinate along the x axis directed normal to the bisectrix of the 2θ angle between the beams (Fig. 2a); Λ is the spatial period (Fig. 2b), *i.e.*, the distance between the bright fringes [or constructive interference fringes, where $\cos(2\pi x/\Lambda) = 1$] along the x axis

$$\Lambda = \frac{\lambda}{\sin \theta},$$

$\lambda = \lambda_0/n$ is the optical wavelength in the polymer; λ_0 is the free-space wavelength; and n is the refractive index of the polymer.

A feature of systems exhibiting photoelectric sensitivity is photogeneration of charge carriers in the constructive interference regions. The number of charge carriers generated is proportional to the light intensity modulation, m (Ref. 5)

$$m = 2 \frac{(I_1 I_2)^{0.5}}{I_1 + I_2}.$$

The necessary condition for the PR effect is considerable difference between the mobilities of photochemically generated electrons and holes. For most polymeric media the mobility of electrons is much lower than that of holes. Electrons are trapped in the regions of bright fringes, while holes drift in the constant electric field E_0 towards the dark regions [or the destructive interference regions, where $\cos(2\pi x/\Lambda) = -1$]. This leads to separation of charge carriers in space and to the appearance of a periodic space-charge electric field E_{sc} , which is directed perpendicular to the bisectrix of the angle between the incident beams and shifted in phase by ψ relative to the fringe pattern (see Fig. 2b)

$$E_{sc} = E_{sc}^0 \cos\left(\frac{2\pi x}{\Lambda} - \psi\right). \quad (2)$$

The E_{sc}^0 field is proportional to the concentration of charge carriers generated in bright regions or, ultimately, to the light intensity modulation

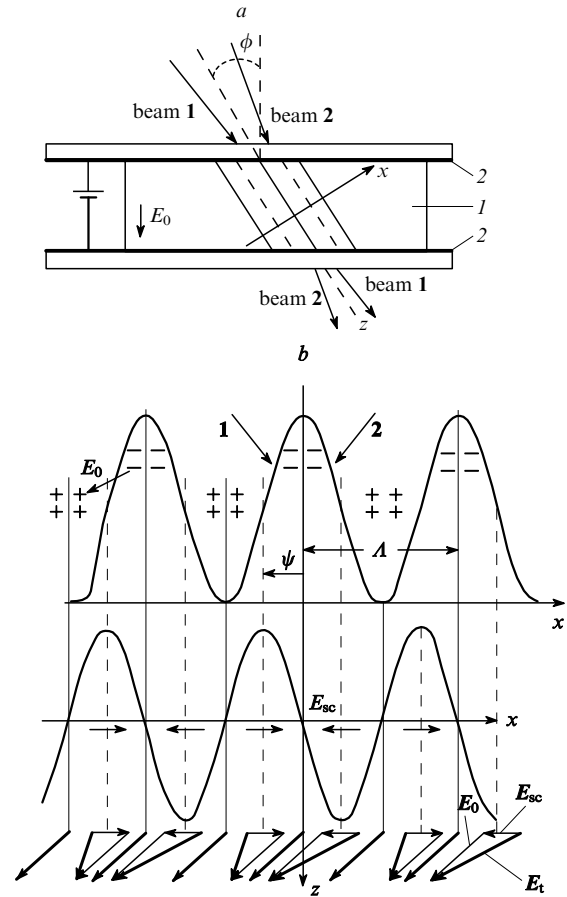


Figure 2. Measuring cell geometry (a) and a scheme illustrating the nature of the PR effect in polymeric systems (b);

(a) polymer layer (1), electrodes made of transparent conducting $\text{In}_2\text{O}_3:\text{Sn}$ film supported by glass slides; regions of constructive and destructive interference in the polymer layer are denoted by the solid and dashed lines, respectively; (b) the fringe pattern and photogeneration of charge carriers, the E_{sc} field distribution along the x axis and the distribution of the total field, $E_t = E_{sc} + E_0$, in the polymer layer (thick arrows); the ‘-’ signs in the interference-maximum regions denote trapped electrons; the ‘+’ signs denote holes migrated to the interference-minimum regions in the E_0 field; ψ is the shift in space of the phase of the E_{sc} field relative to the fringe pattern; the E_{sc} vector is parallel to the x axis and the E_0 vector is directed from the anode to the cathode.

$$E_{sc}^0 \sim 2 \frac{(I_1 I_2)^{0.5}}{I_1 + I_2}. \quad (2a)$$

If positive charges are located at the midpoints of dark regions, the E_{sc} field has maxima at the midpoints between bright and dark fringes, *i.e.*, these maxima are shifted by $x = \Lambda/4$ or by a phase of $\psi \approx \pi/2$ in space relative to the bright fringes. However, the phase shift is usually less than $\pi/2$.

If a composite contains chromophores possessing nonlinear optical properties or anisotropy of the linear polarisability, the E_{sc} field induces a periodic distribution of the refractive index. Indeed, the refractive index is related to the linear electric susceptibility of a unit volume of a polymeric composite $[\chi^{(1)}]$ as follows:

$$n^2 = 1 + 4\pi\chi^{(1)}. \quad (3)$$

The electric susceptibility,

$$\chi^{(1)} = \frac{P(\omega)}{E(\omega)},$$

characterises the linear polarisation, $P(\omega)$, of a unit volume of a substance, induced by the electric component, $E(\omega)$, of the electromagnetic field vector of the light wave. As will be shown below, $\chi^{(1)}$ becomes a variable quantity in a constant electric field.

A feature of non-centrosymmetric chromophores (dipole molecules containing electron-donor and electron-acceptor groups) is that displacement of the electron density from the donor group to the acceptor group induced by the $E(\omega)$ field is larger than in the opposite direction. If the dipole chromophores in the bulk of a substance are aligned in some way during the preparation of a polymer layer, stimulated radiation of an ensemble of such chromophores is anharmonic and can be represented by a set of Fourier components with frequencies ω , 2ω , *etc.*^{6–9} Otherwise, the dipole chromophores are disordered. The second-order susceptibility is given by the formula

$$\chi^{(2)} = Nf(\omega)\beta\langle\cos^3\varphi\rangle,$$

where N is the number of chromophores per unit volume; $f(\omega) = (n^2 + 2)/3$ is the correlation factor relating the external electric field of electromagnetic wave to the field in the medium; β is the second-order molecular polarisability; and $\langle\cos^3\varphi\rangle$ is a parameter characterising the averaged value of the angle of rotation of the dipole moments of chromophores about a specified axis.

For centrosymmetric media (random distribution of the dipole moments of N chromophores), $\langle\cos^3\varphi\rangle = 0$ and the second-order nonlinear susceptibility vanishes. If rotational diffusion of chromophores is possible in a medium, they are aligned in the electric field E_0 . Rotational diffusion of chromophores in polymeric systems is efficient only at temperatures above the glass transition temperature (T_g); therefore, experiments with high- T_g polymers require preliminary alignment in the polarising electric field E_p at $T_p > T_g$. Such an alignment is retained on subsequent cooling ('freezing') of the system in the field E_p down to temperatures below T_g . According to the Langevin formula,

$$\langle\cos^3\varphi\rangle = \frac{f(0)E_p\mu_g}{5kT},$$

where $f(0)$ is the correlation factor relating the external applied field E_p to the field in the polymer layer,

$$f(0) = \varepsilon \frac{n^2 + 2}{2\varepsilon + n^2}$$

(ε is the dielectric constant); and μ_g is the ground-state dipole moment of the chromophore. The formula for the second-order nonlinear volume susceptibility of high- T_g polymers has the form

$$\chi^{(2)} = \frac{Nf(\omega)f(0)\beta E_p\mu_g}{5kT}. \quad (4)$$

At room temperature, chromophores in plasticised polymers (T_g is below the temperature of the experiment, $\sim 20^\circ\text{C}$) are in the mobile state and their alignment makes no sense, since they again become randomly distributed after switching the E_p field off. In such polymers the second-order susceptibility arises only in a constant field. Taking into account the fact that the $\chi^{(2)}$ value is determined by the total field

$$E_t = E_{sc} + E_0,$$

we get

$$\chi^{(2)} = \frac{Nf(\omega)f(0)\beta E_t\mu_g}{5kT}. \quad (4a)$$

The distributions of the E_t field and the E_{sc} and E_0 components along the x axis are shown in Fig. 2b.

The E_t field is involved in the electronic polarisation of a molecule along with the light wave field, $E(\omega)$; therefore, the expression for the volume polarisation, $P(E)$, can be written as follows:

$$\begin{aligned} P(E) = & [\chi_E^{(1)}(-\omega, \omega) + \chi^{(2)}(-\omega, \omega, 0)f(0)E_t + \\ & + \chi^{(3)}(-\omega, \omega, 0, 0)f^2(0)E_t^2]f(\omega)f(-\omega)E(\omega) + \\ & + [\chi^{(2)}(-2\omega, \omega, \omega) + \\ & + \chi^{(3)}(-2\omega, \omega, \omega, 0)f(0)E_t]f^2(\omega)f(-2\omega)E^2(\omega) + \\ & + \chi^{(3)}(-3\omega, \omega, \omega, \omega)f^3(\omega)f(-3\omega)E^3(\omega). \end{aligned} \quad (5)$$

Here $\chi_E^{(1)}$ is the linear volume susceptibility in the constant field; $\chi^{(2)}$ and $\chi^{(3)}$ are the second- and third-order nonlinear volume susceptibilities, respectively; $(-\omega)$, (-2ω) and (-3ω) are the frequencies of the first, second and third harmonics of stimulated radiation of the ensemble of oscillating dipoles when the laser operates at the fundamental frequency ω .

Taking into account formula (5), the linear electric susceptibility in the presence of a constant field E_0 and the E_{sc} field is

$$\chi^{(1)} = \chi_E^{(1)} + f(0)E_t[\chi^{(2)} + \chi^{(3)}f(0)E_t],$$

while relationship (3) takes the form

$$n_E^2 = 1 + 4\pi[\chi_E^{(1)} + E_t(\chi^{(2)} + \chi^{(3)}E_t)]. \quad (5a)$$

[hereafter the $f(0)$ factor is omitted].

The refractive index modulation (grating amplitude) is determined by the difference between expression (5a) in the presence of the E_t field and expression (3) in the presence of the E_0 field, when $\chi^{(1)} = \chi_0^{(1)}$,

$$\Delta n = \frac{n_E^2 - n^2}{n_E + n}.$$

Assuming $n_E + n = 2n$, we get

$$\Delta n = \frac{2\pi}{n} [E_{sc}(\chi^{(2)} + \chi^{(3)}E_t) + \chi_E^{(1)} - \chi_0^{(1)}]. \quad (6)$$

This relation demonstrates that generally three effects contribute to the creation of the phase grating. The first and second effects (the first two terms) are the refractive index modulations due to the Pockels electro-optic effect (PEO) and the quadratic Kerr electro-optic effect (KEO)

$$\Delta n_1 = \Delta n_{PEO} + \Delta n_{KEO}, \quad (7)$$

where

$$\Delta n_{PEO} = \frac{2\pi}{n} \chi^{(2)} E_{sc},$$

$$\Delta n_{KEO} = \frac{2\pi}{n} \chi^{(3)} E_{sc} E_t.$$

According to the known formula⁶ of the electro-optic effect,

$$\Delta n_1 = \frac{n^3}{2} E_t(r + sE_t)$$

the linear Pockels electro-optical coefficient r is proportional to the susceptibility, $\chi^{(2)}$, while the quadratic Kerr electro-optical coefficient s is related to the $\chi^{(3)}$ susceptibility.

The other terms in formula (6)

$$\Delta n_2 = \frac{2\pi(\chi_E^{(1)} - \chi_0^{(1)})}{n}$$

are the refractive index modulations due to alignment of dipole chromophores along the E_t field. This effect is characteristic of plasticised layers only and is not observed in high- T_g polymeric

systems. Due to orientational birefringence, OB, the refractive index modulation is described as follows:^{10–13}

$$\Delta n_{OB} = \frac{2\pi}{n} (\chi_E^{(1)} - \chi_0^{(1)}) = \frac{2\pi}{n} N \Delta \alpha \left(\langle \cos^2 \varphi \rangle - \frac{1}{3} \right) \approx \quad (8)$$

$$\approx \frac{2\pi}{n} \frac{4Nf^2(0)f(\omega)}{45} \Delta \alpha(-\omega, \omega) \left(\frac{\mu_g E_t}{kT} \right)^2,$$

where $\Delta \alpha$ is the anisotropy of the linear polarisability

$$\Delta \alpha = \alpha_{||} - \alpha_{\perp},$$

and $\alpha_{||}$ and $\alpha_{\perp}$ are the molecular polarisabilities along and normal to the principal axis of a dipole chromophore, respectively.

For an isotropic medium, $\langle \cos^2 \varphi \rangle = 1/3$; therefore, the volume anisotropy of the linear polarisability vanishes [see formula (8)]. A two-level model of polarisation¹⁴ describes the anisotropy of polarisability, $\Delta \alpha(-\omega, \omega)$, by the relationship

$$\Delta \alpha(-\omega, \omega) = \Delta \alpha(0) \frac{E_{ge}^2}{E_{ge}^2 - (\hbar\omega)^2},$$

where $\Delta \alpha(0) = 2\mu_{ge}^2/E_{ge}$ and μ_{ge} and E_{ge} are the dipole moment and energy of transition from the ground state to the excited state, respectively. Since the OB is due to rotational diffusion of a dipole chromophore during the formation of the E_t field, the parameter Δn_{OB} significantly contributes to the refractive index modulation of those liquid crystals or plasticised polymers whose glass transition temperatures are low (close to room temperature).^{10, 12, 15} Creation of orientational grating was established in liquid-crystalline media^{16–18} and polymeric composites.¹⁰ Liquid crystals are characterised by the largest orientational refractive index modulation due to strong dielectric anisotropy.^{11, 13, 17–19}

The photorefractive effect in nonlinear optical materials is determined by the spatial modulation of the refractive index (see above).⁴

Creation of a grating in polymer layers of thickness d meeting the following criterion

$$Q = \frac{\pi d \lambda}{\Lambda^2 n} > 1,$$

(more preferable, $Q > 5$, see Ref. 12) is accompanied by self-diffraction of beams due to the Bragg scattering (reflection). Beam 1 is reflected towards beam 2, while beam 2 is reflected towards beam 1. For the measuring cell geometry shown in Fig. 2a the reflected beam 1 is in phase with beam 2. Beam mixing causes an increase in the intensity of the output beam 2 and a decrease in the intensity of the output beam 1 because the reflected beam 2 and beam 1 are out of phase.

The main formulae suitable for estimation of the PR parameters (e.g., the two-beam coupling gain Γ , phase shift of the grating, etc.), were obtained by solving the Kogelnik coupled-wave equations,²⁰ according to which a change in the amplitude (or $I^{0.5}$) of each beam along the z axis is proportional to the amplitude of the other beam and the refractive index modulation, Δn (see Refs 5, 20–23)

$$\frac{\partial(I_1)^{0.5}}{\partial z} = -\left(\frac{\pi \Delta n}{\lambda}\right) (I_2)^{0.5}, \quad (9)$$

$$\frac{\partial(I_2)^{0.5}}{\partial z} = -\left(\frac{\pi \Delta n}{\lambda}\right) (I_1)^{0.5}. \quad (10)$$

The most important relationships were obtained for the PR effect in inorganic crystals assuming that $\Delta n \sim E_{sc}$.^{5, 21, 22} Taking into account formulae (2) and (2a), in this case one can write^{5, 22–28}

$$\Delta n = \Delta n_{\max} \frac{2(I_1 I_2)^{0.5}}{I_1 + I_2} \cos\left(\frac{2\pi x}{\Lambda} - \psi\right).$$

Beam 2 reflected from the PR grating in the $\Delta n_{\max}$ region travels now in the same direction as does beam 1 (the angle of incidence equals the angle of reflection), i.e., towards positive x values (see Fig. 2b). Therefore Eqn (9) can be rewritten as follows:²²

$$\frac{\partial(I_1)^{0.5}}{\partial z} = -2\left(\frac{\pi \Delta n_{\max}}{\lambda}\right) \frac{(I_2)^{0.5} (I_1 I_2)^{0.5}}{I_1 + I_2} \cos\left(\frac{2\pi x}{\Lambda} - \psi\right). \quad (9a)$$

Simultaneously the reflected beam 1 propagates in the same direction as does beam 2 (towards negative x values). Then, formula (10) takes the form²²

$$\frac{\partial(I_2)^{0.5}}{\partial z} = -2\left(\frac{\pi \Delta n_{\max}}{\lambda}\right) \frac{(I_1)^{0.5} (I_1 I_2)^{0.5}}{I_1 + I_2} \cos\left(-\frac{2\pi x}{\Lambda} - \psi\right). \quad (10a)$$

In accord with the energy conservation law

$$I_1(0) + I_2(0) = \frac{I_1(z) + I_2(z)}{\exp(-\alpha z)} = \frac{I_1(L) + I_2(L)}{\exp(-\alpha L)}.$$

Here $I_1(z) \equiv I_1$ and $I_2(z) \equiv I_2$; $\alpha = 2.3A/d$ is the absorption coefficient (A is the optical absorption at the laser wavelength and d is the layer thickness); $I_1(0)$, $I_2(0)$ and $I_1(L)$, $I_2(L)$ are the intensities of the input and output beams, respectively; $L = d/\cos(\phi - \theta)$ is the optical path of beam 2 (see Fig. 2a). Let us denote $I_1(0) + I_2(0) = I_0$. To simplify the solutions, suppose that $\alpha = 0$; then, after replacing I_2 by $(I_0 - I_1)$ in Eqn (9a) we get

$$\frac{\partial(I_1)^{0.5}}{I_1^{0.5}(I_0 - I_1)} = -2 \frac{\pi \Delta n_{\max}}{\lambda I_0} \partial z \times \left[\cos\left(\frac{2\pi x}{\Lambda}\right) \cos \psi + \sin\left(\frac{2\pi x}{\Lambda}\right) \sin \psi \right]. \quad (11)$$

Analogous substitution into Eqn (10a) for beam 2 ($I_1 = I_0 - I_2$) gives

$$\frac{\partial(I_2)^{0.5}}{I_2^{0.5}(I_0 - I_2)} = -2 \frac{\pi \Delta n_{\max}}{\lambda I_0} \partial z \times \left[\cos\left(\frac{2\pi x}{\Lambda}\right) \cos \psi - \sin\left(\frac{2\pi x}{\Lambda}\right) \sin \psi \right]. \quad (11a)$$

Relationships (11) and (11a) thus obtained are unsymmetric, namely, the second terms on the right-hand sides of the equations (they are responsible for energy transfer from beam 1 to beam 2) have opposite signs (negative sign for beam 1 and positive sign for beam 2).²² The energy transfer coefficient, or the two-beam coupling gain, can be found by subtracting relationship (11) from Eqn (11a). After integration of this difference at a particular x value (e.g., at $x = \Lambda/4$), one gets⁵

$$\ln \frac{I_2(L)\beta}{I_1(L)} = \Gamma L, \quad (12)$$

where $\beta = I_1(0)/I_2(0)$,

$$\Gamma = \frac{4\pi \Delta n_{\max} \sin \psi}{\lambda}. \quad (12a)$$

From Eqn (12) it follows that

$$I_1(L) = I_2(L)\beta e^{-\Gamma L}.$$

Hence

$$I_1(L) + I_2(L) = I_2(L)\beta e^{-\Gamma L} + I_2(L) = I_2(L)(1 + \beta e^{-\Gamma L}).$$

At the same time, in accord with the energy conservation law one has

$$I_2(L) + I_1(L) = [I_2(0) + I_1(0)]e^{-\alpha L} = I_2(0)(1 + \beta)e^{-\alpha L},$$

i.e.,

$$I_2(L)(1 + \beta e^{-\Gamma L}) = I_2(0)(1 + \beta)e^{-\alpha L}$$

or

$$\frac{I_2(L)}{I_2(0)} = \frac{(1 + \beta)e^{-\alpha L}}{1 + \beta e^{-\Gamma L}}. \quad (13)$$

Formula (13) serves for estimation of the amplification of the information beam 2 at different β , Γ and α . Experimental estimation of the gain involves measurements of the beam coupling ratio (γ_0)

$$\gamma_0 = \frac{I_2(L)_t}{I_2(L)_{t=0}}. \quad (14)$$

Here the $I_2(L)_t$ value (beam 1 is on) is determined by relationship (13). If beam 1 is switched off [$I_1(0) = 0$ and $\beta = 0$], one gets $I_2(L)_{t=0} = I_2(0)\exp(-\alpha L)$. Thus, the formula (14) for the beam coupling ratio takes the form

$$\gamma_0 = \frac{1 + \beta}{1 + \beta \exp(-\Gamma L)}.$$

From here the two-beam coupling gain, Γ , can be calculated using the formula

$$\Gamma L = \ln \frac{\gamma_0 \beta}{1 + \beta - \gamma_0}. \quad (15)$$

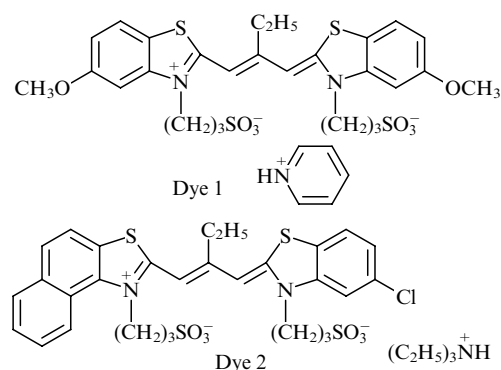
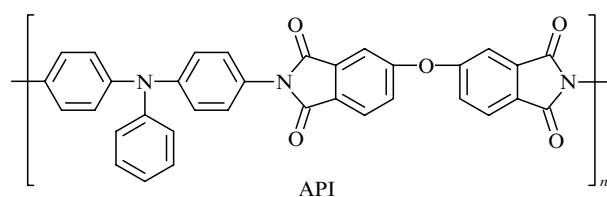
The γ_0 value is estimated from that portion of the kinetic curve, which corresponds to saturation of the beam coupling ratio.

Thus, a shift of the phase grating in space relative to the constructive interference fringes provides amplification of beam 2 due to attenuation of beam 1. As the polarity of the applied voltage (i.e., the E_0 sign) changes (see Fig. 2a), photogenerated mobile holes migrate in the opposite direction relative to that shown in Fig. 2b and the grating is shifted by a phase of ψ towards positive x values

$$\Delta n = \Delta n_{\max} \left[\frac{2(I_1 I_2)^{0.5}}{I_1 + I_2} \right] \cos \left(\frac{2\pi x}{A} + \psi \right).$$

In this case beam 1 is amplified, while beam 2 becomes the pump beam. The beam directed from the fringe to the grating is amplified (see Fig. 2a).

As will be shown below, polymeric composites containing nanocrystalline J-aggregates of cyanine dyes (dipole molecules aligned to form the 'head-to-tail' chains) occupy a special position among photorefractive polymeric materials. Figure 3 presents the kinetic curves for two-beam coupling measured for aromatic polyimide (API) containing J-aggregates of thiacyanine dyes (Dye 1 and Dye 2, respectively).^{29, 30}



Measurements were carried out at $\beta = I_1(0)/I_2(0) = 1$. The experimental design was as follows. The first experiment involved measurements of the beam 1 intensity. First, beam 1 was switched on. At $t = 0$, the E_0 field was applied to the sample and then beam 2 was switched on (upward arrow). This resulted in a decrease in the beam 1 intensity (curve 1). The intensities of the output beam 1 with beam 2 off and on are denoted as $I_1(L)_{t=0}$ and $I_1(L)_t$, respectively. After the curve reached saturation, beam 2 was switched off (downward arrow) and, as can be seen, the initial beam 1 intensity, $I_1(L)_{t=0}$, was restored. Then the same operations were repeated for beam 2. First, beam 2 was switched on and then the E_0 field was applied, the $I_2(L)_{t=0}$ value was measured and beam 1 was switched on. This led to an increase

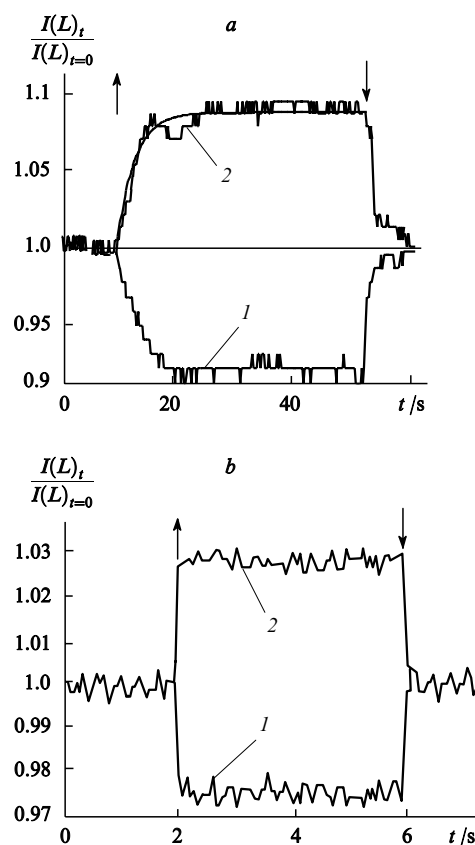


Figure 3. Kinetic curves for two-beam coupling in a polymeric composite [API containing J-aggregates of Dye 1 (a) and Dye 2 (b)].^{29, 30} Experimental conditions: an Ar-Kr laser (647 nm), $I_1(0) = I_2(0) = 0.03 \text{ W cm}^{-2}$, $E_0 = 16 \text{ V } \mu\text{m}^{-1}$. Changes in the beam 1 intensity upon switching beam 2 on (upward arrow) and off (downward arrow) (1) and changes in the beam 2 intensity upon switching beam 1 on (upward arrow) and off (downward arrow) (2).

in the beam 2 intensity, $I_2(L)_t$ (curve 2). After switching beam 1 off the intensity of beam 2 took its initial value $I_2(L)_t = 0$. The $I_2(L)_t/I_2(L)_{t=0}$ ratio is the beam coupling ratio, γ_0 , at saturation [see Eqn (14)]. As the refractive index modulation is created, the intensity of beam 1 (pump beam) decreases, while the intensity of beam 2 (signal beam) increases to nearly the same extent (see Fig. 3). This unambiguously points to writing of a phase grating, which is shifted in space relative to the fringe pattern (see Fig. 2b).

The most important characteristics of the PR effect are the two-beam coupling gain, Γ (more rigorously, the net internal gain, $\Gamma - \alpha$), $\Delta n_{\max}$, the diffraction efficiency, η , and the response time, τ , of the polymeric composite to the two-beam coupling. The last-mentioned parameter is 3 s for the API/Dye 1 composite (see Fig. 3a) and less than 20 ms (the temporal resolution of the experimental setup) for the API/Dye 2 composite (see Fig. 3b).

The diffraction efficiency (in %) is defined by the following relation:²¹

$$\eta = 100 \sin^2 \left(\frac{\pi \Delta n_{\max} d}{\lambda \cos \theta} \right). \quad (16)$$

Experiments on determination of the diffraction efficiency involve the use of two writing beams to create a grating which is read out with the third beam (readout beam of intensity I_3) propagating parallel to beam 1 (or 2). Beam 3 diffracts towards beam 2 (or 1) with an intensity of I_{01} . The diffraction efficiency is determined as follows:

$$\eta = 100 \frac{I_{01}}{I_{01} + I'_3},$$

where I'_3 is the intensity of the non-distorted readout beam passed through the photorefractive layer under diffraction. A salient feature of the PR media is the possibility of fast writing dynamical holograms with $\eta \approx 100\%$ (the writing time is of the order of several milliseconds).^{31–34} It should be noted that the diffraction efficiency contains no information on the phase shift of the grating relative to the fringe pattern. Below we will consider creation of a grating with a zero phase shift in the system exhibiting both photoelectric and nonlinear optical properties.³⁴ Therefore, only analysis of the kinetic curves for two-beam coupling with amplification of one beam at the attenuation of the other beam (see Fig. 3) provides an unambiguous proof of the PR effect.

III. The figure of merit of nonlinear optical chromophores

Choosing a chromophore involves estimation of its Figure of Merit (FOM), which characterises the ability of the chromophore to generate the PR effect.^{15,35–41} Criteria for choosing chromophores with high FOM have been reviewed.¹⁵ Photorefraction in inorganic crystals is primarily due to the Pockels electro-optic effect; therefore, in this case one deals with the FOM_{PEO} .⁴ As to the polymeric media, the Δn_{PEO} and Δn_{KEO} and Δn_{OB} parameters can contribute largely to the refractive index modulation. In the case of non-plasticised high- T_g polymeric systems containing low-molecular-mass chromophores with small FOM_{KEO} after alignment of the chromophores in the field E_p the refractive index modulation Δn is due to the Pockels electro-optic effect only and here we have to deal with

$$\text{FOM}_{\text{PEO}} = \frac{\beta \mu_g}{M},$$

where M is the molecular mass. Generally, various polarisation mechanisms of nonlinear optical chromophores^{35–40} contribute to the refractive index modulation

$$[\text{FOM}] = \text{FOM}_{\text{OB}} + \text{FOM}_{\text{PEO}} + \text{FOM}_{\text{KEO}}.$$

Combining different contributions of the polarisation to the overall FOM requires the appearance of some constants in

addition to the corresponding molecular characteristics; therefore, the FOM in the case of low-molecular-mass chromophores (FOM_{KEO} is negligible) is given by the following relationship^{15,16,39,40}

$$[\text{FOM}] = \frac{1}{M} \left[2\Delta\alpha(0) \frac{\mu_g^2}{kT} + 9\mu_g \beta(0) \right].$$

The figure of merit depends on the degree of charge transfer δ in the nonlinear optical chromophore.^{35–41} Indeed, the molecule of such a chromophore incorporates an electron-donor (D) and an electron-acceptor (A) group linked by a system of conjugated bonds, $\text{D}^{+\delta} - \text{Sp} - \text{A}^{-\delta}$ (Sp is a spacer). The structural formulae of some of the most widely used chromophores are presented below. The degree of charge transfer is determined by the contributions of two resonance structures, without $(\text{D} - \text{Sp} - \text{A})$ and with full charge transfer $(\text{D}^{+1} - \text{Sp} - \text{A}^{-1})$, to the ground state⁴²

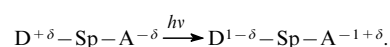
$$\text{D}^{+\delta} - \text{Sp} - \text{A}^{-\delta} = a(\text{D} - \text{Sp} - \text{A}) + b(\text{D}^{+1} - \text{Sp} - \text{A}^{-1}), \quad (17)$$

where

$$\delta = \frac{b^2}{a^2 + b^2} = c^2.$$

When choosing an optimum chromophore, one should study how the contributions of various FOMs depend on the mixing parameter (c^2 parameter, MIX) of these two structures.^{38,40,41} As parameter is also given the bond length alternation in the conjugated molecule^{35,43–46} (namely, the difference, Δr , between the average lengths, r , of the single and double carbon-carbon bonds, which in turn depends on the degree of charge transfer in the chromophore). The orientational polarisability is positive at any Δr value. According to Marder *et al.*,⁴⁴ the bond lengths in polyenes ($c^2 = 0$) are as follows: $r(\text{C} - \text{C}) = 1.45$, $r(\text{C} = \text{C}) = 1.34$ and $\Delta r = 0.11$ Å. Introduction of the D and A groups causes an increase in c^2 and a decrease in the Δr value; in this case β and the third-order molecular polarisability (γ) are positive. At $c^2 = 0.5$, the bond lengths equilibrate ($\Delta r = 0$); i.e., the molecular structures become symmetric (the so-called cyanine limit). At this degree of charge transfer, $\beta = 0$ while γ reaches its maximum negative value. On going to zwitterionic structures at $c^2 > 0.5$ the Δr and β values become negative. As a consequence, the Δn_{OB} and Δn_{PEO} parameters of this type of chromophore have opposite signs.

Photoexcitation of a chromophore containing the D and A groups causes a change in the degree of charge transfer from δ to $1 - \delta$ due to electron transfer (see Ref. 42)



Here $h\nu = E_{\text{ge}}$. The ground-state and excited-state dipole moments of the chromophore are respectively

$$\mu_g = e\delta r_{\text{DA}},$$

$$\mu_e = e(1 - \delta)r_{\text{DA}},$$

where e is the charge of an electron and r_{DA} is the distance between the D and A groups. Thus, the difference

$$\Delta\mu = \mu_e - \mu_g$$

approaches μ_e at $\delta \approx 0$, decreases down to zero for centrosymmetric chromophores ($\delta = 0.5$) and becomes negative at $\delta > 0.5$.

Numerous studies on the 'guest-host' photorefractive polymeric systems containing dipole chromophores have been reported.^{4,12} As mentioned above, alignment of chromophores in the bulk of high- T_g polymers requires the prepoling in a constant field E_p at a temperature T_p , which is 2 to 20 °C higher than T_g .⁴¹ On subsequent cooling of the system below T_g in the presence of the polarising field E_p the chromophore alignment is 'frozen'.

It should be noted that, depending on the properties of the polymer matrix, ‘unfreezing’ of rotational diffusion can occur at temperatures much below T_g . For instance, the intensity of the second laser harmonic generated in a poly(methyl methacrylate) (PMMA) layer doped with poly(ethylene oxide) and nonlinear optical chromophore 4-anilino-4'-nitroazobenzene (DO-3 dye) substantially increases after heating of the system at 52–57 °C and reaches the same values as those obtained after heating at temperatures above T_g (92–95 °C).⁴⁷ This effect is due to an increase in the volume expansion coefficient of the polymer blend in the temperature range 52–57 °C.⁴⁸

After alignment of the oligomeric chromophores in the E_p field the refractive index modulation is due to the Pockels and Kerr electro-optic effects. If we go to the molecular polarisabilities, formula (7) takes the form⁴¹

$$\Delta n_1 = \Delta n_{PEO} + \Delta n_{KEO} = \frac{2\pi}{n} \frac{N f^2(0) f(\omega) E_{sc}}{5} \left[\beta(-\omega, \omega, 0) \frac{\mu_g E_p}{k T_p} + \gamma(-\omega, \omega, 0, 0) E_0 \right], \quad (18)$$

where

$$\beta(-\omega, \omega, 0) = \beta(0) \frac{E_{ge}^2 [3E_{ge}^2 - (h\omega)^2]}{3[E_{ge}^2 - (h\omega)^2]^2},$$

$\omega = 2\pi/\lambda$, λ is the laser wavelength at which the PR effect is measured and $\beta(0)$ is the static contribution to the second-order molecular polarisability extrapolated to $h\omega = 0$.^{7, 16–19} The two-level polarisation model¹⁴ defines the molecular polarisabilities as follows:

$$\beta(0) = \frac{6\mu_{ge}^2 \Delta\mu}{E_{ge}^2}, \quad (19)$$

$$\gamma(0) = \frac{24(\Delta\mu^2 - \mu_{ge}^2)\mu_{ge}^2}{E_{ge}^3} + \frac{24\mu_{ge}^2 \mu_{ce'}^2}{E_{ge'} E_{ge}^2},$$

where $\Delta\mu = \mu_e - \mu_g$, $\mu_{ce'}$ is the dipole moment of the transition from the first to the second excited level and $E_{ge'}$ is the energy of transition from the ground state to the second excited state.^{43–46, 49}

Taking into account the net FOM, formula (18) can be written as follows:

$$\Delta n_1 = \Delta n_{PEO} + \Delta n_{KEO} = \frac{2\pi}{n} \frac{N f^2(0) f(\omega) E_p}{5k T_p} [\text{FOM}],$$

where

$$[\text{FOM}] = \text{FOM}_{PEO} + \text{FOM}_{KEO} = \mu_g \beta(0) + \frac{E_0 k T_p}{E_p} \gamma(0), \quad (20)$$

where $E_0 k T_p / E_p$ is a constant.

At room temperature, anisotropic chromophores in low- T_g polymers are in the mobile state and can be aligned during measurements of the PR effect in the E_t field, which changes both its direction and amplitude (see Fig. 2b). In this case a doubled FOM_{PEO} value is introduced into Eqn (20) (see Refs 35, 40, 41, 45)

$$[\text{FOM}] = \text{FOM}_{PEO} + \text{FOM}_{KEO} = 2\mu_g \beta(0) + k T \gamma(0). \quad (20a)$$

As mentioned above, the refractive index modulation arises in the low- T_g polymeric composites due to the linear orientation polarisation of a dipole chromophore in the E_t field. Therefore, the expression for the net refractive index modulation must contain an additional term Δn_{OB} [see formula (8)]

$$\Delta n = \Delta n_{OB} + \Delta n_{PEO} + \Delta n_{KEO} = \frac{4\pi}{n} \frac{N f^2(0) f(\omega) E_t^2}{45k T} [\text{FOM}], \quad (21)$$

where

$$[\text{FOM}] = \text{FOM}_{OB} + \text{FOM}_{PEO} + \text{FOM}_{KEO},$$

$$\text{FOM}_{OB} = \frac{\Delta\alpha(0)\mu_g^2}{k T}.$$

Since the net modulation, Δn , is quadratically dependent on E_t , it was assumed^{15, 16, 39, 40} that creation of a grating in low- T_g composites is due to the Kerr electro-optic effect only. By substituting Eqn (20a) into relationship (21) we get

$$[\text{FOM}] = \text{FOM}_{OB} + \text{FOM}_{PEO} + \text{FOM}_{KEO} = \Delta\alpha(0) \frac{\mu_g^2}{k T} + 9\mu_g \beta(0) + \frac{9}{2} k T \gamma(0). \quad (21a)$$

This expression is, as a rule, used when comparing the contributions of various polarisation mechanisms to the amplitude of the refractive index modulation.⁴¹

To prepare photorefractive polymeric systems, chromophores possessing the maximum net FOM are chosen. The parameters in formula (21a) are determined from ellipsometric measurements, by analysing the optical and electro-optical absorption spectra in solution^{15, 16, 39–41} and from quantum-chemical calculations.^{35–38, 43–46}

1. Photorefractive polymeric systems with low glass transition temperatures

The FOM values of typical chromophores used in studies of the PR effect are listed in Table 1. When choosing nonlinear optical chromophores for photorefractive composites based on both low- and high- T_g polymers, these data allow estimation of the relative contributions of various polarisation mechanisms to the creation of a phase grating using formulae (20) and (21a). As can be seen, for all chromophores

$$\text{FOM}_{OB} \gg \text{FOM}_{PEO} + \text{FOM}_{KEO},$$

i.e., low- T_g polymers must have a much higher refractive index modulation and, hence, PR-characteristics than the samples with high T_g .

Analysis of the data listed in Table 1 also reveals that if chromophores incorporated into high- T_g polymers (in this case $[\text{FOM}] = \text{FOM}_{PEO} + \text{FOM}_{KEO}$) are preliminarily aligned in the E_p field at $T_p \gg T_g$, the Pockels electro-optic effect makes major contribution to the creation of a grating. Otherwise the phase grating amplitude in high- T_g polymeric systems is determined only by the Kerr electro-optical coefficient whose contribution to the net FOM allows one to assume that the PR-characteristics, e.g., Γ [see formula (12)] should be much lower than the corresponding characteristics obtained for polymer composites with low T_g .

Since 1994 (see Ref. 10), the vast majority of photorefractive materials were synthesised using polymers with glass transition temperatures close to room temperature. Most of them are based on plasticised poly(vinylcarbazole) (PVCz),^{12, 19, 31–33, 50–54} carbazoyl-substituted polysiloxanes (PSX-Cz)^{55–57} and polyethers.^{58, 59} In such polymeric media the major contribution to the creation of a phase grating comes from the linear orientation polarisation. Under these conditions, the diffraction efficiency buildup rate is determined by rotational diffusion of the chromophore and is described as follows:^{60, 61}

$$\eta(t) \sim \sin^2 \left[A_1 \left(1 - e^{-D_1 t} \right) + A_2 \left(1 - e^{-D_2 t} \right) \right],$$

where

$$A_1 + A_2 = \frac{\pi}{2},$$

and D_1 and D_2 are coefficients: $D_n = n(n+1)D$ at $n = 1$ and 2 ; and D is the rate constant for rotational diffusion.

Table 1. Figure-Of-Merit values (in 10^{-46} e.s.u.) for chromophores of various structure.

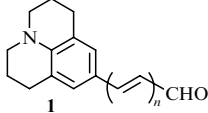
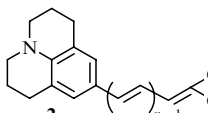
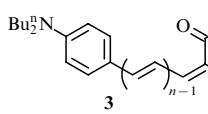
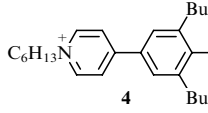
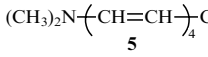
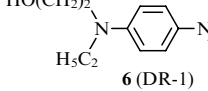
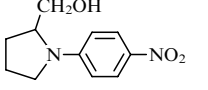
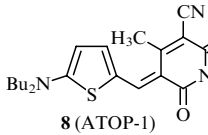
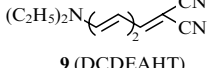
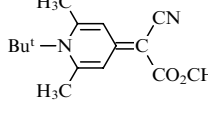
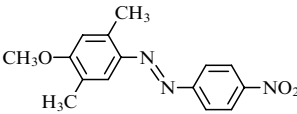
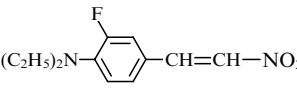
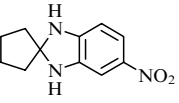
Chromophore formula	<i>n</i>	Solvent	FOM _{PEO} (sec ^a)	FOM _{KEO} (sec ^a)	FOM _{OB} (sec ^a)	[FOM]	$\frac{\text{FOM}_{\text{OB}}}{[\text{FOM}]} 100$ (%)	Ref.
	1	dioxane	32	2.2	180	214	84	41
	2	"	50	4.5	216	270	80	41
	3	"	130	18	378	528	71.6	41
	1	"	63	4.5	576	639	90	41
	2	"	170	9	810	989	82	41
	3	"	280	41	1229	1550	79.3	41
	4	"	540	68	1548	2156	72	41
	5	"	1233	189	2341	3763	62	41
	1	"	86	-2.25	545	629	86.6	41
	1	chloroform	110	—	810	920	88	37
	2	dioxane	274	9	1161	1444	80.4	41
	2	chloroform	295	—	1400	1695	82.6	37
	3	dioxane	549	76.5	1305	1930	67.6	41
	3	chloroform	630	—	2335	2965	78.8	37
	4	dioxane	927	184.5	1710	2821	60.6	41
	4	chloroform	1070	—	2920	3990	73.2	37
	5	dioxane	1800	580	2254	4634	48.6	41
	5	chloroform	2190	—	3270	5460	60	37
		"	—	—	970	—	—	38
		dioxane	-2.5	—	1500	—	—	38
		THF	-50	—	1640	1590	103	38
		chloroform	-50	—	2105	2055	102	38
		acetone	-100	—	2205	2105	104	38
		DMSO	-170	—	3015	2845	106	38
		methanol	-160	—	2885	2725	106	38
		see ^b	—	—	530	—	80	35
		chloroform	486	—	1620	2106	77	36
		"	54	—	380	435	87.4	36
		dioxane	45	-9	2354	2390	98.5	41
		"	90	-4.5	1431	1516	94.4	41
		see ^b	—	—	530	—	99.3	39

Table 1 (continued).

Chromophore formula	Solvent <i>n</i>	FOM _{PFO} (see ^a)	FOM _{KFO} (see ^a)	FOM _{OB} (see ^a)	[FOM]	FOM _{OB} [FOM] 100 (%)	Ref.
 11 (DMNPAA)	see ^b	—	—	285	—	88.1	39
 12 (FDEANST)	"	—	—	357	—	75.4	39
 13 (DTNBI)	"	—	—	350	—	87.4	39

^a FOM_{PFO} = $9\mu_g\beta(0)$, FOM_{KFO} = $9kT\gamma(0)/2$ and FOM_{OB} = $\Delta\alpha(0)\mu_g^2/kT$ [see formula (21a)]. ^b Obtained from quantum-chemical calculations.

The determining role of plasticiser was demonstrated taking composites prepared from carbazolyl-substituted polysiloxane, 2,4,7-trinitro-9-fluorenone (TNF) and indole derivatives (chromophores) as examples. The major contribution (97%) to the net FOM of this system comes from the FOM_{OB}.⁵⁷ In the absence of plasticiser this composite has $T_g = 34^\circ\text{C}$ and the net internal gain ($\Gamma - \alpha$) is close to 2 cm^{-1} . Doping with a small amount of plasticiser (ethylcarbazole, ECz) causes lowering of the T_g value down to 23°C and an increase in ($\Gamma - \alpha$) to 25 cm^{-1} (see Ref. 57). The steady-state value of the net internal gain is achieved about 1 s after the start of two-beam coupling, which is believed to correspond to the reorientation time of nonlinear optical chromophores in the E_t field. It was also pointed out⁶² that nonlinear optical chromophores form aggregates, which cannot be oriented in the applied field E_0 ; as a consequence, the PR effect is weakened. For this reason, the side butyl groups are introduced into the chromophore molecule (see Table 1, compound 8) to preclude dimerisation.

2. Photorefractive polymeric systems with high glass transition temperatures

The data for compound 2 (see Table 1) show that an increase in the number of conjugated bonds from 1 to 5 causes a respective increase in the FOM_{PFO} and FOM_{KFO} values by a factor of 19.6 and 42. The third-order molecular polarisability of acetylene oligomers with the number of conjugated bonds varying from $n = 1$ to 31 increases with an increase in the length of the conjugated system as follows:^{49, 63–65}

$$\gamma(0) = \gamma_1(0)n^{2.5 \pm 0.2}. \quad (22)$$

J-Aggregates of cyanine dyes are known to have a very high third-order susceptibility.^{66–69} The corresponding dependence

$$\chi^{(3)} \sim n^{2.36},$$

coincides with relationship (22) within the limits of experimental error. The third-order volume susceptibility, $\chi^{(3)}$, of J-aggregates of dyes can be as high as nearly $2.7 \times 10^{-13}\text{ C m J}^{-3}$ (in SI units).⁶⁶ This value is due to co-operative electronic excitation of molecules and delocalisation of the excitation along the whole length of the J-aggregate, which comprises n conjugated bonds.^{66–69} Orientational diffusion of dipole chromophores in high- T_g polymers is restricted; therefore, after application of the field E_t the major contribution to the refractive index modulation [see Eqns (21) and (21a)] should be expected only from the third-

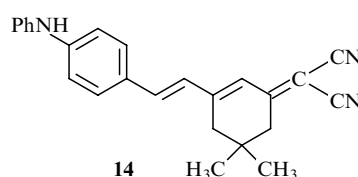
order electronic polarisation. It is the use of J-aggregates of cyanine dyes as nonlinear optical chromophores that allowed the obtention of high PR-characteristics of composites based on aromatic polyimide with $T_g \approx 230^\circ\text{C}$,^{29, 30} which are comparable with the corresponding parameters of plasticised composites based on PVCz.

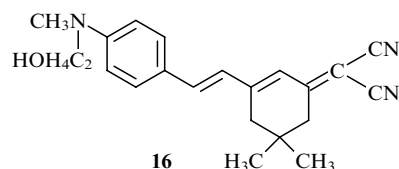
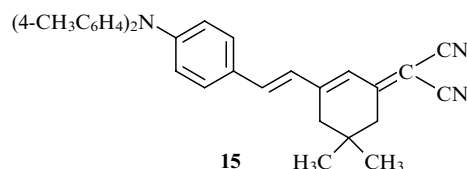
Poly(diacetylenes)^{49, 70–72} and polyenes of various structures⁷³ are also characterised by rather high $\chi^{(3)}$ values; however, they are several orders of magnitude lower than those of J-aggregates.

IV. Interrelation between the photorefractive effect and the photoelectric and electron transport properties

Depending on the composition of a system, the PR-characteristics can be related in a different manner to the rate of charge photo-generation, charge carrier mobility or to the rate of rotational diffusion of a nonlinear optical chromophore in the field E_t . When creating dynamical holograms, it is essential to achieve a short response time of the polymer layer to the two-beam coupling. Therefore, it seems likely that polymeric systems with electronic polarisation rather than orientational effects, which are limited to rotational diffusion of the chromophore in the matrix, should be more promising in this case.

Note that the ionisation potential of the chromophore (I_D) influences the high two-beam coupling gain coefficients and diffraction efficiency more strongly than the nonlinear optical characteristics responsible for the FOM values.^{33, 74} This was established taking composites prepared from PVCz containing the donor carbazolyl groups (Cz), acceptor (2,4,7-trinitro-9-fluorenylidene)malonodinitrile (TNFDM) and the chromophores **14–16** as examples.

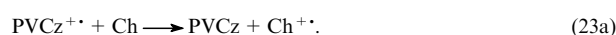
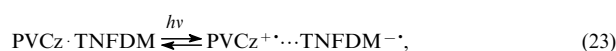




The donor–acceptor complex PVCz·TNFDM is responsible for the photoelectric sensitivity of these composites. The ionisation potentials of the carbazolyl group, Cz, and chromophores **14–16**, their FOM values, and the most important PR-characteristics of the composites are listed in Table 2. The refractive index modulation $\Delta n_{\max}$ was estimated from the η values measured in the presence of chromophores **14–16** using formula (16), which was modified to include the sample geometry and had the form^{33, 74}

$$\eta = \sin^2(586 \Delta n_{\max}).$$

The product $\Delta n_{\max} \sin \psi$ was calculated using the measured two-beam coupling gain coefficients Γ and formulae (15) and (12a). Therefore, by comparing η and Γ it is possible to determine the phase shift ψ (see Table 2), which decreases in the series of the chromophores **14–16**. Analysis of the measured η values showed that the $\Delta n_{\max}$ values increase by a factor of 1.6 and 2.2 if the chromophore **14** is replaced by **15** and the chromophore **15** is replaced by **16**, respectively. Taking into account the fact that these replacements cause a much smaller increase in the FOM value (by a factor of 1.06 and 1.2, respectively), it was concluded that the $\Delta n_{\max}$ value is primarily determined by the space-charge field E_{sc} rather than FOM (the larger the ionisation potential difference between the carbazolyl group and the nonlinear optical chromophore, the stronger the E_{sc} field). It was hypothesised^{33, 74, 75} that the increase in E_{sc} is due to an increase in the quantum yield of holes, which can be related to the hole jump to chromophore (Ch) during the reactions

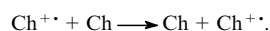


Hole jump to chromophore by reaction (23a) precludes its disappearance *via* recombination of the radical ion pair following reaction (23), thus increasing the quantum yield of holes. The molecules of acceptor, TNFDM, act as deep electron traps; therefore they persist in the region of bright fringes. When present in low concentrations, chromophores act as hole traps; however, at high concentrations (28.5% of the composite mass) they serve as charge transport agents^{33, 74, 75}

Table 2. Ionisation potentials and FOM values for chromophores **14–16** and the most important characteristics of polymeric photorefractive composites based on PVCz,^a TNFDM and chromophores **14–16** at 60 V μm^{-1} (see Refs 33 and 74).

Chromophore	I_D / eV	FOM (rel.u.)	Composite characteristics		
			η (%)	Γ / cm^{-1}	ψ / deg
14	5.59	1.0	25	70	37
15	5.46	1.06	40	88	29
16	5.40	1.27	85	167	25

^a The ionisation potential of the carbazolyl group is 5.90 eV.



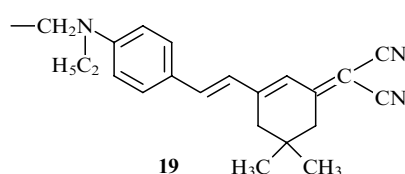
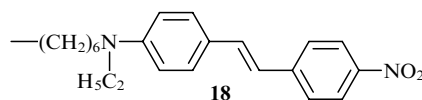
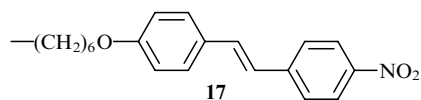
The photoconductivity and the quantum yield of mobile holes in the composite prepared from PVCz, sensitiser (TNFDM), plasticiser (ECz) and a nonlinear optical chromophore were shown⁷⁵ to increase by nearly an order of magnitude upon replacement of TNFDM by C₆₀ fullerene. This is due to the corresponding decrease in the probability of recombination of charge carriers by reaction (23).

The larger the difference

$$\Delta I_D = I_D(\text{Cz}) - I_D(\text{Ch}),$$

the higher the probability that efficient deep hole traps will be formed.^{33, 74, 75} Therefore, a decrease in $I_D(\text{Ch})$ causes shortening of the hole path length and a corresponding decrease in the phase shift ψ (see Table 2). The limiting case, *viz.*, a decrease in phase ψ down to zero was found for a composite prepared from PVCz, TNF (acceptor) and nonlinear optical chromophore 2-(4-nitro-phenyl)-4,5-bis(4-methoxyphenyl)imidazole (Lophine-1, 33 mass %) (see Ref. 34). The effect is due to the fact that, similarly to an electron, a hole trapped by the chromophore by reaction (23a) remains immobile in the region of bright fringes and, hence, no PR effect occurs. The formation of a Lophine-1⁺...TNF^{−•} radical ion pair is accompanied by the appearance of the corresponding band in the optical absorption spectrum and changes the layer composition, thus causing creation of the amplitude and phase gratings with zero phase shift ($\psi = 0$), similarly to conventional photochemical writing of a hologram.

In poly(methyl methacrylate) with carbazolyl-containing side groups and the chromophores **17–19**,

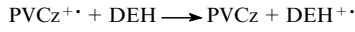


the T_g value was changed by introduction of different amounts of liquid-crystalline plasticiser 4-C₇H₁₅C₆H₄C(O)OC₆H₄CN-4. It was found that the larger the $T_e - T_g$ difference (T_e is the temperature of the experiment), the higher the photoconductivity and the phase shift ψ . It was concluded that raising the temperature causes an increase in the hole path length (until trapping by deep traps), which in turn leads to an increase in ψ . If at a constant temperature of the experiment ($T_e = 21^\circ\text{C}$) the $(T_e - T_g)$ difference increased due to a decrease in T_g caused by an increase in the concentration of plasticiser, Γ increased more slowly than η .⁷⁶ This is due to a decrease in the phase shift ψ as a result of reduction of the mobility of charge carriers on dilution of carbazolyl transport groups with neutral plasticiser molecules. Experiments with a composite prepared from PVCz, TNF and the nonlinear optical chromophore *N,N*-diethyl-*p*-nitroaniline (EPNA) and doped with 4-(diethylamino)benzaldehyde diphenylhydrazone (DEH) showed that the phase shift depends on the dopant concentration in a complex manner. The ionisation potential of DEH is somewhat lower than that of PVCz.⁷⁷ Comparison of the Γ and η values obtained at 633 nm revealed that $\psi = 32^\circ$ for the undoped material, decreases to 8° upon doping with about 2×10^{-3} mass % of DEH and down to nearly zero at 2 mass % of DEH but then increases and reaches a value of 45° at a DEH

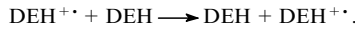
concentration of 20 mass %. The effect is due to the fact that photogenerated holes, which did not undergo recombination by reaction (23), migrate from one carbazolyl group of PVCz to another by the hopping mechanism



When present in low concentrations, the DEH molecules act as traps of mobile holes



and thus restrict the free path of charge carriers. However, as the DEH content increases to ~ 8 mass % and the average distance between neighbouring molecules is correspondingly shortened, they provide hole transportation by the hopping mechanism



In a composite prepared from PVCz, TNF and the nonlinear chromophore 1-(2'-ethylhexyloxy)-2,5-dimethyl-4-(4''-nitrophenylazo)benzene the chromophore molecules also play the role of hole traps at low concentrations but become responsible for hole transportation in the PR layers if the chromophore concentration reaches 47.5 mass %. Under these conditions the hole mobility ($2 \times 10^{-6} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) remains unchanged upon replacement of the PVCz matrix by the dielectric polycarbonate matrix.⁷⁸

The grating buildup speed can be related to the quantum yield of charge carriers (φ) and to the time it takes for a charge carrier (t_{tr}) to travel the distance $\Lambda/2\cos\phi$ as follows:

$$\frac{\partial E_{sc}}{\partial t} \sim \frac{\partial N_h}{\partial t} = \frac{\varphi I_0 (1 - 10^{-A}) \lambda^2 \cos\theta}{A h c} - \frac{N_h}{t_{tr}}, \quad (24)$$

where $\Lambda/2\cos\phi$ is the distance from the bright fringe to the midpoint between the interference-maximum regions along the direction of the E_0 field (see Fig. 2a); N_h is the concentration of the photogenerated holes determining the photocurrent j_{ph} ; I_0 is the laser light intensity; $(1 - 10^{-A})$ is the fraction of light energy absorbed within the layer (A is the optical absorption); and hc/λ is the light quantum energy. Formula (24) was derived assuming $\psi = \pi/2$; i.e., the hole distribution in Fig. 2b is centred at the midpoint between the bright fringes.

In the API-based composites containing J-aggregates of carbocyanine dyes the free carrier generation rate determines the kinetic characteristics of photorefraction, as demonstrated by analogy between the kinetic curves for the growth of photocurrent (Fig. 4) and the kinetic curves for two-beam coupling (see Fig. 3).^{29, 30, 79, 80} The curve for the growth of photocurrent measured for the API/Dye 1 composite (see Fig. 4a) is described by a biexponential dependence

$$\frac{j_{ph} + j_d}{j_d} = 14 - 7 \exp\left(-\frac{t}{3}\right) - 6 \exp\left(-\frac{t}{45}\right)$$

with the time constants $\tau = 3$ and 45 s. In the case of two-beam coupling (see Fig. 3a) the intensity $I_2(L)$, increases synchronously with the fast component of photocurrent

$$\frac{I_2(L)_t}{I_2(L)_{t=0}} = 1 + 0.125 \left[1 - \exp\left(-\frac{t}{3}\right) \right]$$

(time constant $\tau = 3$ s). The diffraction efficiency also increases with the time constant $\tau = 3$ s. Thus, in these composites the rate of hole accumulation, $\partial N_h/\partial t$, determines the time constant for the growth of the intensity $I_2(L)_t$. This is additionally confirmed by the correspondence between the rapid increase in the gain coefficient $I_2(L)_t/I_2(L)_{t=0}$ for the API/Dye 2 composite, for which $\tau < 20$ ms (see Fig. 3b), and the equally rapid appearance of a steady-state photocurrent as the laser is switched on (see Fig. 4b). In this case the speed of writing of the grating can be limited by the mobility of charge carriers μ . The available data on the mobility of charge carriers in composites of close compositions show that

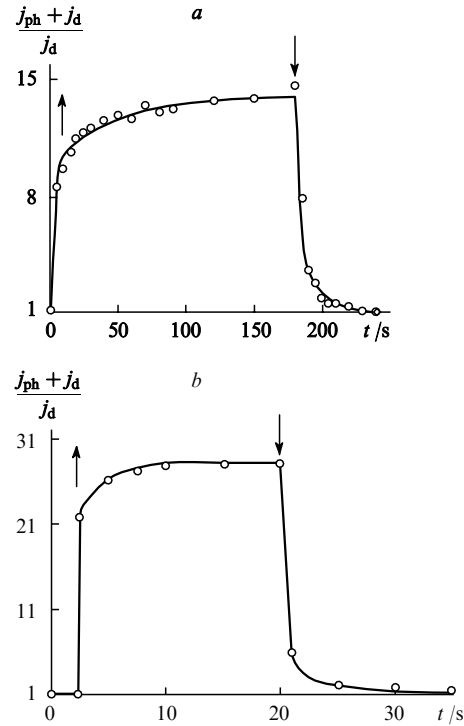


Figure 4. Changes in the $(j_{ph} + j_d)/j_d$ ratio (j_d is the dark current) for the API/Dye 1 (a) and API/Dye 2 (b) composites upon switching an Ar–Kr-laser beam (647 nm, $I_0 = 0.06 \text{ W cm}^{-2}$) on (upward arrow) and off (downward arrow).^{79, 80}

$\mu \approx 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ (see Refs 81 and 82); this allows one to conclude that the time a charge carrier takes to travel a distance $\Lambda/2\cos\phi$ ($\Lambda = 1653 \text{ nm}$) is

$$t_{tr} = \frac{\Lambda}{2E_0\mu\cos\phi}. \quad (25)$$

At $E_0 = 16 \text{ V } \mu\text{m}^{-1}$, the time t_{tr} is $\sim 6 \times 10^{-6} \text{ s}$, which is much shorter than the response time ($\tau = 3 \text{ s}$) to the two-beam coupling (see Fig. 3a).

It should be noted that if the photocurrent is measured under conditions corresponding to attainment of the steady-state value $(j_{ph} + j_d)/j_d$, i.e., when $\partial N_h/\partial t = 0$ in Eqn (24), deep traps are filled and the lifetime of the photogenerated charge carriers is not trap-limited. Since the photoconductivity is related to the photocurrent as follows

$$\sigma_{ph} = \frac{j_{ph}}{E_0} = N_h e \mu,$$

at $\partial N_h/\partial t = 0$ formula (24) can be rewritten so that it allows estimation of the quantum yield of mobile charge carriers (photo-generation efficiency)

$$\varphi = \frac{j_{ph} h c}{e \lambda I_0 (1 - 10^{-A})}. \quad (26)$$

The efficiency of photogeneration of transportation centres, measured using the field dependence of the photocurrent, coincided with the efficiency estimated using the xerographic discharge curves. In the latter case no negative electrode was available and φ was determined from the rate of discharge of the surface potential, V_0 , which appeared upon deposition of negatively charged CO_3^- ions formed in the corona discharge in air near the surface of the layer on the free surface of the polymer

layer. The parameter $(dV/dt)|_{V_0}$ was estimated at different V_0 values from the difference

$$\left. \frac{dV}{dt} \right|_{V_0} = \left. \frac{dV}{dt} \right|_{V_0(\text{light})} - \left. \frac{dV}{dt} \right|_{V_0(\text{dark})},$$

where $(dV/dt)|_{V_0(\text{light})}$ and $(dV/dt)|_{V_0(\text{dark})}$ are the initial fall-off rates of the surface potential upon switching on the light and in the dark, respectively. In contrast to the method involving measurements of the field dependence of the photocurrent (the steady-state photocurrent value is attained after full occupation of deep traps, see above), xerography allows measurements of φ with empty traps. The quantum yield of charge carriers is proportional to the initial potential drop $(dV/dt)|_{V_0}$

$$\varphi(V) = \frac{\varepsilon \varepsilon_0 h c}{e \lambda I_0 (1 - 10^{-4}) d} \left. \frac{dV}{dt} \right|_{V_0}. \quad (26a)$$

The $j_{\text{ph}}(E_0)$ dependence measured in the API/Dye 1 composites has the form^{79,80}

$$j_{\text{ph}} = a (E_0)^{3.5}, \quad (27)$$

where a is a constant. In accordance with this relationship the photoconductivity,

$$\sigma_{\text{ph}} = \frac{j_{\text{ph}}}{E_0},$$

and the photoelectric sensitivity (photoconductivity per unit of light intensity),

$$S = \frac{\sigma_{\text{ph}}}{I_0},$$

depend on the field E_0

$$\sigma_{\text{ph}} = a(E_0)^{2.5},$$

$$S = \frac{a(E_0)^{2.5}}{I_0}.$$

The field dependence of the quantum yield of mobile charge carriers [see Eqn (26)] is also described by a power function

$$\varphi = b \varphi_0 (E_0)^{3.5}. \quad (28)$$

Here b is a constant and φ_0 is the quantum yield of the bound, isolated and thermalised electron–hole pairs with the initial electron–hole distance r_0 . To estimate the φ_0 and r_0 values, the probability that the electron–hole pair escapes recombination was calculated using the Onsager equations for Brownian motion of charges in the field E_0 with inclusion of the Coulombic attraction. Since the experimental field dependence of φ is linear in the $\varphi - (E_0)^{3.5}$ coordinates, a method for solving the Onsager equations expanded of up to the $(E_0)^4$ term⁸³ was employed.

Figure 5a presents the quantum yield, φ , of mobile charge carriers plotted vs. the applied field E_0 determined from the photocurrent for the API/Dye 1 composite. The curve calculated using the Onsager equation at $\varphi_0 = 0.2$ and $r_0 = 12 \text{ \AA}$ fits well the experimental points. As can be seen in Fig. 5b, the experimental φ values estimated both from the photocurrent [see Eqn (26)] and xerographically [see Eqn (26a)] virtually coincide. This is due to the fact that for both experimental methods trapping by deep traps imposes no limitations on the lifetime of photogenerated charge carriers, since, as mentioned above, in the former case they are fully occupied while in the latter they are empty and the measurement time is shorter than the trapping time of the charge carriers. It should be noted that Melz⁸⁴ related the parameter r_0 to the exponent, m , in the formula

$$\varphi = b \varphi_0 (E_0)^m$$

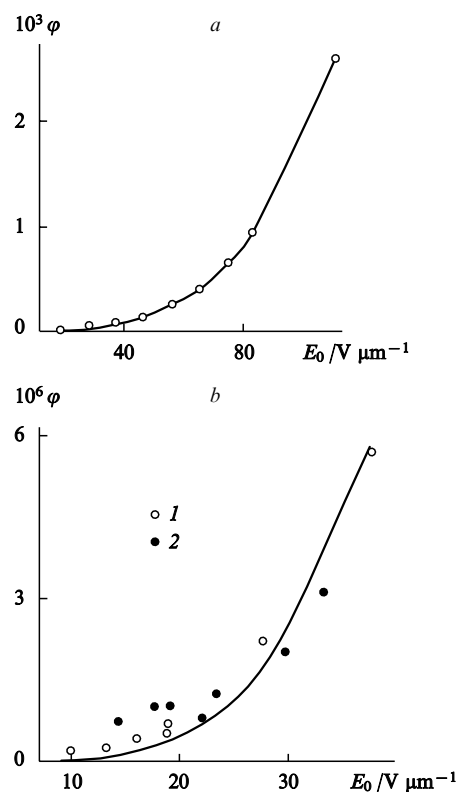


Figure 5. Quantum yield (φ) vs. E_0 plot for the API/Dye 1 composite: overall curve (a) and its initial portion (b).^{79,80}

(a) φ values were estimated from photocurrent using formula (26) (points); (b) φ values were estimated from the photocurrent using formula (26) (1) and from xerographic curves using formula (26a) (2); solid lines were obtained from calculations using the Onsager formula with $\varphi_0 = 0.2$ and $r_0 = 12 \text{ \AA}$.

at $\varepsilon = 3$ and $T = 23 \text{ }^\circ\text{C}$ using the Onsager theory. He also found that if the distance between charge carriers is $\sim 12\text{--}13 \text{ \AA}$, $m = 3.5$. Thus, the r_0 value obtained^{79,80} with this m coincides with the calculated value.

Detailed analysis of the studies on charge photogeneration and transport in polymeric systems can be found in some monographs (see, e.g., Refs 85 and 86).

The linear dependence φ on the applied field was obtained for the polysiloxane PR layers bearing side carbazolyl groups (PSCz) and doped with trinitrofluorenone and the chromophores FDEANST or DTNBI.⁸⁷ The hole mobility in these layers is nearly $2 \times 10^{-7} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ at $E_0 = 16 \text{ V } \mu\text{m}^{-1}$. Estimation using formula (25) showed that the time taken to travel the distance $\lambda/(2\cos\phi)$ is $1\text{--}2 \text{ ms}$, which is nearly 100 times shorter than the experimentally determined time constant for the growth of the signal beam intensity.⁸⁸ It seems likely that in this polymeric system the rate of photogeneration charge also determines the speed of writing of the grating.

The mobility of charge carriers in the PR composites comprised of a polystyrene matrix, the nonlinear optical chromophore 2,2-dimethyl-4-(4-nitrophenylazo)phenol and various low-molecular-mass transport dopants is reduced by more than two orders of magnitude as the dipole moment of the dopant molecules increases from 1 to 4 D.⁸⁸ The highest mobility ($4 \times 10^{-6} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) at $16 \text{ V } \mu\text{m}^{-1}$ was obtained for hole transport with 1,1-bis(di-4-tolylaminophenyl)cyclohexane while the lowest one ($2 \times 10^{-8} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$) was obtained for electron transport along the 1,1'-dioxo-2-(4-methylphenyl)-6-phenyl-4-(dicyanomethylidene)thiopyran molecules. Such a change in the mobility corresponds to extension of the t_{tr} time from 1 to 200 ms; in the latter case the speed of writing of the grating can be limited

by transport of charge carriers. To identify the stage responsible for the speed of writing, the kinetic curves of the growth of the diffraction efficiency in the PVCz/TNF/DMNPAA system doped with high concentration of plasticiser (ethylcarbazole, $T_g = 10^\circ\text{C}$) were measured under different writing conditions.⁸⁹ The efficiency $\eta = 0.85\eta_{\text{max}}$ was observed after 73.2 s if both beams were switched on and then the E_0 field was switched on and after 2.18–5.54 s if the E_0 field was switched on 30 min before switching on both beams. Such a shortening of the response time was associated with the fact that chromophores pre-oriented in the E_0 field are only slightly reoriented as E_{sc} increases and that this reorientation occurs much faster than reorientation from the disordered state.

The dependence $j_{\text{ph}} \sim E_0^m$ corresponding to the Onsager theory is masked in the presence of ionic components. Indeed, in contrast to the systems considered above experiments with poly(phenylenevinylene) containing sensitisers, tri(bipyridyl)ruthenium complexes $\text{Ru}(\text{bipy})_3^{2+}(\text{PF}_6^-)_2$, and fragments with nonlinear optical chromophores ($T_g = 16^\circ\text{C}$) in the main chain the photocurrent initially increases with increasing E_0 but substantially slows down at $E_0 > 40 \text{ V } \mu\text{m}^{-1}$.⁹⁰ In this E_0 range the two-beam coupling gain coefficient and the diffraction efficiency reach saturation and become equal to $\Gamma = 25 \text{ cm}^{-1}$ and $\eta = 0.5\%$, respectively. This was explained by peculiar features of reorientation of the $\text{Ru}(\text{bipy})_3^{2+}(\text{PF}_6^-)_2$ dipole in the E_t field. As E_t increases, the PF_6^- anion changes its position relative to the cation and the direction of the dipole moment of this ion group changes. The dipole induces an internal local electric field. The stronger the E_0 field, the better the dipole alignment along the E_t direction and the stronger the internal local field. The local field is directed oppositely to the E_t field; therefore, the growth of the effective field E_t' responsible for the creation of a grating is restricted.⁹⁰

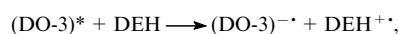
V. The gain coefficient and diffraction efficiency in photorefractive polymeric systems

The most important characteristics of recently developed photorefractive polymeric systems are listed in Table 3. The two-beam coupling gain coefficients of these composites were measured both at equal beam intensities [$\beta = I_1(0)/I_2(0) = 1$, see formula (15)] and at $\beta > 1$ to avoid 'depletion' of the pump beam.

Taking the PVCz/TNF-composites containing the chromophores *N,N*-diethyl-*p*-nitroaniline or 4-(hexyloxy)nitrobenzene as examples, it was shown⁹¹ that the two-beam coupling gain coefficient in the PR layers is independent of β and close to 10 or 3 cm^{-1} , respectively, in the range of β variation from 0.8 to 81. A very weak dependence of Γ on β (Γ increases from 5 to 10 cm^{-1} as β increases from 1 to ~ 500) was found for inorganic crystals.⁵

Currently, PR-materials with low glass transition temperatures (*i.e.*, close to room temperature or below it) have been the subject of intensive research and development. The T_g values were lowered by introducing plasticisers. In such composites the grating is created due to the orientation polarisation of chromophores in the E_t field.^{10, 12, 31–33, 52, 56, 62, 73, 74, 76, 87, 92–105} The composites listed in Table 3 (except for the composite No. 14 with triphenylamino transport groups incorporated into the main chain¹⁰⁰) include polymers such as PVCz, polysiloxanes or polyacrylates with the carbazolyl transport groups in the side chains. In these systems phototransfer of an electron by reaction (23) is followed by hole hopping from bright fringes to the dark regions in the E_0 field (see Fig. 2*b*). Fullerene C_{60} and a charge transfer complex between the donor carbazolyl group of the polymer and the acceptors, TNF or its derivative TNFDM, are used as sensitisers. The composites sensitised with C_{60} fullerene are characterised by high quantum yields of charge carriers, since the recombination stage of reaction (23) is impeded due to the long distance between the charges owing to electron delocalisation over the bulky C_{60} molecule.¹⁰³ A feature of the composite No. 12 is the possibility of simultaneously writing the PR-grating and a

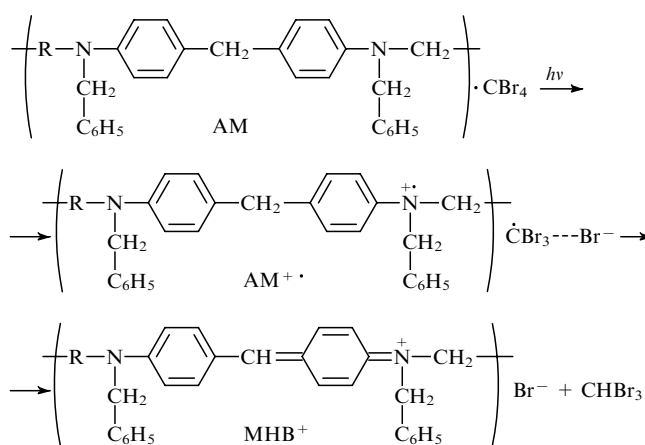
local photochemical grating.⁹⁹ The creation of the latter is due to energy transfer from the triply excited fullerene to the nonlinear optical chromophore, which occurs simultaneously with the process (23). The excited chromophore enters into the [2+2]-cycloaddition reaction with the non-excited chromophore, thus creating a photochemical phase grating which is not shifted in phase relative to the bright fringes. Simultaneous creation of two gratings was also found in the composite comprised of neutral PMMA, DEH and a nonlinear optical chromophore (DO-3 dye).¹⁰⁴ Laser-induced photoexcitation of the dye at 514 nm is followed by phototransfer of an electron, its trapping by the acceptor group of the dye (NO_2^-), generation of a mobile hole (DEH^+)



thus causing the appearance of photocurrent and the refractive index modulation.

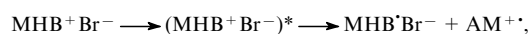
The γ_0 value at an external field strength of $8 \text{ V } \mu\text{m}^{-1}$ is 1.065. The PR effect is masked by the effect of a reversible increase in the intensities of both beams by 12%. The latter effect is due to *trans*–*cis*-photoisomerisation of the DO-3, which is accompanied by a nearly seven-fold decrease in the absorption coefficient.¹⁰⁵

A single-component photorefractive polymer layer was obtained by photochemical modification (PM) of poly(hydroxy-aminoether), PHAE (see Table 3, compound No. 22).^{106–109} The layers comprised of PHAE with donor amino groups (AM) incorporated into the main chain and the CBr_4 acceptor groups were photochemically modified. The amino group and CBr_4 form photosensitive charge-transfer complexes characterised by optical absorption in the region 330–500 nm. Exposure to light in this spectral region results in the formation of chromophores of the Michler hydrol (MHB^+) type due to phototransfer of charge.

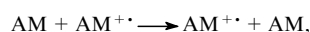


Here R is the hydroxyether fragment responsible for the adhesive and other properties.

After removal of CBr_4 from the layer by heating, the exposed areas of the polymer layer consisted of the PHAE with the modified main chain containing conjugated MHB^+Br^- fragments that absorb light in the region 560–700 nm and are responsible for the photoelectric sensitivity of PM PHAE¹¹⁰ and for the second-order nonlinear optical properties.¹¹¹ When writing a PR-grating using two beams of an Ar–Kr laser ($\lambda = 647 \text{ nm}$), photoexcitation of MHB^+Br^- in the region of bright fringes is followed by phototransfer



which is accompanied by trapping of electrons (MHB^+Br^-) and the formation of mobile holes



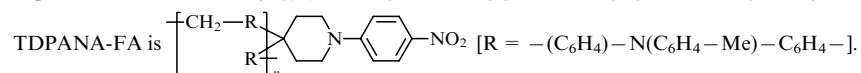
which migrate in the E_0 field and are trapped in the dark regions, thus forming the space-charge field E_{sc} .

Table 3. Most important characteristics of polymeric photorefractive composites comprising a polymer, a sensitizer, a plasticiser and a chromophore.

No.	Polymer	Sensitiser	Plasticiser	Chromophore	β	$T_g / ^\circ\text{C}$	$d / \mu\text{m}$	λ / nm	α / cm^{-1}	$E_0 / \text{V } \mu\text{m}^{-1}$	Γ / cm^{-1}	$10^3 \Delta n$	τ_e / s	$\eta (\%)$	$(\Gamma - \alpha) / \text{cm}^{-1}$	Ref.
1	PVCz	TNF	ECz	11	1, 3	21	105	675	13	90	220	5.5	—	86	207	12, 31
2	PVCz	C ₆₀	BBP	PDCST	1	28	75	676	12	120	200	—	0.05		188	32, 94, 95
3	PVCz	TNF		BDMNPAB	1	20	100	633	~13	92.4	195	4.3	~3	15	182	52
4	PSX-Cz	TNF		11	1	25	40	670	—	80	220	10	5	60	~220	56
5	PVCz	TNF	ECz	11	1	20	105	675	—	60	—	1.2	~3	86	—	96
6	PVCz	TNFDM	ECz	DHADC-MPN	1	20	105	830	—	59	—	1.5	~3	74	—	96
7	PVCz	TNF	ECz	11 + 8	100	21	105	790	15	60	140	2	2	85	125	62
8	PVCz	C ₆₀	BBP	DCST	37	28	135	676	9	50	60	—	0.057	—	51	93
9	PSX-Cz ^a				1	43	100	676	5.4	40	22	—	2.8	—	16.6	97
10	PVCz	C ₆₀	TCP	APSS	1	20	180–195	488, 514	48, 33	65	63, 110	—	~3	—	15, 37	98
								633	8		51	—	~3	—	43	98
11	PVCz	C ₆₀	BBP	AODCST	1	20	100	647	9	100	235	1.3	0.05	—	226	51, 53
		C ₆₀	BBP	AODCST	2000	20	260	647	~26	77	166	—	0.033	—	140	92
12	PVCz	C ₆₀	BBP	Lemke-e	1	26	75	675	—	82	156	1.3	1	50	~156	99
13	PVCz	C ₆₀	TCP	7	1	20	100	633	3.3	80	107	0.6	0.35	15.5	104	100
14	TDPANA-FA	C ₆₀	TCP	—	1	20	100	633	4.7	80	36.1	—	0.004	—	31.4	100
15	PVCz	TNFDM	ECz	MHADC-MPN	1	21	125	780	13	60	167	1.6	0.72	86	154	73
16	PVCz	TNFDM	ECz	14	1	21	102	780	—	60	70	0.9	—	25	~70	33, 74
		TNFDM	ECz	15	1	21	102	780	—	60	88	1.4	—	40	~88	33, 74
		TNFDM	ECz	16	1	21	102	780	—	60	167	3.1	—	85	~167	33, 74
17	PSX-Cz	TNFDM		4	1	25	105	633	42	33.3	72	—	~600	—	30	38
18	PSX-Cz	TNF		12	1	30	100	676	33	80	130	—	~0.5	—	97	87
		TNF		13	1	28	150		20		80	—		—	60	87
19	PSX-Cz	TNF		DB-IP-DC	1	27	100	633	—	30	—	3	~10	92	—	101
20	CPA	TNF	ECz		1	20	100	633	—	92.4	93	0.5	—	12	~93	102
21	PMMA-Cz	TNFDM	LC (20% by mass)	17	1	15	125	780	—	48	70	—	—	—	~70	76
				18, 19	1	10	125	780	—	48	35	—	—	—	~35	76
22	PM PHAE	MHB ⁺	MHB ⁺		1	74	19.4		66	26	189	—	19	—	117	106–109
23	API	J-aggregates	Dye 1		1	230	5	514	362	16	480	5	3	2.3	118	29, 30
		J-aggregates	Dye 1		1	230	5	647	37	123	398	—	2.5	—	361	80
		J-aggregates	Dye 2		1	230	4	633	75	50	218	4	0.02	3	143	80

^a With chromophore side groups.

Note. BBP is butyl benzyl phthalate; PDCST is 4-piperidinodicyanostyrene-malononitrile; BDMNPAB is 1-*n*-butoxy-2,5-dimethyl-4-(4'-nitrophenylazo)benzene; DHADC-MPN is 2-*N,N*-dihexylamino-7-dicyanomethylidenyl-3,4,5,6,10-pentahydronaphthalene; DCST is dicyanostyrene; APSS is 4-[*N*-(2-hydroxyethyl)-*N*-methylamino]-4'-(6-hydroxyhexylsulfonyl)stilbene; TCP is tricresyl phosphate; AODCST is aminodicyanostyrene; Lemke-e is (3-{2-[4-(*N,N*-diethylamino)phenyl]vinyl}-5,5-dimethylcyclohex-2-enylidene)malonodinitrile; MHADC-MPN is *N,N*-methylhexylamino-7-dicyanomethylidenyl-3,4,5,6,10-pentahydronaphthalene; DB-IP-DC is 3-{(E)-2-dibutylaminovinyl}-5,5-dimethylcyclohex-2-enylidene)malononitrile; CPA is a copolymer of carbazoyl acrylate and 1-(acryloxyethoxy)-2,5-dimethyl-4-(nitrophenylazo)benzene;



The PM PHAE layers generate the second harmonic at 532 nm under the action of pulses of a Nd–YAG laser ($\lambda = 1064$ nm).¹¹¹ This is due to the fact that in Ch^+X^- compounds the outer anion X^- causes a displacement of the electron density in the cationic fragment.⁴³ The dipole moment thus induced interacts with the E_0 field. This interaction is responsible for the appearance of a predominant orientation of the dipole moments of the MHB^+ cations in the bulk of the polymer layer, and, hence, for the volume susceptibility $\chi^{(2)}$. The second- and third-order volume susceptibilities provide the refractive index modulation

$$\Delta n_1 = \Delta n_{\text{PEO}} + \Delta n_{\text{KEO}} = \frac{2\pi E_{\text{sc}}(\chi^{(2)} + \chi^{(3)} E_{\text{t}})}{n}.$$

The MHB^+ cation can exhibit orientational polarisability despite the fact that this nonlinear optical chromophore is incorporated into the polymer chain of PM PHAE and its diffusive motion is restricted. The polarisability is due to the interaction between the cation and the mobile Br^- anion, which is displaced relative to the cation during the formation of the E_{t} field and changes the direction of the induced dipole moment of the MHB^+ cation, thus contributing of Δn_{OB} to the refractive index modulation.

A peculiarity of PM PHAE is that the transport centres and the photogeneration and nonlinear optical fragments formed upon exposure are embedded into the main chain. This substantially decreases the probability of the formation of dimers, which are deep hole traps. Besides, as mentioned above, compensation of dipole moments in the case of dimerisation of low-molecular-mass chromophores reduces the orientational polarisability.⁶²

Table 3 lists the most important characteristics of a photorefractive polymeric material (API containing nanocrystalline J-aggregates of carbocyanine dyes) with a high glass transition temperature ($T_{\text{g}} = 230$ °C). J-Aggregates form a centrosymmetric structure in the polymer matrix. As mentioned above, this structure is characterised by a very high third-order susceptibility,⁶⁶ so the refractive index modulation is governed by the contribution of the Kerr electro-optic effect, Δn_{KEO} [see Eqn (7)]. Therefore, in contrast to most polymer composites listed in Table 3, in this case there is no need for pre-poling of J-aggregates in the electric field or use of viscous low- T_{g} polymers. As can be seen in Table 3, the PR-polymeric material with J-aggregates has a large two-beam coupling gain coefficient, the net internal gain having a record value of 361 cm^{-1} .

VI. Practical applications of polymeric photorefractive materials

Organic (in particular, polymeric) materials have long been thought as inefficient, unstable and insufficiently pure for electronic and photonic applications. Because of this the emphasis was placed on inorganic crystalline and amorphous semiconductors and dielectrics. However, considerable advances in the synthesis of and research on new organic compounds achieved during the last two decades have introduced radical changes in the situation. Suffice it to say that currently nearly 90% of photoreceptors for copiers, laser printers and digital presses are made of organic polymeric materials. What is more, novel polymers, organic compounds and materials based on them possessing photoelectric and optical properties are considered as rather promising for use in electroluminescent devices, solar energy converters, etc.

Such characteristics of photorefractive polymeric materials as high photoelectric sensitivity, beam coupling ratio, refractive index modulation, diffraction efficiency and short (millisecond range) hologram writing times, as well as the possibility of repeated real-time hologram writing/erasure cycles make these materials promising for photonic applications. In particular, dynamical holograms can be written with a diffraction efficiency

of nearly 100% and erased by illuminating the PR-layer in the absorption band of a photogenerator. Some other applications include, e.g., a unique image amplification effect, a laser-based method for detection of ultrasonic oscillations of various media⁹³ and a method for storage of digital information by one- and two-photon excitation of a photorefractive polymeric material.¹¹² It is of interest to consider the prospects for use of these materials in everyday life, which go beyond the scope of the photonics area, in more detail.

Protection of documents and goods from forgery and counterfeit is a topical problem. Current holographic techniques are no longer a solution to this problem, since holograms can be readily copied. Peyghambarian *et al.*¹¹³ proposed a photorefractive method for security verification of objects of various nature, which is based on the ability of photorefractive polymeric materials to write dynamical holograms. A transparent phase mask of size 5×5 mm and thickness $1\text{--}2 \mu\text{m}$ is placed on an object to be verified. The mask is an array of a rather large number of pixels, the pixel size being of the order of several tens of micrometres. Such pixels are photolithographically or in another manner formed in an initial mask material in a specified order or randomly and differ from the latter in refractive index value. Using a simple optical laser correlator, the mask with a secret code is compared with the reference mask encoded exactly in the same way as the test mask. The main element of such a device is the photorefractive polymer layer (for the layer composition, see Table 3, No. 1). First, a photorefractive hologram of the test phase mask is written on the polymer by the interference of the pump beam and the signal beam and serves as a holographic filter. Then the laser beam transmitted through the reference mask passes through the polymer layer from the opposite side. This beam undergoes diffraction towards the pump beam. If the images of the reference mask and the test mask in the photorefractive polymer layer match each other, the intensity of the diffracted beam increases dramatically. The advantages of this system are low cost, nearly full protection from copying information recorded on the mask, real-time operation (response time is about 1 s), confident verification (even if 90% of information recorded on the mask is erased) and the possibility of using a small-size semiconductor laser diode for writing dynamic holograms.

Energy transfer between interfering beams in photorefractive polymer layers is used for image amplification in video-rate optical processing applications.⁹² Using a conventional optical scheme with the pump and the signal beams interfering in a photorefractive polymer layer (beam intensity ratio $\beta = 2000$ at a signal beam intensity of 0.5 mW cm^{-2}), a net increase in image intensity by a factor of 37 was observed within a video frame at a $E_0 = 77 \text{ V } \mu\text{m}^{-1}$ field applied to the layer. The frame exposure time is determined by the time taken to reach the maximum net intensity gain during creation of a phase hologram in the PR layer (the layer composition is listed in Table 3, No. 11) and is 33 ms, which nearly coincides with the frame illumination time when watching a movie. As the polarity of the external field applied to the photorefractive polymer layer changes, energy is transferred from the signal beam to the pump beam. As a consequence, only moving objects can be visualised using the image-bearing laser beam. Indeed, by imaging static objects a hologram is created in the photorefractive layer and the signal beam energy is transferred to the pump beam, thus diminishing the image. If objects move faster than the photorefractive response time, the hologram has no time to be created, so no energy transfer from the signal beam occurs and the moving object can be clearly seen on a screen. Clearly, by varying the hologram writing speed in the PR layer it is possible to change the speed threshold necessary for visualisation of moving objects.

A photorefractive method of medical diagnosis has been proposed.⁹⁶ It is known that biological tissues strongly scatter radiation over the whole optical region and at the same time are transparent in the near-IR region (700 to 900 nm). Hence, tissue diagnosis requires separation of the scattered radiation from the

unscattered radiation carrying useful information about absorption centres in the medium. In addition, the material for writing dynamic holograms must be near-IR sensitive. This problem can be solved using a photorefractive polymeric material (for the composition, see Table 3, No. 6). The technique employs a time delay of the scattered radiation with respect to the unscattered radiation in the signal beam due to extension of the optical path in the scattering medium. The source of IR radiation was either a pulsed femtosecond Ti:sapphire laser ($\lambda = 830$ nm) or a semiconductor laser diode capable of generating a continuous-wave (cw) low-coherence beam. The hologram is formed only when the unscattered radiation of the signal beam overlaps with the pump beam. When using a pulsed laser, the delayed scattered radiation reaches the PR layer after the pump beam pulse; when using a cw laser, coherent portions of the unscattered beam and the pump beam interfere, while the delayed scattered radiation reaches the PR layer simultaneously with the non-coherent radiation of the signal beam. In both cases the hologram is formed only when the signal and the pump beams overlap within the coherence length of a laser source. The hologram can be reconstructed using the probe laser beam counterpropagating with the pump beam and a conventional optical scheme.

In all the systems considered above, low- T_g photorefractive polymers were used. In addition to their advantages (see above) photorefractive polymeric systems have a fundamental drawback, which precludes wide industrial applications of such materials and consists in a relatively short lifetime of stable photorefractive parameters (about six months at room temperature even when encapsulated and protected from moisture).^{11,3} This is due to crystallisation of chromophore and phase separation within the layer. A possible solution to this problem is to work with high- T_g polymeric systems. This is of course associated with loss of alignment of the dipole chromophores in the modulated space-charge field responsible for additional increase in Δn . Therefore, search for new polymeric systems with high nonlinear susceptibilities is required. A promising avenue of investigations is the incorporation of chromophores with high third-order susceptibility into photorefractive polymeric systems. For instance, J-aggregates of carbocyanine dyes have been used.^{29, 30, 80} As mentioned above, during the synthesis of a PR material J-aggregates form a centrosymmetric structure, which has a very high third-order susceptibility $\chi^{(3)}$. Hence there is no need for alignment of J-aggregates in the electric field, which is necessary if one operates with photorefractive polymers possessing linear orientational polarisability and second-order nonlinearity. The refractive index modulation, Δn , is determined by the Kerr electro-optic effect and is proportional to $E_1^2 \chi^{(3)}$; hence, there is no need to use low- T_g polymers.

Besides, the electronic nature of optical nonlinearity allows one to expect a substantial shortening of the writing time of dynamical holograms, which in this case is not related to the orientational motion of bulky chromophores. It should also be noted that, depending on their structure, carbocyanine dyes absorb in the whole visible region and in the near IR region. J-Aggregates of carbocyanine dyes are nanocrystalline particles, which absorb the electromagnetic radiation at wavelengths that are 100–300 nm longer than the absorption wavelengths of the corresponding monomeric dye molecules. Thus, in principle the long-wavelength limit of the sensitivity of photorefractive polymeric materials can be estimated at 1550 nm. The fact that optical fibre communication operates at this wavelength significantly extends the range of practical applications of such materials. Oligomeric triacetylene and diacetylene compounds characterised by high third-order susceptibility (see above) can also be used as chromophores.

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^a — *J. Exp. Theor. Phys. Lett. (Engl. Transl.)*

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^c — *High Energy Chem. (Engl. Transl.)*

^d — *Polym. Sci. (Engl. Transl.)*

^e — *Sci. Appl. Photogr. (Engl. Transl.)*

Synthesis and reactions of halogen-containing chromones

V Ya Sosnovskikh

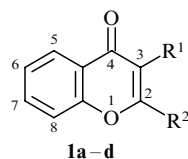
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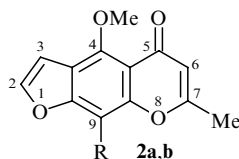
Abstract. Published data on the synthesis and reactivity of halogen-containing chromones, flavones, thiochromones and furochromones are generalised. The bibliography includes 220 references.

I. Introduction

Chromone (4*H*-chromen-4-one, 4*H*-1-benzopyran-4-one, **1a**) is a parent compound for an important class of oxygen-containing heterocyclic compounds with a benzoannulated γ -pyrone ring. This heterocyclic system is frequently encountered in the vegetable world, most often as flavone (2-phenylchromone, **1b**), flavonol (3-hydroxy-2-phenylchromone, **1c**) and isoflavone (3-phenylchromone, **1d**) derivatives, which form the group of flavonoids — flower and fruit pigments.¹ These compounds exhibit various types of biological activities² and find use as substrates in the preparation of many pharmaceuticals including some antitumour drugs.³ Alkylchromones are less naturally abundant; nevertheless, some of them are also known to be biologically active. For example, of therapeutic interest are 3-methyl- and 2,5,8-trimethylchromones.² The natural furochromones khellin (**2a**) and visnagin (**2b**) are the active substances of the plant *Ammi visnaga* L., known for its therapeutic properties since antiquity.^{4,5}

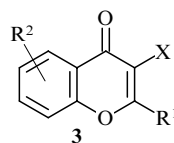


$R^1 = R^2 = H$ (**a**);
 $R^1 = H, R^2 = Ph$ (**b**);
 $R^1 = OH, R^2 = Ph$ (**c**);
 $R^1 = Ph, R^2 = H$ (**d**).

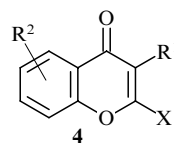


$R = MeO$ (**a**), H (**b**).

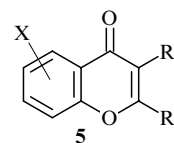
Among halogen derivatives of chromone **1a**, compounds acting as stimulators for the central nervous system^{6,7} and exhibiting high antiviral,⁸ antimicrobial,^{9,10} antimycotic,^{9,10} anti-allergic^{11–13} and neuroleptic¹⁴ activities have been found. The enhanced interest in the chromone chemistry is indicated by publication of a series of reviews^{15–18} and monographs.² However, halogenated chromone derivatives (halochromones and haloalkylchromones) are the subjects of only one chapter in the book² published in 1977. In recent years, a fairly large number of studies dealing with the chemistry of halochromones containing halogen atoms attached directly to the carbon atoms of the chromone system and haloalkylchromones in which halogen atoms occur in the side chains have been reported. However these data have not yet been reviewed or analysed. This review is meant to fill this gap. Here we consider chromones **3–5**, where R^1 , R^2 are any substituents containing no halogen atoms.



$X = Hal, CH_2Hal, COCH_2Hal.$



$X = Hal, R^F, CCl_3, CH_2Hal.$



$X = Hal, CH_2Hal.$

Derivatives **5**, containing a halogen or a halomethyl group in the benzene ring, differ little in methods of synthesis and reactivity from the appropriate halogenated benzene derivatives and are of secondary importance for the chromone chemistry, which is mainly determined by the γ -pyrone ring having two electrophilic centres, the C(2) and C(4) atoms. Therefore, attention will be focused on halo- and haloalkylchromones **3** and **4**, containing a halogen-containing substituent in the γ -pyrone ring. The presence in the ring of a halogen atom, which is a good leaving group, or a 2-polyhaloalkyl group, which increases the electrophilicity of the C(2) atom, extends appreciably the synthetic potential of chromones and makes them valuable substrates for the synthesis of new heterocyclic compounds with a broad range of useful properties.

To complete the picture, the review covers the most important publications of the 1960s–1970s not included in the monograph² and also the sparse data available on halo-containing thiochromones and furochromones. The methods of synthesis and chemical properties of chromones with the perfluorinated benzene ring have been covered in a number of reviews;^{2,18,19} therefore, we do not consider them here. The reactions of heteroanalogues of

V Ya Sosnovskikh Department of Chemistry, A M Gor'ky Urals State University, prosp. Lenina 51, 620083 Ekaterinburg, Russian Federation. Fax (7-343) 261 59 78. Tel. (7-343) 261 68 24. E-mail: Vyacheslav.Sosnovskikh@usu.ru

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isoflavones containing a trifluoromethyl group at the 2-position with alkalis, hydrazines, amidines and hydroxylamine have been described in a review published previously.¹⁵

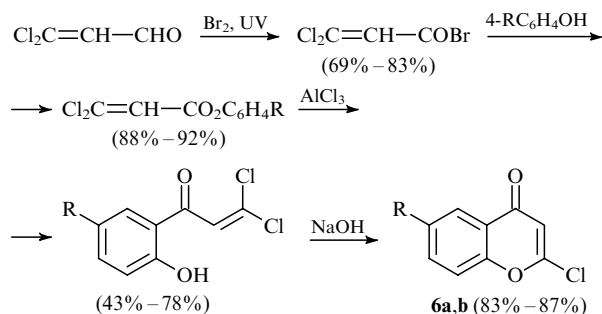
II. Methods for the synthesis of halochromones

The most convenient methods for the formation of the chromone system include the Claisen condensation of 2-hydroxyacetophenones with esters,²⁰ the Baker–Venkataraman rearrangement of *O*-acyl derivatives of 2-hydroxyacetophenones²¹ and the Kostanecki–Robinson method, consisting of the reaction of the same ketones with carboxylic acid anhydrides.¹⁴ This gives rise to compounds that exist either in the open β -diketone form or in the cyclic 2-hydroxychromanone form, depending on the conditions and the nature of the substituents. Upon dehydration in an acid medium, they yield the corresponding chromones. The introduction of halogen atoms into the pyrone and benzene rings and into the side chains can be performed both during the synthesis of chromones (by using halo-containing ketones and esters) and by treatment of chromones or their precursors (β -diketones) with halogenating agents.

1. Synthesis of 2-halochromones

2-Halochromones represent a group of halo-derivatives of chromone difficult to access, as the introduction of the halogen atom into the 2-position of the chromone system is usually a more complicated synthetic task than halogenation of the benzene ring activated by electron-donating groups.

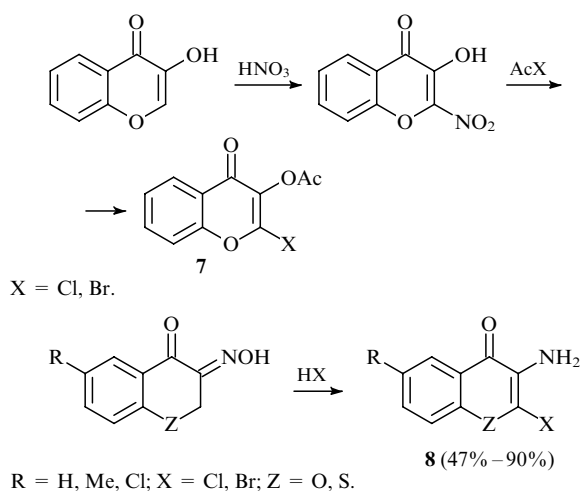
The first representatives of chromones containing a halogen atom at the 2-position [2-chloro- (**6a**) and 6-methyl-2-chlorochromones (**6b**)] were prepared in 1960 from β,β -dichloroacrolein and the corresponding phenols.²² The key step of the synthesis is the Fries rearrangement of aryl dichloroacrylate on treatment with AlCl_3 at 130 °C followed by cyclisation of *o*-hydroxyketones in an alkaline medium to give 2-chlorochromones **6**.



R = H (**a**), Me (**b**).

Subsequently, α,β,β -trichloro- and α -bromo- β,β -dichloroacroleins^{23,24} and also α,β,β -trichloro- and α,β -dichloroacryloyl chlorides²⁵ have been involved in this reaction. The intra- and intermolecular acylation of phenols with these reagents resulted in the synthesis of 2- and 3-halo- and 2,3-dihalochromones. For example, 2,3-dichloro-7-methoxy- or 3-chloro-7-methoxychromones were prepared from 1,3-dimethoxybenzene and α,β,β -trichloro- or α,β -dichloroacryloyl chloride.²⁵

Other methods for the introduction of a halogen atom into the 2-position are also known. The presence of the 3-hydroxy group facilitates the electrophilic attack on the C(2) atom; as a result, bromination of 3-hydroxychromone affords 2-bromo-3-hydroxychromone in a good yield,² while its nitration furnishes 3-hydroxy-2-nitrochromone. By treatment with acetyl halides, the latter product can be converted into 2-chloro- and 2-bromo-3-acetoxychromones (**7**).²⁶ The reactions of chromane-3,4-dione 3-oximes and thiochromane-3,4-dione 3-oximes with hydrogen halides yield 3-amino-2-chloro- and 3-amino-2-bromochromones and -thiochromones (**8**).²⁷

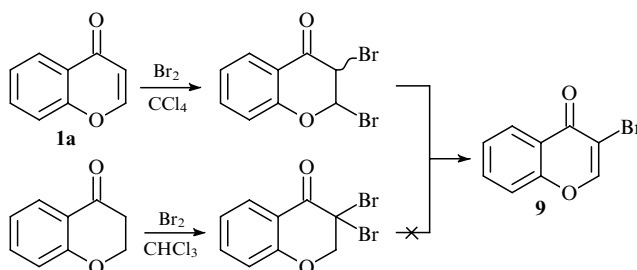


It is noteworthy that all the known methods for the synthesis of 2-halochromones proposed 30–40 years ago were based on initial compounds difficult to prepare and in most cases, the methods were not generally applicable. In recent years, no significant progress in the development of new approaches to the preparation of these compounds has been made either. Only in one study,²⁸ was the Fries rearrangement used to prepare 2-chloro-6-methylchromone,²² which was then introduced in reactions with α -amino ketones and α -aminoacetals (see Section III.1).

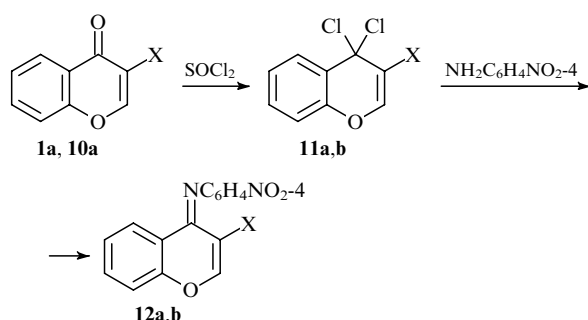
2. Synthesis of 3-halochromones

Due to the vigorous development of transition metal-catalysed cross-coupling reactions giving C–C bonds, which open up the way to complex natural molecules, the interest in the synthesis of 3-halochromones has been enhanced and they have become available compounds. 3-Halochromones can be prepared by halogenation of either chromones or their precursors, *i.e.*, β -diketones and β -aminovinyl ketones containing 2-hydroxyaryl substituents at the carbonyl group (in most cases, the latter route is preferred).

The reaction of chromones with halogens or some halogenating reagents usually starts with the halogen addition to the double bond of the pyrone ring, which is followed by dehydrohalogenation (either spontaneous or base-induced), resulting in the target 3-halochromones. For instance, the reaction of chromone **1a** with bromine in CCl_4 gives 2,3-dibromochroman-4-one, which is readily converted into 3-bromochromone (**9**).²⁹ Chromanone reacts with bromine in CHCl_3 to give 3,3-dibromochromanone; however, this product could not be converted into chromone **9** in a plausible yield.³⁰



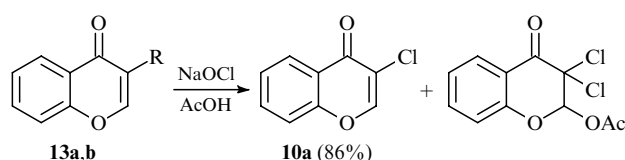
Treatment of chromone **1a** with sulfonyl chloride with cooling gives rise to 2,3-dichlorochroman-4-one, which is smoothly converted into 3-chlorochromone (**10a**) on treatment with triethylamine.³¹ Interestingly, chromones **1a** and **10a** react with thionyl chloride to give 4,4-dichloro- (**11a**) and 3,4,4-trichloro-4*H*-chromenes (**11b**), whose reaction with 4-nitroaniline affords the corresponding *N*-(4*H*-chromen-4-ylidene)anilines (**12a, b**), the first representatives of the chromeneimine series.³¹



X = H (**1a**, **11a**, **12a**), Cl (**10a**, **11b**, **12b**).

The reaction of 6-nitrochromone with a potent electrophilic brominating agent, in particular, the dibromoisocyanuric acid–sulfuric acid system, results in the formation of 3,8-dibromo-6-nitrochromone, whereas chromone **1a** gives only 6-bromochromone under similar conditions due to protonation of the pyrone ring. With a greater amount of dibromoisocyanuric acid, the transformation of chromone **1a** yielded 5,6,8-tribromo- and 3,5,6,8-tetrabromochromones.³²

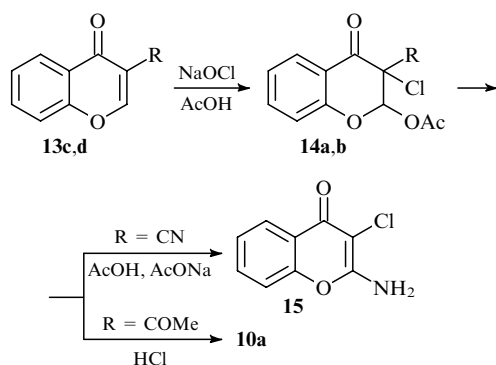
Treatment of chromone-3-carbaldehyde (**13a**) or chromone-3-carboxylic acid (**13b**) with sodium hypochlorite in acetic acid gives 3-chlorochromone **10a** with a 2-acetoxy-3,3-dichlorochroman-4-one impurity.



R = CHO (**13a**), CO₂H (**13b**).

Under similar conditions, 3-formylchromones substituted in the benzene ring form the corresponding 3-chlorochromones in 43%–82% yields.^{33, 34}

The transformation of 3-acetylchromone (**13c**) and chromone-3-carbonitrile (**13d**) under the same conditions gives 2-acetoxy-3-acetyl- (**14a**) and 2-acetoxy-3-cyano-3-chlorochroman-4-ones (**14b**). On treatment with HCl, the acetyl derivative **14a** furnishes chromone **10a**, while nitrile **14b** is converted into 2-amino-3-chlorochromone (**15**) in aqueous acetic acid in the presence of AcONa. In this case, the reaction is accompanied by opening of the pyrone ring followed by cyclisation involving the cyano group.³⁴

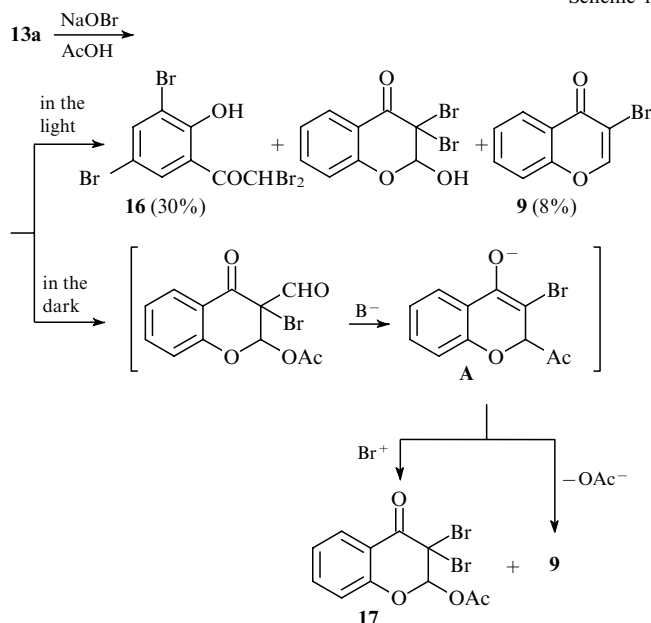


R = COMe (**13c**, **14a**), CN (**13d**, **14b**).

Chromone-3-carbaldehyde (**13a**) reacts with sodium hypobromite in the light to give a mixture of three products where 2,2,3',5'-tetrabromo-2'-hydroxyacetophenone (**16**) is the major

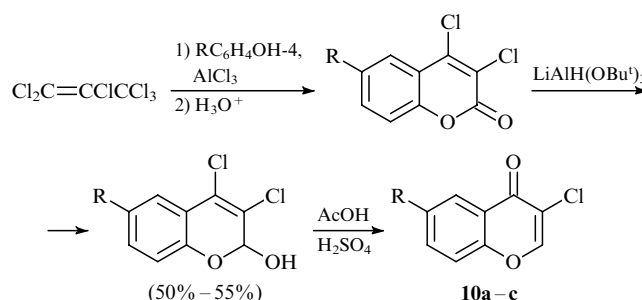
product (30%), while the expected 3-bromochromone **9** is formed in a low yield (8%). The researchers believe³⁴ that tetrabromoacetophenone results from radical opening of the pyrone ring, because the same reaction carried out in the dark gave only bromo-derivatives **9** and **17** in 32% and 29% yields, respectively (Scheme 1). The reaction mechanism includes the addition of acetyl hypobromite and subsequent elimination of the formyl group under the action of a base. The elimination of molecule AcOH from intermediate **A** affords chromone **9**, while its bromination leads to chromanone **17**.

Scheme 1



B is base.

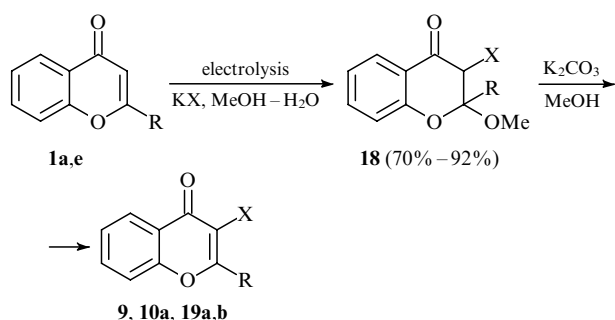
The reduction of 3,4-dichlorocoumarins, prepared by treatment of phenols with perchloropropylene in the presence of aluminium chloride,³⁵ with lithium tri(*tert*-butoxy)aluminium hydride produces lactols, which are easily transformed into 3-chlorochromones **10a–c** when heated in acetic acid in the presence of catalytic amounts of H₂SO₄.^{36, 37}



R = H (**a**), Me (**b**), Cl (**c**).

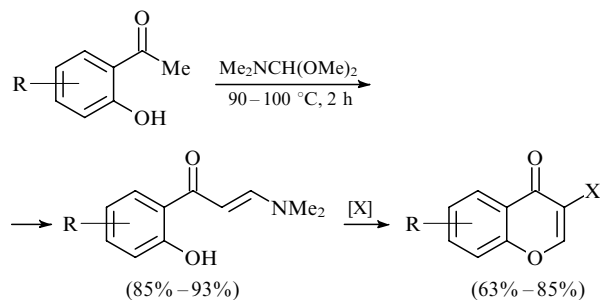
When chromone **1a** is subjected to oxidative chlorination (*m*-chloroperbenzoic acid, HCl, DMF, ~20 °C), 3-chlorochromone **10a** is formed in 96% yield.³⁸ This method is suitable for introducing chlorine into the α-position of both cyclic and acyclic α,β-enones.

Electrolysis of chromone (**1a**) and 2-methylchromone (**1e**) in a methanol–water mixture (4:1) containing potassium halide yields 3-halo-2-methoxychroman-4-ones **18**, which are unstable during storage. On treatment with K₂CO₃ in methanol, they pass almost quantitatively into the corresponding 3-chloro- (**10a**, **19a**) and 3-bromochromones (**9**, **19b**).³⁹



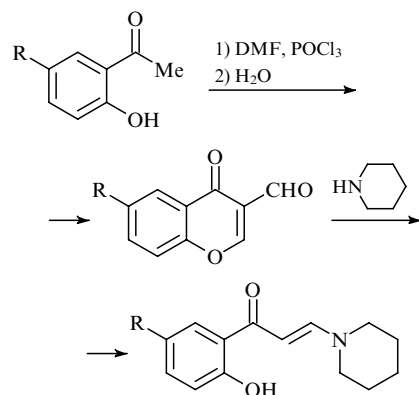
$\text{R} = \text{H, Me; X} = \text{Cl, Br}$.

The most general protocol used to prepare 3-halochromones (which also appears most attractive from the preparative standpoint) is halogenation of β -aminovinyl ketones containing a 2-hydroxyaryl group at the carbonyl carbon atom.⁴⁰ To prepare 3-halochromones containing no substituents at the 2-position, 2-hydroxyacetophenones are condensed with excess dimethylformamide dimethyl acetal. The 1-(2-hydroxyaryl)-3-dimethylaminoprop-2-en-1-ones thus formed are halogenated with *tert*-butyl hypochlorite, bromine or iodine in CHCl_3 ⁴⁰ or with *N*-fluoro-2,4,6-trimethylpyridinium triflate in a $\text{CH}_2\text{Cl}_2 - \text{MeCN}$ mixture.¹⁴



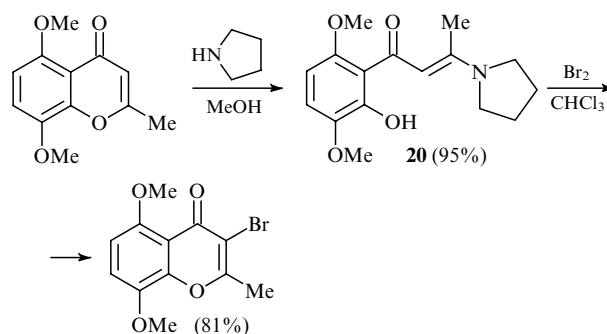
$\text{R} = \text{H, Me, Cl, MeO; X} = \text{F, Cl, Br, I}$.

When electrophiles with good leaving groups such as iodine chloride or trifluoro- and trichloroacetic anhydrides are used in the reaction with aminovinyl ketones, 3-chloro- and 3-trihaloacetylchromones are formed.⁴¹ The use of expensive dimethylformamide dimethyl acetal can be avoided by preparing aminovinyl ketones in two steps *via* chromone-3-carbaldehydes,⁴² which are readily deformylated by opening the heterocycle under the action of piperidine.⁴³



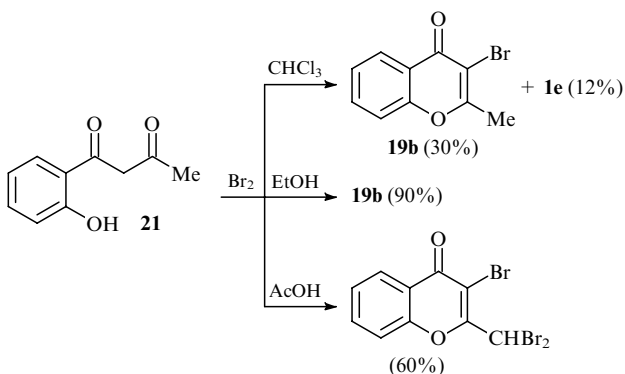
$\text{R} = \text{H, Me, Cl}$.

The reaction of 5,8-dimethoxy-2-methylchromone with piperidine in boiling methanol yields aminovinyl ketone **20**, which reacts with bromine in CHCl_3 being converted into 3-bromo-5,8-dimethoxy-2-methylchromone.⁴⁰

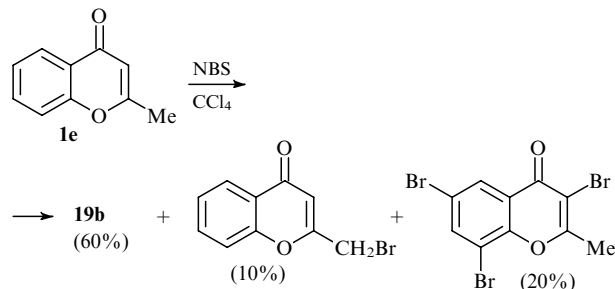


This reaction was used as an example to demonstrate that halogenation of enamines of 2-hydroxyacetophenones can be employed to obtain 2-substituted 3-halochromones.

3-Bromo-2-methylchromone (**19b**) was prepared in a relatively low yield, as a mixture with 2-methylchromone (**1e**) from β -diketone **21** under similar conditions (treatment with bromine in CHCl_3).⁴⁴ The outcome of this reaction proved to be substantially dependent on the nature of the solvent in which bromination took place. Indeed, when chloroform was replaced by ethanol, the yield of chromone **19b** increased to 90%, while the reaction performed in acetic acid in the presence of excess bromine led to 3-bromo-2-dibromomethylchromone.⁴⁵



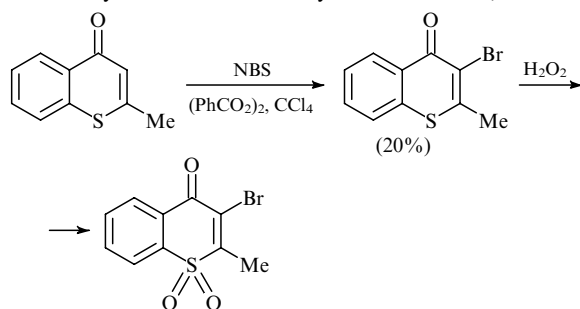
In the reaction of 2-methylchromone (**1e**) with bromine in AcOH , chromone **19b** is formed in a low yield (25%).² Upon an attempt to prepare compound **19b** from 2-methylchromone (**1e**) and *N*-bromosuccinimide in CCl_4 , as described in an earlier publication,⁴⁶ three products were isolated, namely, chromone **19b**, 2-(bromomethyl)chromone and 3,6,8-tribromo-2-methylchromone.⁴⁷



NBS is *N*-bromosuccinimide.

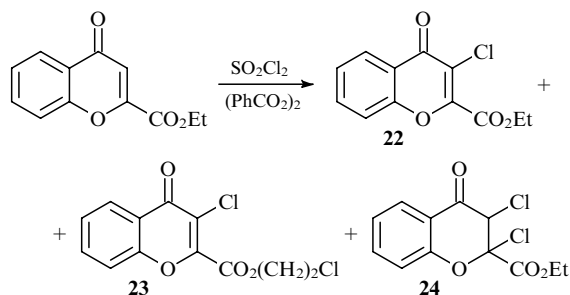
In the case of 6-methyl- and 6-methoxy-2-methylchromones, the reaction proceeds more unambiguously giving rise to 6-substituted 3-bromo-2-methylchromones (yields 90%–92%), together with small amounts of 2-(bromomethyl)chromones (5%–8%).⁴⁷ The reaction of 6-hydroxy-2-methylchromone with bromine in concentrated H_2SO_4 (25°C , 6 h) gives 5-bromo-6-hydroxy-2-methylchromone (yield 73%). In acetic acid ($45 - 50^\circ\text{C}$, 8 h) and in the presence of excess bromine, 3,5-dibromo-6-hydroxy-2-methylchromone is formed (yield 53%).⁴⁸

Ziegler bromination of 2-methylthiochromone gives 3-bromo-2-methylthiochromone, which is oxidised at sulfur on treatment with H_2O_2 to yield 3-bromo-2-methylthiochromone 1,1-dioxide.⁴⁹



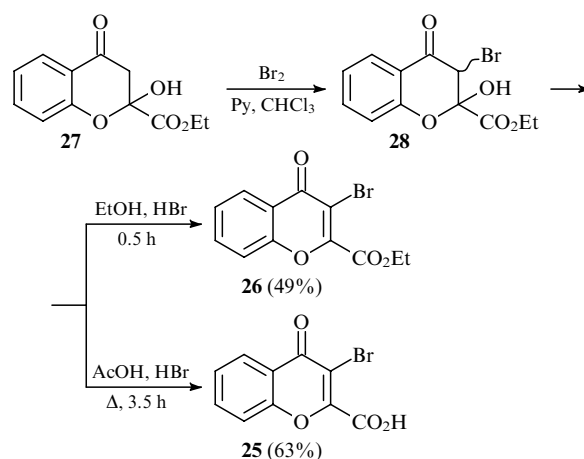
Treatment of 6-substituted 2-methylchromone and chromone-2-carbaldehyde with an aqueous solution of sodium hypochlorite in the presence of AcOH gives the corresponding 3-chlorochromones[†] in 61%–93% yield.⁵⁰ *N*-Trichloroacetyl- and *N*-ethoxycarbonyl-2-aminochromones are selectively chlorinated at the C(3) atom on treatment with SO_2Cl_2 in CHCl_3 at $\sim 20^\circ\text{C}$.⁵¹ In the I_2 – HIO_4 system, *N*-ethoxycarbonyl-2-aminochromone affords the 3-iodo-derivative in a yield of 78%.⁵²

Refluxing a solution of ethyl chromone-2-carboxylate in sulfuryl chloride in the presence of benzoyl peroxide for 10 h gives a mixture consisting of approximately equal amounts of mono- (**22**) and di-chloro (**23**, **24**) derivatives.⁵³ Chromanone **24**, which is a product of free radical addition of chlorine at the double bond, easily loses an HCl molecule on treatment with pyridine, being thus converted into 3-chloro derivative **22**.



Under similar conditions, methyl chromone-2-carboxylate yields only methyl 3-chlorochromone-2-carboxylate (yield 69%)⁵⁴ and chromone-2-carbonitrile is converted into 3-chlorochromone-2-carbonitrile (yield 63%), which was used to prepare 3-chloro-2-(5-tetrazolyl)chromone, exhibiting an antiallergic activity.⁵⁵

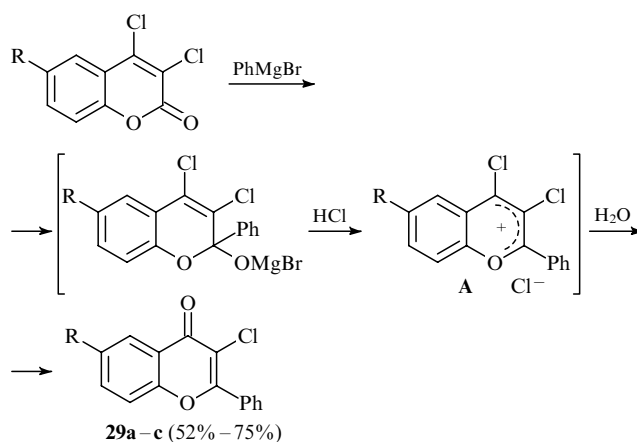
3-Bromochromone-2-carboxylic acid (**25**) and its ethyl ester (**26**) have been synthesised by two procedures.⁵⁴ According to one procedure, the condensation product obtained from 2-hydroxyacetophenone and diethyl oxalate and existing in the cyclic chromanone form **27** is made to react with bromine in chloroform in the presence of pyridine at -3°C . This yields a mixture of *cis*- and *trans*-isomers of 3-bromochromanone **28** in 72:28 ratio. When compound **28** is refluxed in an EtOH–HBr mixture, ethyl 3-bromochromone-2-carboxylate (**26**) is formed in 49% yield, while refluxing of **28** in an AcOH–HBr mixture gives the acid **25**. The ester **26** can also be obtained by the above-described method⁴⁰ from ethyl chromone-2-carboxylate and pyrrolidine via aminovinyl ketone but in a lower yield.⁵⁴



Bromination of ethyl 7-hydroxychromone-2-carboxylate with bromine in acetic acid (75 – 80°C , 5 h) furnishes a mixture of 8-bromo-, 6,8-dibromo- and 3,6,8-tribromo-7-hydroxychromone-2-carboxylate, whereas bromination of the corresponding acid stops after the formation of 8-bromo-7-hydroxychromone-2-carboxylic acid under the same conditions (yield 94%).⁵⁶

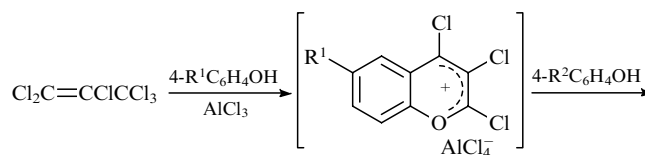
3. Synthesis of 3-halo flavones

Interestingly, 3-chloroflavones were first obtained⁵⁷ by the reaction of 3,4-dichlorocoumarins³⁵ with phenylmagnesium bromide rather than by chlorination of flavones. The key intermediate in this reaction is benzopyrylium salt **A**, which is hydrolysed at the 4-position to give 3-chloroflavones **29a–c**. This was the first example of direct transformation of the coumarin system into the chromone one.

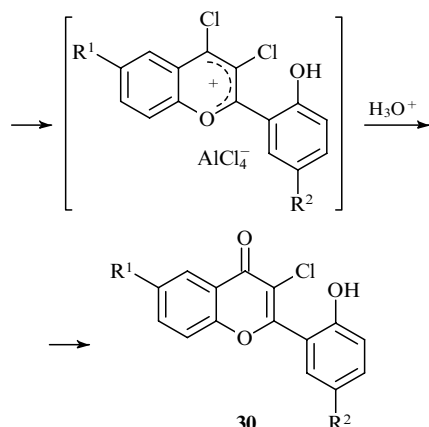


R = H (**a**), Me (**b**), Cl (**c**).

A modification of this method is treatment of the benzopyrylium salts formed *in situ* from phenols, perchloropropene and AlCl_3 with substituted phenols. This procedure was used to prepare 2'-hydroxy-3-chloroflavones **30**.⁵⁸

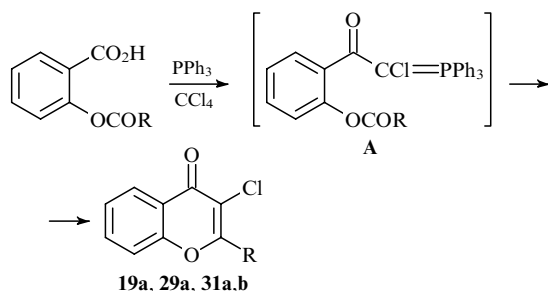


[†] In the case of 6-substituted chromone-2-carbaldehyde (unlike chromone-3-carbaldehyde³⁴), the 2-formyl group is retained.



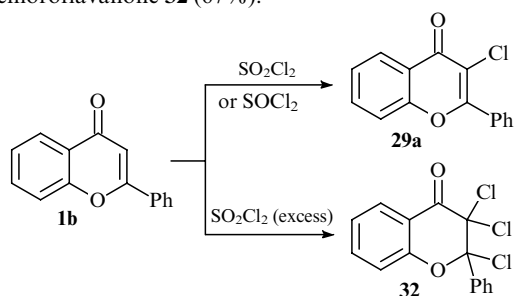
$R^1, R^2 = \text{Me, Cl.}$

Acetylsalicylic acid and *O*-aroylsalicylic acids cyclise in the $\text{PPh}_3\text{--NEt}_3\text{--CCl}_4\text{--CH}_2\text{Cl}_2$ system at $\sim 20^\circ\text{C}$ over a period of several hours to give 3-chloroflavone (**29a**) and its derivatives **19a** and **31a,b** (yields 43%–60%). In the researchers' opinion,⁵⁹ these products are formed *via* ylide type intermediate **A**. This reaction allows one to obtain 3-chlorochromone compounds in one step.



$R = \text{Me (19a), Ph (29a), 4-ClC}_6\text{H}_4 \text{ (31a), 3-C}_5\text{H}_4\text{N (31b).}$

3-Chloroflavone (**29a**) is also formed on refluxing flavone (**1b**) with suluryl chloride (CHCl_3 , 1 h, 65%)³¹ or thionyl chloride (PhH , 15 h, 70%).⁶⁰ With excess SO_2Cl_2 in the presence of benzoyl peroxide (16 h, $\sim 20^\circ\text{C}$), flavone (**1b**) is converted into 2,3,3-trichloroflavanone **32** (67%).³¹

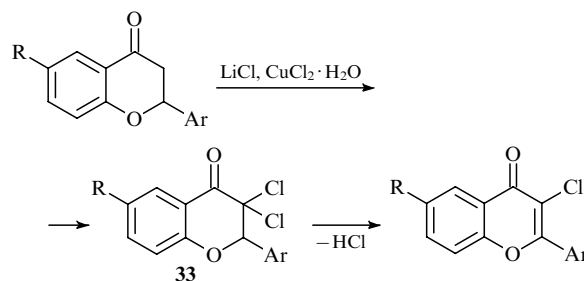


Compound **32** can also be prepared without benzoyl peroxide by refluxing flavone **1b** or **29a** with excess SO_2Cl_2 in benzene for 15 h.⁶¹

6- and 7-Chloroflavones react with thionyl chloride to give 3,6- and 3,7-dichloroflavones. 6-Chloroflavone reacts with suluryl chloride giving rise to 2,3,3,6-tetrachloroflavanone. The reaction of 7-hydroxyflavone with SOCl_2 in boiling benzene affords a mixture of 7-chloro- and 3,7-dichloroflavones, while its reaction with SO_2Cl_2 leads to 3,6,8-trichloro-7-hydroxyflavone.⁶² When 6-methylflavone is refluxed with SO_2Cl_2 in CCl_4 for 15 h, 3-chloro-6-dichloromethylflavone is the major reaction product. 2,3,3-Trichloro-6-dichloromethylflavanone is formed as a minor product. The reaction of SO_2Cl_2 with 6-methoxyflavone results in a complex mixture of four chloro derivatives of flavone and flavanone.⁶³ A general and an efficient method for the synthesis

of 3-chlorinated derivatives of flavone, chromone and thioflavone has been proposed. The procedure implies treatment with SO_2Cl_2 ⁶⁴ and the use of montmorillonite K10 as the catalyst.

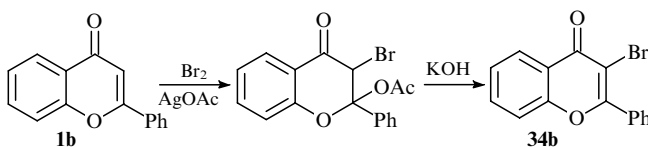
Oxidative chlorination of flavones has been carried out using LiCl as a source of chloride ions and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ^{65,66} or $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ ⁶⁷ as the oxidant. The process afforded 3,3-dichloroflavanones **33**, which are readily dehydrogenated yielding 3-chloroflavones.



$\text{Ar} = \text{Ph}; R = \text{H, Me, OMe, Cl, Br}; \text{Ar} = 4\text{-MeOC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4; R = \text{H.}$

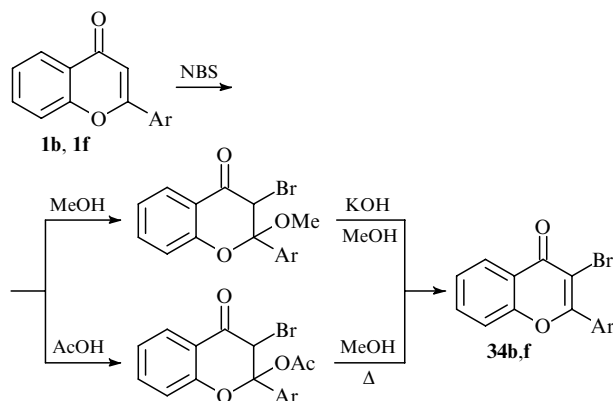
On refluxing in the $\text{CuCl}_2\text{--DMSO}$ system, flavanones and their linear isomers, 2'-hydroxychalcones, are immediately converted into 3-chloroflavones **29** in 80%–85% yields. Dichloro derivatives are not formed under these conditions.⁶⁸

Treatment of flavone **1b** with bromine in chloroform in the presence of silver acetate produces 2-acetoxy-3-bromoflavanone, which is easily transformed into 3-bromoflavone (**34b**) on treatment with KOH in aqueous alcohol.⁶⁹



Upon direct bromination of flavone **1b** with bromine in boiling acetic acid, 3-bromoflavone **34b** (75%) and 3,8-dibromoflavone (10%) were isolated.⁷⁰ However, attempts to prepare substituted 3-bromoflavones and their heteroanalogues have not met with success.⁷¹ During bromination of flavones in the $\text{Br}_2\text{--AcOH}$ system, the addition of $\text{Hg}(\text{OAc})_2$ is recommended.⁷² Preparation of 3-bromoflavones by the reaction of flavone with bromine in pyridine has been reported;⁷³ the product yields were not given in the publication.

Good results have been attained by using *N*-bromosuccinimide as the brominating agent. For instance, 3-bromoflavones **34b,f** were prepared in high yields by the reaction of flavones **1b** and **1f** with *N*-bromosuccinimide in methanol or acetic acid.⁷⁴

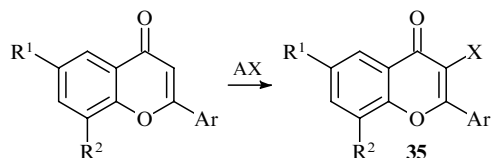


$\text{Ar} = \text{Ph (b), 4-MeOC}_6\text{H}_4 \text{ (f).}$

This method was used successfully to prepare 3,8-dibromo-7-butoxy-6-nitroflavones. These compounds were used to demon-

strate that the introduction of a bromine atom in the 3-position of flavones increases their antibacterial activity.⁷⁵

Substituted 3-bromoflavones **35** were prepared by treatment of appropriate flavones with *N*-bromosuccinimide in CHCl_3 or CuBr_2 in an $\text{AcOEt}-\text{CHCl}_3$ mixture (the yield of compounds **35** reached 50%–80%).^{71, 76–78}

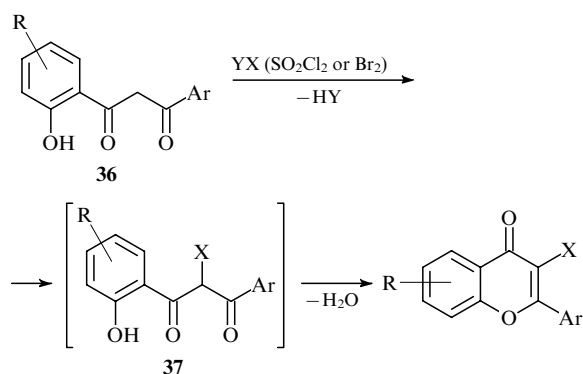


$\text{R}^1 = \text{H, Me, MeO, Cl, Br, F}$; $\text{R}^2 = \text{H, Me, Br}$; $\text{Ar} = \text{Ph, 4-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 4\text{-FC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-AcNHC}_6\text{H}_4, 2\text{-MeOC}_6\text{H}_4, 2\text{-C}_4\text{H}_3\text{O, 2-C}_4\text{H}_3\text{S}$; $\text{AX} = \text{NBS, CuBr}_2, \text{C}_5\text{H}_5\text{NH}^+\text{Br}_3^-$, $\text{PhI}(\text{OAc})_2-\text{Me}_3\text{SiX}$ ($\text{X} = \text{Cl, Br}$).

Recently, it was found that the reaction of flavones with pyridinium tribromide in pyridine and CH_2Cl_2 ($\sim 20^\circ\text{C}$, 16–48 h)⁷⁹ or with diacetoxy- λ^3 -iodanylbenzene in the presence of trimethylsilyl halides and pyridine (0°C , 4 h)⁸⁰ provides the corresponding 3-bromo- and 3-chloroflavones **35** in 60%–86% yields. In the latter case, halogenation can be carried out on a polymer substrate.

Bromination of flavones with 2,4,4,6-tetrabromocyclohexa-2,5-dienone proceeds under mild conditions to give the corresponding 3-bromoflavone in good yields.⁸¹

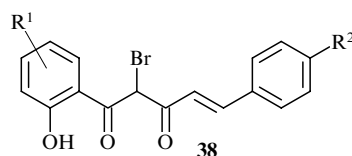
A facile and versatile method for the synthesis of 3-halo-flavones is based on halogenation of flavone precursors, diketones **36**.^{76, 82–86} For example, substituted 3-chloroflavones are formed on treatment of diketones **36** with sulfuryl chloride in dioxane and 3-bromoflavones, on treatment with bromine in dioxane.⁸² The reaction involves intermediates **37**, which undergo cyclodehydration in the presence of the hydrogen halide evolved in the reaction to give 3-halo-flavones in 60%–70% yields. Subsequently, this procedure has been utilised to prepare 2-styryl-,⁸⁴ 2-(α -furyl)- (see Refs 71, 83) and 2-(α -thienyl)-3-halochromones,⁷¹ as the double bond and the heterocyclic ring of 2-substituents are not halogenated under these conditions.



$\text{R} = \text{H, Me, Cl, Br}$; $\text{Ar} = \text{Ph, 4-MeOC}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4, 2\text{-C}_4\text{H}_3\text{O, 2-C}_4\text{H}_3\text{S, PhCH=CH, 4-MeOC}_6\text{H}_4\text{CH=CH}$; $\text{X} = \text{Cl, Br}$.

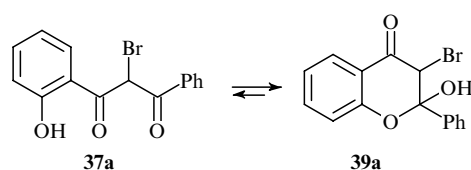
It should be noted that the reaction between 2-styrylchromones and pyridinium tribromide in AcOH at $\sim 20^\circ\text{C}$ starts with bromination of the double bond of the styryl substituent; only after this, does bromination of C(3) take place.⁸⁷

In the bromination of 5-aryl-1-(2-hydroxyaryl)pent-4-ene-1,3-diones in DMF (which traps the HBr evolved), intermediate α -bromodiketones **38**, existing in the linear form in CDCl_3 (according to ^1H NMR data), were isolated.⁸⁴

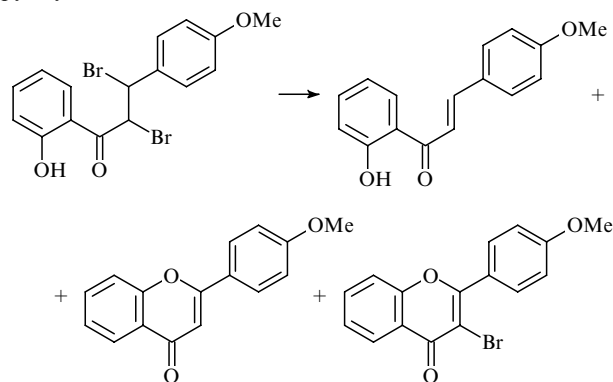


$\text{R}^1 = \text{H, Me}$; $\text{R}^2 = \text{H, MeO}$.

The same compounds are formed upon bromination of styryl diketones in the $\text{Br}_2-\text{AcOH}-\text{AcONa}$ system, whereas treatment with *N*-bromosuccinimide in CCl_4 yields a mixture of compounds **34** and **38** that are difficult to separate.⁸⁵ It is noteworthy that, unlike diketones **38**, 2-bromo-1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (**37a**) produced in the reaction of diketone **36a** ($\text{R} = \text{H, Ar} = \text{Ph}$) with bromine in chloroform in the presence of K_2CO_3 exists in the crystalline state as cyclic semiketal **39a**, while in CDCl_3 , it exists as a mixture of ring-chain tautomers **37a** and **39a** in a 3 : 11 ratio, respectively.⁸⁸

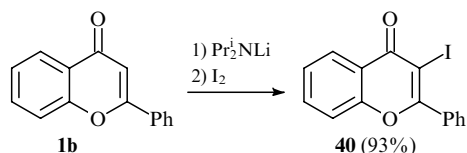


Treatment of flavanone with the complex $[(\text{C}_6\text{H}_7\text{NO})_3 \cdot \text{HBr} \cdot \text{Br}_2]$ in THF is an efficient method for the synthesis of 3-bromoflavanone, which is formed as a mixture of *cis*- and *trans*-isomers. Treatment of 4'-methoxy- and 4',7-dimethoxyflavanones with this complex in DMSO results in product mixtures consisting of the corresponding flavones and 3-bromoflavones.⁸⁹ Pyrolysis of 2'-hydroxy-4-methoxydihydrochalcone dibromide at 150°C yields a mixture of three products, namely, 2'-hydroxy-4-methoxychalcone, 4'-methoxyflavone and 3-bromo-4'-methoxyflavone; the last-mentioned product is formed upon bromination of 4'-methoxyflavone under conditions of pyrolysis.⁹⁰

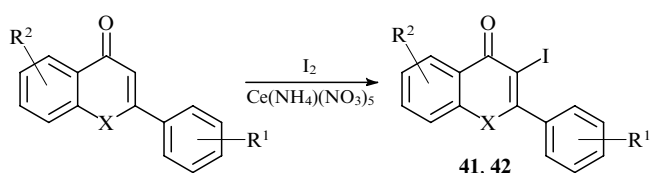


The reaction of 2'-benzyloxy-6'-hydroxychalcone and 2'-benzyloxy-6'-hydroxy-2-cinnamylideneacetophenone with bromine or iodine (DMSO , Δ , 0.5 h) represents a one-step synthesis of the corresponding flavones and 2-styrylchromones dihalogenated in the benzene ring, which is activated by the hydroxy group at the 5-position; 3-halochromones are not formed under these conditions.⁹¹

Data on the synthesis of 3-iodoflavones (which hold much promise as intermediates in the synthesis of diflavonoids) and 3-fluoroflavones are quite scarce. Unlike chromone **1a**, flavone **1b** is smoothly lithiated at the 3-position on treatment with lithium diisopropylamide (THF , -78°C), which makes it possible to prepare 3-iodoflavone **40** by treating 3-lithioflavone with iodine.⁹²



Recently, the first and still the only one rather general method for the synthesis of 3-iodoflavones **41**, 3-iodothioflavones **42** and 3-iodo-2-(methyl)thiochromones, has been developed.⁹³ The method consists of the treatment of flavones, thioflavones and thiochromones with the $\text{Ce}(\text{NH}_4)(\text{NO}_3)_5$ – I_2 system in anhydrous acetonitrile at 55–60 °C. The yields of 3-iodoflavones **41** vary over broad limits (24%–80%) and reach a maximum (71%–80%) when an electron-donating group occurs at the 4'-position. Thioflavones and 2-(methyl)thiochromones are iodinated under the same conditions almost quantitatively (95%–98%). These results are in good agreement with the mechanism of electrophilic substitution at C(3) involving I^+ .

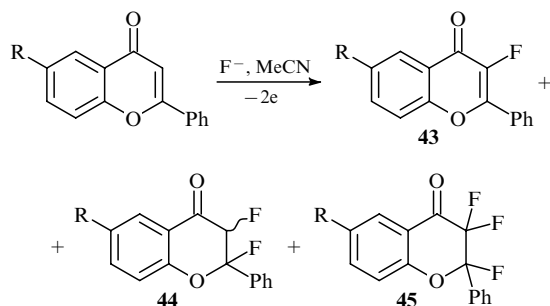


41: X = O: $\text{R}^1 = \text{H}, 4\text{-MeO}, 4\text{-BnO}, 4\text{-Cl}, 2\text{-MeO}$;

$\text{R}^2 = \text{H}, 6\text{-MeO}, 7\text{-MeO}, 5,7\text{-(MeO)}_2$;

42: X = S: $\text{R}^1 = \text{H}$; $\text{R}^2 = \text{H}, 6\text{-Me}$.

3-Fluoroflavone and its 6-substituted derivatives were prepared from appropriate flavones by electrochemical fluorination using the $\text{Et}_4\text{NF} \cdot 4 \text{HF}$ or $\text{Et}_3\text{N} \cdot 3 \text{HF}$ salts in acetonitrile as the source of fluoride anions.^{94,95} Anodic fluorination of flavones affords mono- (**43**), di- (**44**) and tri- (**45**) fluoro derivatives, whose ratio depends on the type of salt used and the temperature of electrolysis. 3-Fluoroflavones **43** are formed upon dehydrofluorination of compounds **44** under the action of triethylamine, while trifluoro derivatives **45** are the products of further fluorination of flavones **43**.

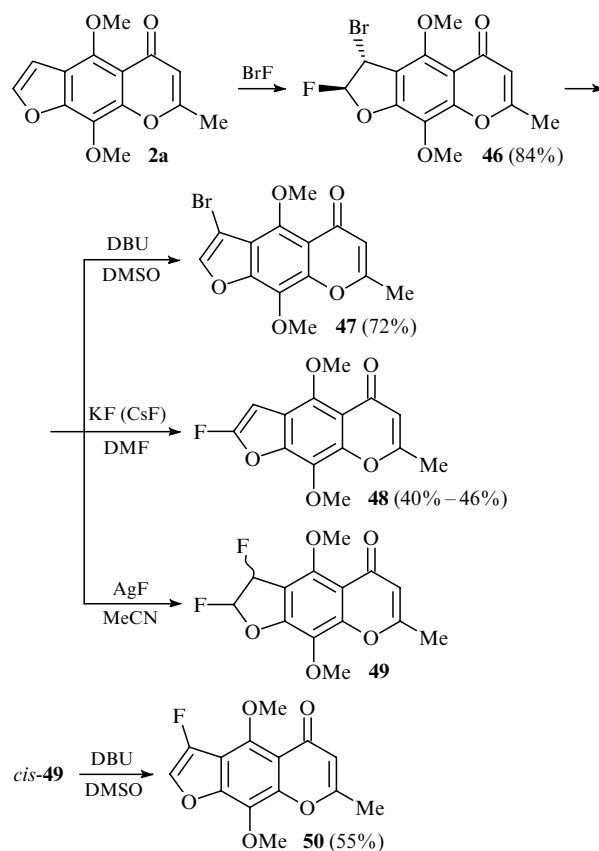


$\text{R} = \text{H}, \text{Me}, \text{Cl}$.

The yields of 3-fluoroflavones **43** vary over a broad range (25%–63%). Nevertheless, due to high regioselectivity, mild reaction conditions and the absence of toxic reagents, which are normally employed in the chemical fluorination, this method is an efficient tool for the synthesis of various fluorine-containing heterocycles.⁹⁵ By anodic fluorination of thioflavone under similar conditions, 3-fluorothioflavone (22%) and 2,3,3-trifluorothioflavanone (42%) have been synthesised.⁹⁶

The synthesis of 3-bromo- and 2- and 3-fluorokhellins from khellin **2a** and BrF has been reported.⁹⁷ The protocol includes the formation of *trans*-3-bromo-2-fluoro-2,3-dihydrokhellin **46** in a high yield. On treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in DMSO, compound **46** is smoothly converted into 3-bromokhellin **47**. The reaction of **46** with KF or CsF gives 2-fluorokhellin **48**, and the reaction with AgF in acetonitrile affords a mixture of *cis*- and *trans*-2,3-difluoro-2,3-dihydro-

khellins **49** (51% and 36%, respectively). When the *cis*-isomer is treated with 1,5-diazabicyclo[5.4.0]undec-5-ene in DMSO, 3-fluorokhellin **50** is formed.

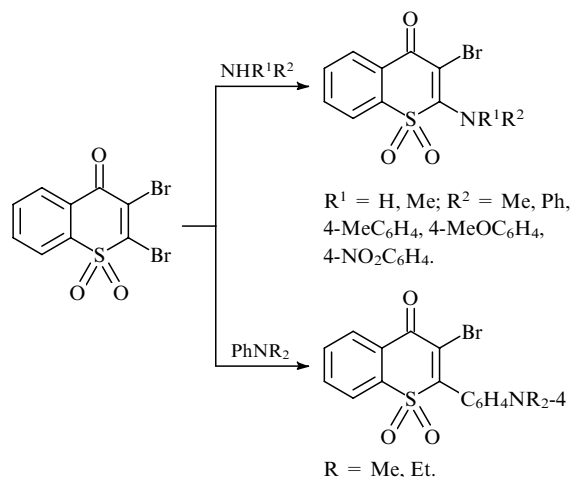


III. Chemical properties of halochromones

1. Reactions of 2-halochromones

As regards the ability of the halogen atom to act as a leaving group, 2- and 3-halochromones markedly surpass chromones halogenated at the benzene ring (except for 5,6,7,8-tetrafluorochromones in which the fluorine atom located in the *para*-position relative to the carbonyl group is susceptible to nucleophilic substitution¹⁸). The halogen atom situated in the β -position with respect to the carbonyl group is the most active; therefore, 2-halochromones surpass 3-halochromones and are similar to acid halides in reactivity.

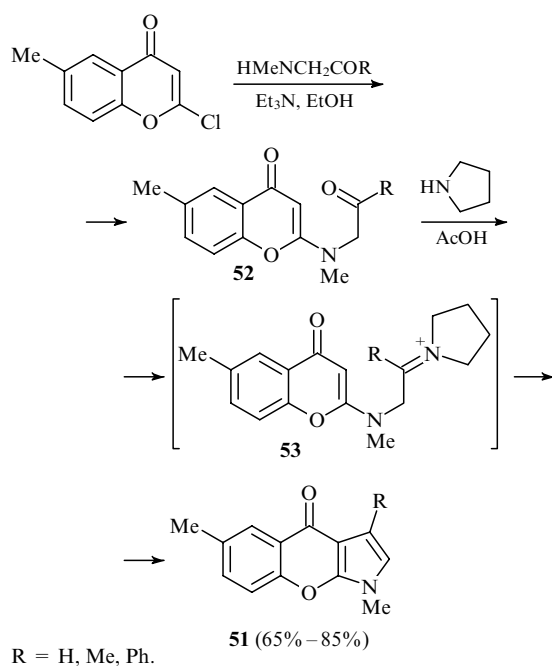
When 2,3-dibromothiochromone 1,1-dioxide is made to react with primary and secondary aliphatic and aromatic amines,⁹⁸ only one bromine atom is replaced, namely, that located at the



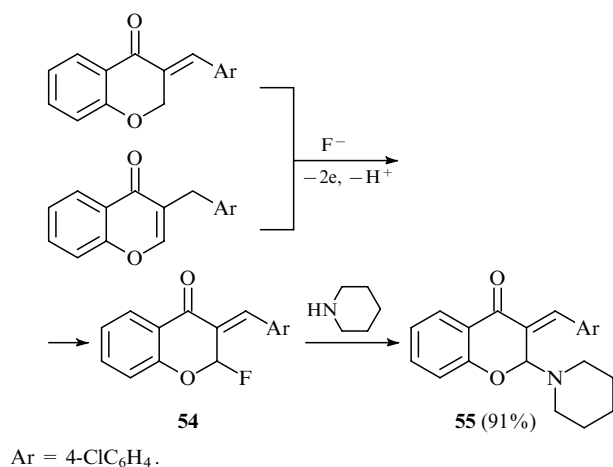
2-position. Tertiary aromatic amines behave in this reaction as C-nucleophiles.⁹⁸

2-Chlorochromones are readily hydrolysed to 4-hydroxycoumarins when treated with water in the presence of acids or bases,²² while 2-chloro-3-hydroxychromone reacts with methylamine, aniline or secondary amines yielding the corresponding 2-amino-3-hydroxychromones (yields 40%–50%).⁹⁹

Recently, chromeno[2,3-*b*]pyrrol-4(1*H*)-ones **51**, analogues of natural products useful for pharmacology, have been prepared from 2-chloro-6-methylchromone and α -aminocarbonyl compounds (as acetals, ketals or hydrochlorides).²⁸ The reaction follows the A_N-E mechanism proceeding through replacement of the chlorine atom by nitrogen giving rise to 2-aminochromone derivatives **52**, which cyclise on heating in a pyrrolidine–acetic acid mixture (1:1). Presumably,²⁸ pyrrolidine activates the carbonyl group through the formation of iminium salt **53** (in the presence of other acids or bases, this reaction does not occur).



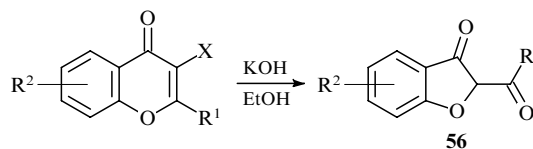
The anodic fluorination of (*E*)-3-(4-chlorobenzylidene)-2,3-dihydrochroman-4-one or isomeric 3-(4-chlorobenzyl)chromone yields the same product — (*E*)-3-(4-chlorobenzylidene)-2-fluoro-2,3-dihydrochroman-4-one (**54**). On treatment with piperidine in acetonitrile at ~20 °C, compound **54** is converted into 3-(4-chlorobenzylidene)-2-piperidino-2,3-dihydrochroman-4-one (**55**).¹⁰⁰



2. Reactions of 3-halochromones

3-Halochromones contain a double bond with geminal arrangement of the carbonyl group and the halogen atom; thus, they can be regarded as geminally activated haloalkenes, which are highly reactive and are widely used in the synthesis of heterocycles and analogues of natural compounds.¹⁰¹ The reactions of nucleophilic reagents with 3-halochromones containing two good leaving groups (the halogen atom at the α carbon atom and the phenolic fragment at the β carbon atom) are more diverse than reactions with haloalkenes. Indeed, haloalkenes react with *N*-nucleophiles along three major pathways including the formation of aziridines and aminoalkenes with a vicinal or geminal (*ipso*-substitution) activating group.¹⁰¹ In the case of 3-halochromones, apart from these pathways, reactions associated with opening and transformation of the γ -pyrone ring can also take place. Note in addition that, whereas the reaction pathway with haloalkenes is governed by the nature of the activating group, in the case of 3-halochromones, the most important factor is the type of the nucleophilic species, together with the size and the electronic properties of the 2-substituent.

Among 3-halochromones, 3-halo-2-hetaryl- and their heterocyclic analogues are least reactive, which is due to the presence of the (het)aryl substituent at the 2-position. For example, the most typical reaction of 3-halo-2-hetaryl- is contraction of the γ -pyrone ring on refluxing with an ethanol solution of KOH to give compounds **56**.

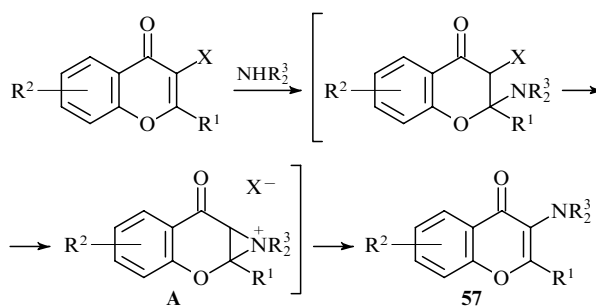


$R^1 = Ar, Het, CH=CHAr; R^2 = H, Me, Cl; X = Cl, Br.$

This ring transformation has been repeatedly used to confirm the structures of 3-bromo-2-hetaryl-,⁸² 3-halo-2-hetaryl-⁸³ and 3-halo-2-styrylchromones.⁸⁴ However, in the case of 3-halochromones devoid of substituent at the 2-position, ring transformation occurs only on treatment with amines (see below). Worthy of note is also the possibility of replacement of the chlorine atom in 3-chloro-2-hetaryl- by a cyano group in the presence of copper(I) cyanide,^{57, 102} which cannot be accomplished for other halochromones.

a. Reactions with N- and S-nucleophiles

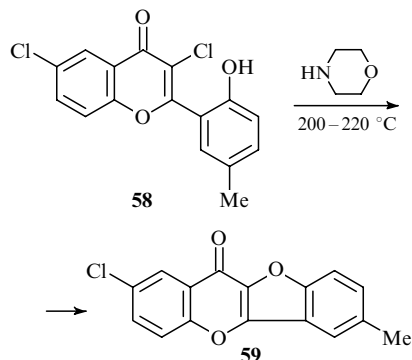
A very important reaction of 3-halochromones is its amination by secondary cyclic amines (pyrrolidine, piperidine, morpholine and *N*-methylpiperazine), which results in the corresponding 3-aminochromones **57**.^{37, 46, 47, 70, 103, 104} Presumably, the *ipso*-replacement of the halogen atom observed in this case follows the 1,4-addition mechanism involving the formation of the aziridinium intermediate **A**, whose subsequent opening gives an amino group at the C(3) atom.^{37, 105, 106}



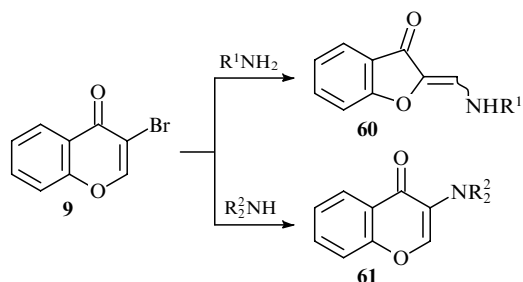
$R^1 = H, Me, Ar; R^2 = H, Me, Cl; X = Cl, Br;$

$NHR_2^3 = HN(CH_2)_Z (Z = CH_2, O, NMe), HN(CH_2)_4.$

The presence of a substituent at the 2-position of the chromone system hampers the reaction; amination of 3-haloflavones is carried out under rather drastic conditions. 3-Bromo derivatives are more reactive than analogous 3-chloro derivatives. 3-Bromoflavone is converted into amino derivatives **57** at $\sim 100^\circ\text{C}$ in 60%–80% yields (6–8 h),⁷⁰ while 3-chloroflavone enters into the reaction with morpholine or piperidine only on heating in *N*-methylpyrrolidone in a sealed tube ($200\text{--}220^\circ\text{C}$, 72–80 h) and the yield does not exceed 30%–44%. Flavone **58** cyclises under these conditions to form tetracyclic derivative **59**.¹⁰⁴

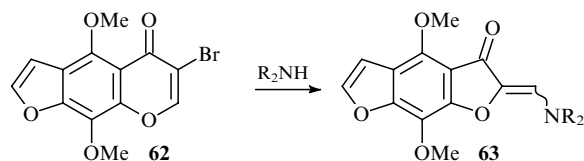


3-Chlorochromones,^{37, 103} 3-bromo-2-methylchromone⁴⁶ and 3-bromoflavone⁷⁰ are aminated on heating without a solvent; however, an attempt to use these conditions for amination of 3-bromochromone (**9**) resulted in a complex mixture of products.¹⁰⁶ A study of amination of 3-halochromones devoid of substituents at C(2), which is the site of the initial nucleophilic attack, has shown that the reaction of 3-bromochromone (**9**) with primary amines in acetonitrile in the presence of K_2CO_3 (added for neutralisation of HBr evolved during the reaction) is accompanied by contraction of the γ -pyrone ring giving benzofuran (coumarone) derivatives **60**. The reaction with secondary amines under the same conditions gives the expected 3-aminochromones **61**.¹⁰⁶ The synthesis of compounds **60** proceeds *via* opening of the pyrone ring induced by the attack by the amine on the C(2) atom followed by replacement of the bromine atom under the action of the phenoxide anion (tautomerism and double bond configuration have not been discussed in the study cited¹⁰⁶).



$\text{R}^1 = \text{Bu}, \text{Bn}, \text{cyclo-C}_6\text{H}_{11}$; $\text{R}_2\text{NH} = \text{HN(CH}_2)_4\text{O}, \text{HN(CH}_2)_3\text{CH}_3$.

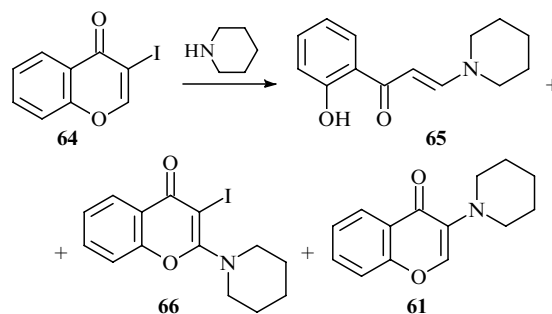
Note that 6-bromonorkhellin **62** reacts with primary and secondary amines with contraction of the pyrone ring to give furocoumarone derivatives **63**.¹⁰⁶



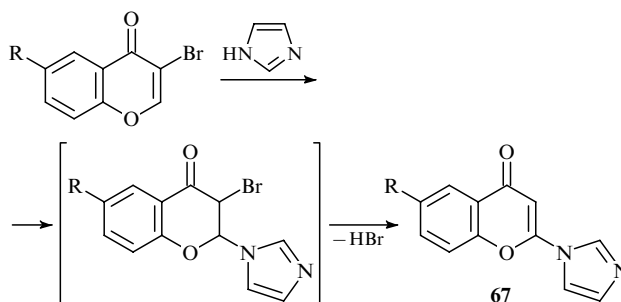
$\text{R}_2\text{NH} = \text{BuNH}_2, \text{cyclo-C}_6\text{H}_{11}\text{NH}_2, \text{HN(CH}_2)_4\text{O}, \text{HN(CH}_2)_3\text{CH}_3$.

Recently, it was shown¹⁰⁷ that replacement of acetonitrile by DMF changes the reaction pathway between secondary cyclic amines and 3-halochromones unsubstituted at the 2-position. Instead of 3-aminochromones **61**, the reaction affords benzofuranones **60** (yields 72%–96%), *i.e.*, the reaction occurs in the same way as that with primary amines in MeCN.

Of 3-halochromones, 3-iodochromone (**64**) is the most reactive. For reactions of halochromones with imidazole, it was shown that on replacement of 3-iodochromone by 3-bromo- or 3-chlorochromone, the reaction rate and the product yield substantially decrease.¹⁰⁸ The reaction of 3-iodochromone with piperidine has been studied in detail.¹⁰⁷ The reaction carried out in MeCN in the presence of K_2CO_3 was found to yield aminovinyl ketone **65** (63%) and 3-iodo-2-piperidinochromone (**66**) (4%). In DMF in the absence of K_2CO_3 , a mixture consisting of compounds **65** (51%), **66** (11%) and 3-piperidinochromone (**61**, $\text{NR}_2^2 = \text{NC}_5\text{H}_{10}$) (13%) is obtained. The diversity of reaction products is explained by a variety of transformations of the Michael adduct formed initially; in particular, iodine elimination with simultaneous ring opening affords compound **65**, iodination followed by elimination of HI gives chromone **66**, and intramolecular replacement of iodine *via* the aziridinium cation leads to chromone **61**. When 3-chloro- or 3-bromochromone is introduced in this reaction, products of types **65** and **66** are not formed.¹⁰⁷



The reaction of 3-bromo- and 3-bromo-6-chlorochromones with excess imidazole in the presence of its silver salt (80°C , 0.5 h) proceeds by Michael addition followed by dehydrobromination and results in 2-imidazolylchromones **67**.¹⁰⁸ Due to the electron-withdrawing nature of the imidazole ring, the acidity of the H(2) atom increases, and the formation of the aziridinium intermediate becomes impossible due to the reduced nucleophilicity of the imidazole nitrogen; apparently, this contributes to the change in the reaction route.

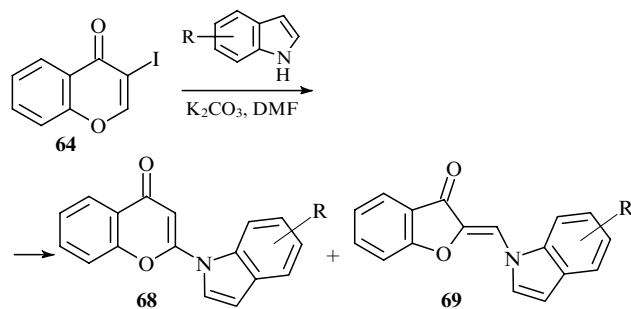


$\text{R} = \text{H}, \text{Cl}$.

3-Bromothiochromones react with imidazole or 2-alkyl-imidazoles giving rise to 2-imidazolylthiochromones and react with secondary amines (piperidine, morpholine and methylethylamine) to give 3-aminothiochromones, *i.e.*, 3-bromochromones and 3-bromothiochromones are equally reactive towards imidazoles and secondary amines.¹⁰⁹

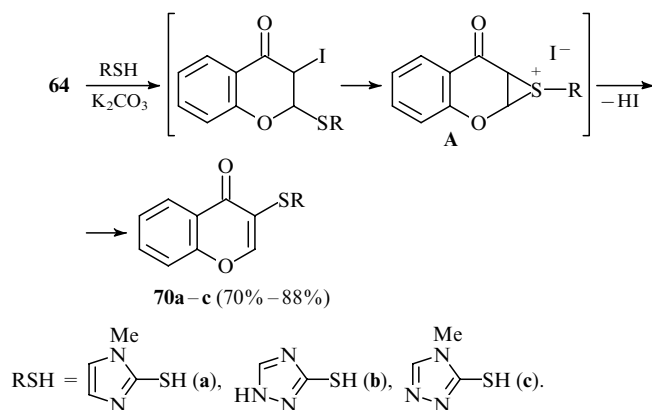
2-(*N*-Azolyl)chromones are prepared by heating 3-iodochromone (**64**) with azoles (imidazole, pyrazole, pyrrole, 1,2,4-triazole, benzimidazole, indazole) in DMF in the presence of K_2CO_3 (80°C , 56%–89%).¹¹⁰ The reaction of 3-iodochromone (**64**)

with indole carried out under the same conditions leads to a mixture of approximately equal amounts of 2-(1-indolyl)chromone (**68**) and 2-(1-indolyl)methylene-3(2*H*)-benzofuranone (**69**). Substituents in the indole system have a substantial influence on the **68** to **69** product ratio. In the presence of electron-donating groups (Me, MeO), the product ratio changes in favour of benzofuranones **69**, whereas electron-withdrawing substituents (Cl, NO₂) promote the proportion of chromones **68**, because in this case, the indole nitrogen atom is depleted of electrons.¹¹⁰

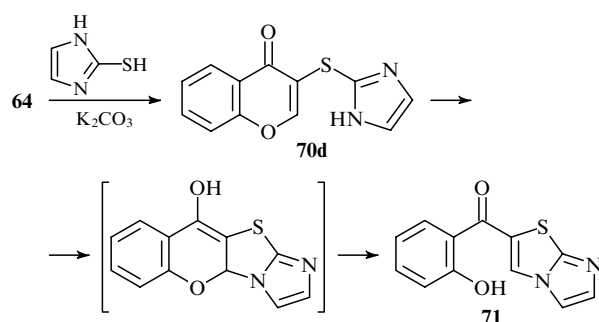


R = H, 3-Me, 5-Me, 5-MeO, 5-Cl, 5-NO₂, 6-NO₂.

The reactions of chromone **64** with 1-methyl-2-sulfanylimidazole, 3-sulfanyl-1,2,4-triazole or 4-methyl-3-sulfanyl-4*H*-1,2,4-triazole (DMF, K₂CO₃, ~20 °C) proceed differently from the reactions with azoles. In this case, 3-azolylsulfanylchromones **70** are formed instead of 2-substituted chromones or benzofuranones.¹¹¹ An analogous compound has also been obtained in the reaction of chromone **64** with 2-thiocytosine.¹¹² The substitution of a sulfur atom for iodine involves the formation of a three-membered episulfonium cation **A** (similarly to the substitution of nitrogen for halogen). The subsequent opening of the three-membered ring furnishes chromones **70a–c**.

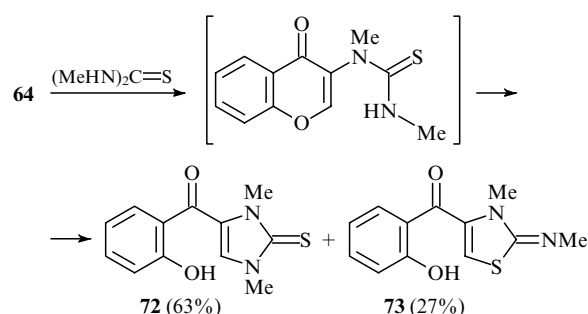


Unexpectedly, the reaction of 3-iodochromone (**64**) with 2-sulfanylimidazole does not stop after the formation of chromone **70d** but proceeds further as an intramolecular ring transformation giving a mixture of products **70d** and **71** in 18% and 62% yields, respectively.¹¹¹



2-Sulfanyl- and 5-methoxy-2-sulfanylbenzimidazoles react with chromone **64** to yield compounds of type **71** as the major products, whereas 5-nitro-2-sulfanylbenzimidazole gives only the corresponding chromone **70**.¹¹¹ When K₂CO₃ is replaced by Bu₄NCl, the reactions with 2-sulfanylimidazole and 2-sulfanylbenzimidazole stop after the formation of 3-substituted chromones **70**.¹¹³

Finally, the reaction of *N,N'*-dimethylthiourea with 3-iodochromone (**64**) produces a mixture of imidazoline **72** and thiazoline **73**; thiourea acts as an N-nucleophile in the first step of the reaction and as either an N- or S-nucleophile in the final step.¹¹⁴

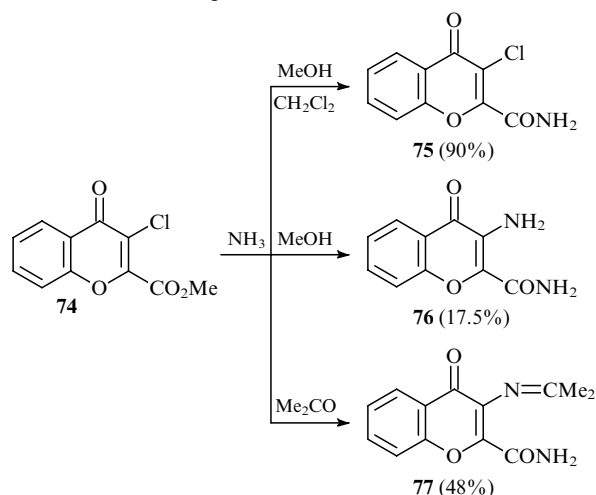


Thus, the transformations of 3-bromo- and 3-iodochromones induced by N- and S-nucleophiles demonstrate the broad synthetic potential of these compounds, the high reactivity of which ensures the existence of several pathways for particular reactions. On the one hand, this diversity of properties complicates prediction of the structures of the final products but, on the other hand, this makes 3-halochromones attractive objects for further investigations.

It should be noted that data on the reactions of 3-halochromones with bisnucleophiles (even with simple ones such as hydroxylamine or hydrazine) are very scarce.

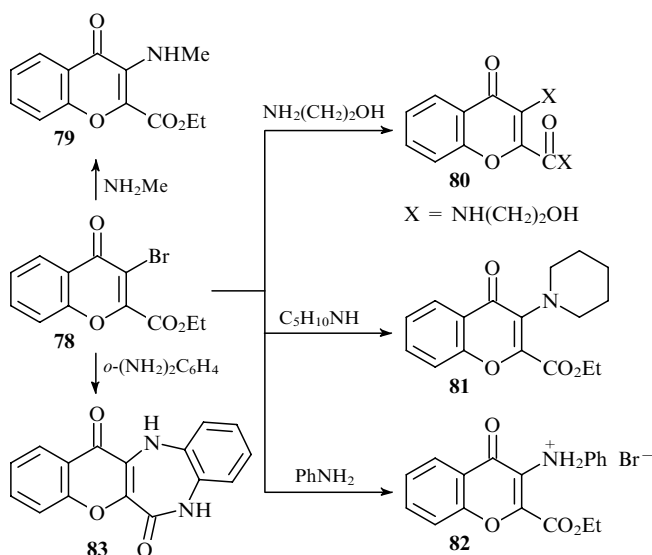
The reaction of 3-bromochromone (**9**) with hydroxylamine has been reported to give the oxime of 3-hydroxy-1-benzofuran-2-carbaldehyde, the structure of which was confirmed by X-ray diffraction data; however, neither the synthetic procedure nor the spectroscopic or physicochemical characteristics were described.¹⁰⁶

Some data on the reactions of alkyl 3-chloro- and 3-bromochromone-2-carboxylates with ammonia and amines have been reported.^{53, 54, 115} Depending on the reaction conditions, methyl ester **74** reacts with ammonia to give products **75–77**; this implies that the reaction first involves the ester group, and then the chlorine atom is replaced by the amino group, which is able to react with acetone to yield Schiff's base **77**.⁵⁴ The yield of amide **76** increases to 66% when the ethyl ester is used as the starting compound instead of the methyl ester, which is due to different solubilities of these compounds in methanol.⁵³



Attempts to replace chlorine in 3-chlorochromone-2-carboxylate by an amino group on treatment with ammonia have failed. In 3-chlorochromone-2-carbonitrile, the group to be replaced is the cyano group; this gives 2-amino-3-chlorochromone, which is hydrolysed in an acid medium to 3-chloro-4-hydroxycoumarin.⁵³ On the basis of these data, it was concluded⁵³ that the reactivity of 2-substituted 3-chlorochromones decreases in the sequence 2-Me < 2-CO₂Et < 2-CN < 2-CO₂H.

The reactions of ethyl ester **78** with methylamine, 2-aminoethanol, piperidine, aniline and *o*-phenylenediamine proceed with replacement of the bromine atom and with retention of the pyrone ring, yielding products **79–83**.^{54, 115}

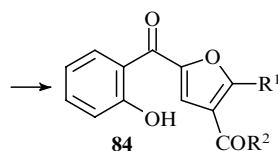
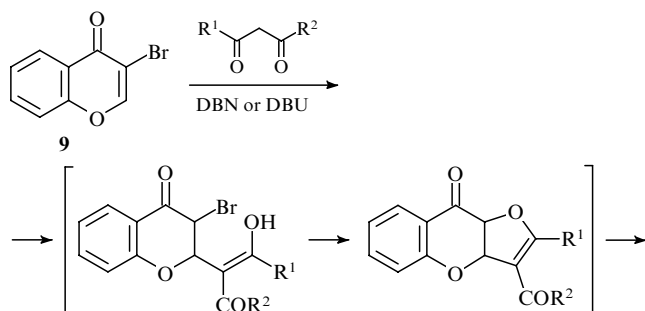


Ester **78** reacts with ammonia giving rise to amide **76** (yield 74%). Due to steric hindrance in the ester group, *tert*-butyl 3-bromochromone-2-carboxylate reacts only at the C(3) atom with replacement of bromine yielding *tert*-butyl 3-aminochromone-2-carboxylate (yield 55%).¹¹⁵

Thus, neither primary nor secondary amines react with 3-halochromone-2-carboxylate with contraction of the pyrone ring to form the furan ring. When secondary amines react with 3-bromo-2-methylchromone and 3-haloflavones, the pyrone ring is also retained.

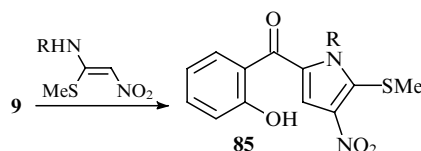
b. Reactions with C-nucleophiles

The reactions of bromochromone (**9**) with C-nucleophiles are highly significant, in particular, for the preparation of pharmaceutically valuable products. Thus the reactions of chromone **9** with β -diketones and β -ketoesters {1,5-diazabicyclo[4.3.0]non-5-ene (DBN) or DBU, CHCl₃, ~20 °C, 0.5–1 h} lead to highly functionalised furans **84**.¹¹⁶ Completion of this reaction requires two equivalents of a base, while replacement of DBN or DBU by Et₃N results in the recovery of the starting compounds. The mechanism of this transformation involves 1,4-addition of the β -dicarbonyl compound to chromone **9** followed by intramolecular *O*-alkylation and opening of the pyrone ring to give 2-salicyloylfurans **84**.¹¹⁶



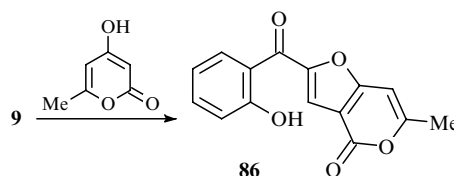
$R^1 = R^2 = \text{Me}$; $R^2 = \text{OEt}$; $R^1 = \text{Me, Ph, CH}_2\text{SPh, CH}_2\text{CO}_2\text{Et}$;
 $R^1 - R^2 = \text{CH}_2\text{CMe}_2\text{CH}_2$.

The reaction of 3-bromochromone (**9**) with nitro enamines resulting in 2-salicyloylpyrroles **85**¹¹⁷ is carried out in the MeCN–K₂CO₃ system (previously, this system was used in reactions with amines¹⁰⁶).

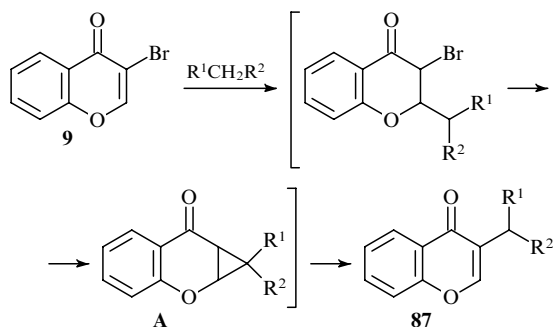


$R = \text{Me, Ph}$.

Heating of chromone **9** with 4-hydroxy-6-methyl-2*H*-pyran-2-one in pyridine for 4–5 h gives furopyrone **86**.¹¹⁷

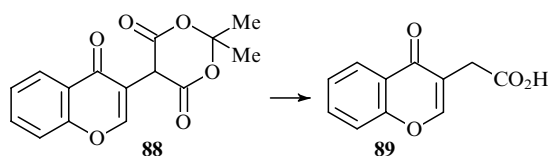


Unlike β -diketones and β -ketoesters, derivatives of malonic acid, more susceptible for C-alkylation, react with 3-bromochromone (DBU, MeCN, 20 °C) *via* the formation of the cyclopropane intermediate **A**. Owing to the anchimeric assistance from the neighbouring oxygen atom, the cyclopropane ring in compound **A** is easily cleaved to give 3-substituted chromones **87**.



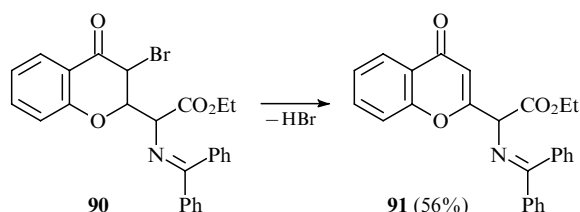
$R^1 = R^2 = \text{CO}_2\text{Et}$; $R^1 = \text{CO}_2\text{Et}$, $R^2 = \text{CN}$;
 $R^1 = \text{CO}_2\text{Bu}^t$, $R^2 = \text{CN}$; $R^1 = \text{CN}$, $R^2 = \text{SO}_2\text{Me}$.

The reaction of 3-bromochromone (**9**) with Meldrum's acid affords chromone **88**, which is converted into acid **89**.¹¹⁸

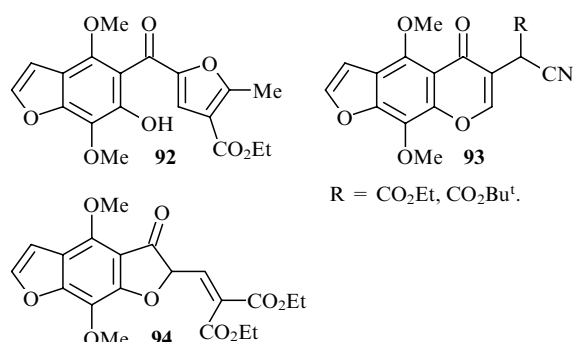


3-Bromo-2-methylchromone (**19b**) reacts with diethyl malonate in the presence of Et₃N in acetone being converted into diethyl (2-methylchromon-3-yl)malonate.⁴⁵ However, the reaction pathway between 3-bromochromone (**9**) and ethyl *N*-(diphenylmethylidene)glycinate changes (apparently, for steric reasons). In this case, elimination of hydrogen bromide from the

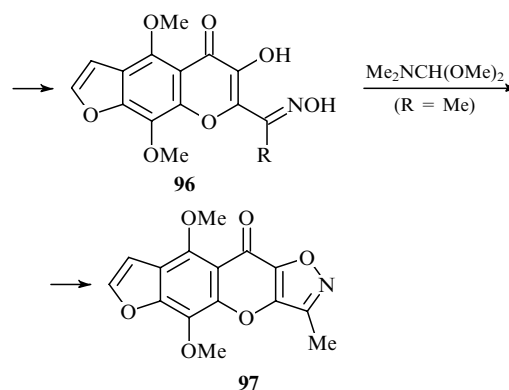
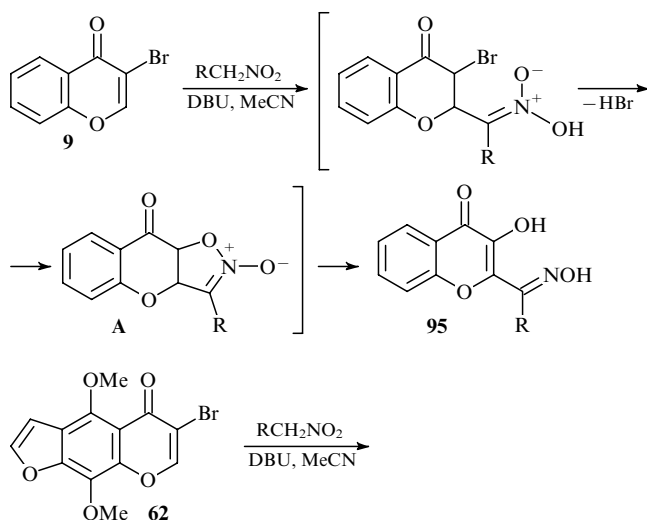
protonated Michael adduct **90** results in the formation of 2-substituted chromone **91**.¹¹⁸



Notably, as in the reactions with amines, 6-bromonorkhellin **62** shows a specific behaviour in reactions with C-nucleophiles; in particular, it reacts with ethyl acetoacetate and ethyl *tert*-butyl cyanoacetates in the same way as 3-bromochromone (**9**), *i.e.*, to give furan **92** and 6-substituted norkhellins **93**, whereas the reaction with diethyl malonate produces furocoumarone derivative **94**.¹¹⁸ Thus, the pyrone fragment of compound **62** is also prone to contraction in reactions with C-nucleophiles.¹⁰⁶



In reactions with the ambident nitronate anions generated from the corresponding nitro compounds, 3-bromochromone (**9**) and 6-bromonorkhellin (**62**) behave in the same way to give chromones **95** (yields 49%–74%) and **96** (yields 39%–90%) containing the oxime function at 2(7)-positions and the hydroxy group instead of the bromine atom.¹¹⁹ As in the case of β -diketones and β -ketoesters, the reactions of nitronate anions with chromones start with the Michael addition, which is accompanied by intramolecular *O*-alkylation and gives intermediate **A**. Subsequently, under the action of the *N*-oxide fragment, the isoxazole (rather than the pyrone) ring in the intermediate **A** is opened, which gives oximes **95** and **96**.

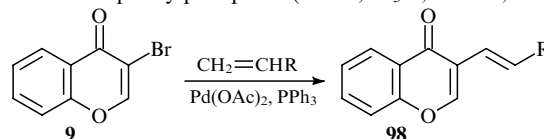


R = Me, Et, CO₂Me, Ph.

The khellin derivative **96** (R = Me) cyclises on heating with dimethylformamide dimethyl acetal at 100 °C for 0.5 h being thus converted into 5,9-dimethoxy-3-methyl-10*H*-furo[3',2':6,7]chromeno[2,3-*d*]isoxazol-10-one (**97**). Similar products were also obtained under the same conditions from chromones **95** (yields 49%–83%).¹¹⁹

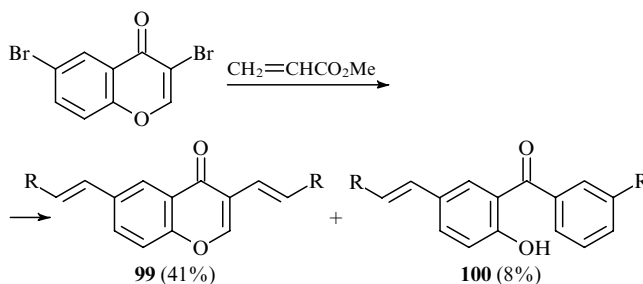
c. Cross-coupling and cycloaddition reactions

In recent years, studies dealing with the use of 3-halochromones in homo- and cross-coupling reactions catalysed by transition metal complexes have been appearing more and more often. These reactions open up a new route to the synthesis of complex molecules incorporating a chromone fragment. For example, derivatives **98**, otherwise difficult to prepare, have been synthesised by vinylation of 3-bromochromone (**9**) with methyl acrylate or styrene in the presence of catalytic amounts of palladium acetate and triphenylphosphine (DMF, Et₃N, 120 °C, 6 h).¹²⁰



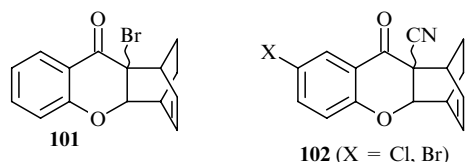
R = CO₂Me, Ph.

Cross-coupling of 3,6-dibromochromone with methyl acrylate involves both bromine atoms and affords a mixture of products — compounds **99** and **100**. The formation of substituted benzophenone **100** is a result of cycloaddition of methyl acrylate to chromone **99** followed by decarboxylation of the adduct, opening of the pyrone ring and dehydrogenation induced by palladium.¹²⁰

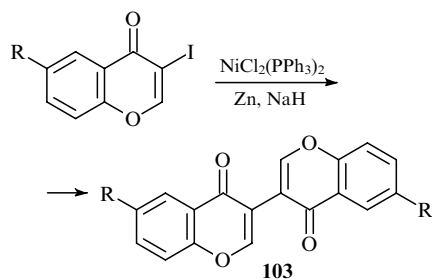


R = CO₂Me.

Chromone **9** proved to be a poor dienophile in the Diels–Alder reaction. Only with 1,3-cyclohexadiene and under rigorous conditions (300 °C, 120 h), does it form adduct **101** with a low stereoselectivity (the isomer ratio is equal to 2:1, yield < 16%). Chromone-3-carbonitrile and especially its 6-chloro- and 6-bromo-substituted derivatives proved to be more reactive. Compounds **102** were synthesised in 44%–50% yield and with 93% stereoselectivity.¹²¹

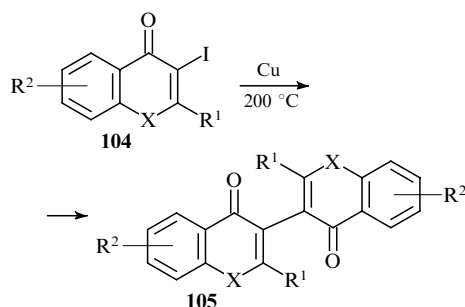


Homo-coupling of 3-iodochromones in the $\text{NiCl}_2(\text{PPh}_3)_2$ – PPh_3 – Zn – NaH – PhMe system occurs almost quantitatively giving rise to bischromones **103**, which are of interest for the synthesis of natural biflavonoids.^{122, 123}



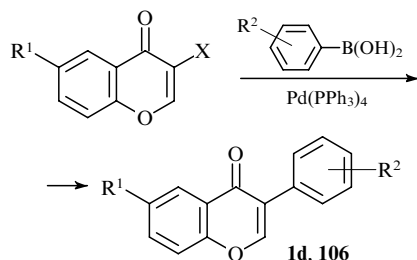
R = H, Me, MeO.

In order to develop a method for the synthesis of natural biflavonoids, homo-coupling of 3-iodo derivatives of flavones, thioflavones and thiochromones **104** under the Ullmann reaction conditions has been studied.¹²⁴ It was shown that heating of these compounds with copper powder at 200–210 °C under argon leads to products **105**, the yields of biflavones and bithioflavones being 71%–86% and the yields of bithiochromones being 31%–33%.



X = O: R¹ = Ph, 4-MeOC₆H₄; R² = H, 7-MeO;
X = S: R¹ = Ph, Me; R² = H, 6-Me.

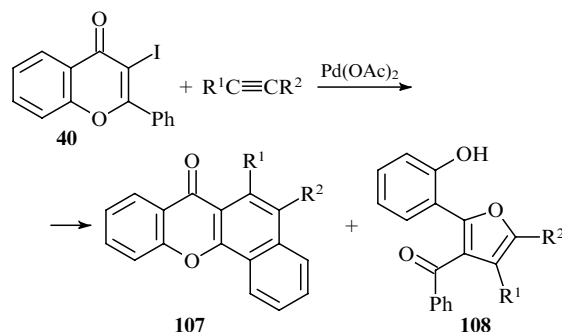
Isoflavone (**1d**) and its derivatives **106**^{125, 126} have been prepared in high yields by cross-coupling of 3-bromo- and 3-iodochromones with arylboronic acids catalysed by tetrakis-(triphenylphosphine)palladium(0) in the presence of Na₂CO₃ (Suzuki reaction).



R¹ = H, MeO, Cl; R² = H, Me, MeO, F, NO₂; X = Br, I.

Annulation of 3-iodoflavone **40** by internal alkynes catalysed by Pd(OAc)₂ in the presence of NaOAc and LiCl yields a mixture of compounds **107** and **108**. In this mixture, the expected benzoxanthenes **107** are the minor products,¹²⁷ while tetrasubstituted furans **108**, resulting from the electrophilic attack on the carbonyl

oxygen atom by the vinylpalladium intermediate followed by pyrone ring opening, are the major products.

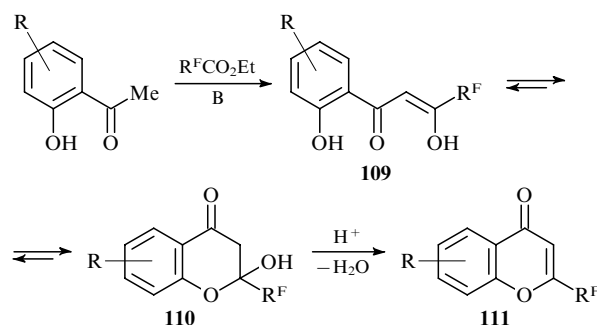


R¹ = R² = Ph; R¹ = Me, R² = Bu^t.

IV. Methods for the synthesis of 2-polyhaloalkyl- and halomethylchromones

1. Synthesis of 2-polyfluoroalkylchromones

The first representatives of 2-trifluoromethylchromones were obtained in 1951 by condensation of substituted 2-hydroxyacetophenones with ethyl trifluoroacetate in the presence of sodium followed by dehydration of the initially formed β-diketones in an acid medium.¹²⁸ It has long been considered¹²⁹ that these diketones have a linear keto-enol structure **109**; however, subsequently, it has been found on the basis of ¹H NMR data^{130, 131} that they exist as cyclic semiketals **110** both in solutions and in crystals. Cyclisation is facilitated by the presence of the electron-withdrawing trifluoromethyl group in the side chain and the hydroxy group in the *ortho*-position of the benzene ring. It was found that open tautomers start to appear in CDCl₃ solutions with an increase in the number of fluorine atoms in the polyfluoroalkyl group.^{132, 133} Indeed, the condensation products of 2-hydroxy- and 2-hydroxy-5-methylacetophenones with H(CF₂)₂CO₂Et in CDCl₃ represent a tautomeric mixture containing the keto-enol and semiketal forms in ~1 : 10 ratio.¹³³ Short-term refluxing of 2-hydroxychromanones **110** in ethanol¹²⁸ or acetic acid¹³⁴ in the presence of concentrated HCl results in 2-polyfluoroalkylchromones **111**.

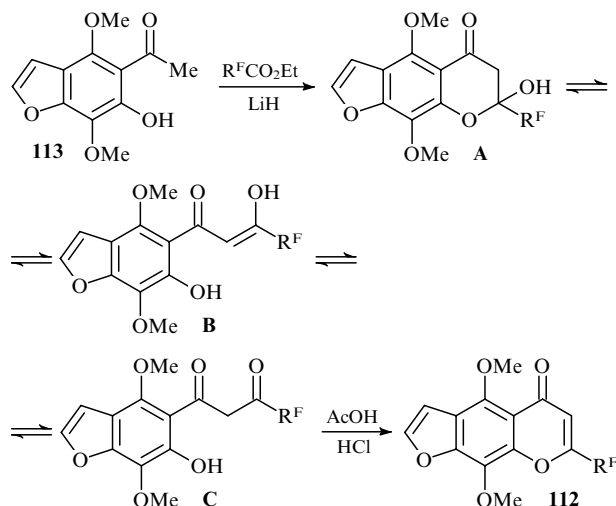


R = H, Me, MeO, Cl, Br;

R^F = CF₂H, CF₃, (CF₂)₂H, C₂F₅, C₃F₇, C₄F₉.

Modification of natural products by replacing an alkyl group by a polyhaloalkyl group has long attracted the attention of researchers, because the electron-withdrawing effect of the halogenated substituent entails electron density redistribution in the molecule and thus changes its reactivity with respect to nucleophilic reagents.¹³⁵ In this connection, of obvious interest is the synthesis of 7-polyfluoroalkylnorkhellins **112**,^{136, 137} which are fluorinated analogues of khellin **2a**, because it opens up the way for the synthesis of a broad range of fluorine-containing heterocyclic derivatives that incorporate the natural benzofuran fragment and are potentially biologically active.

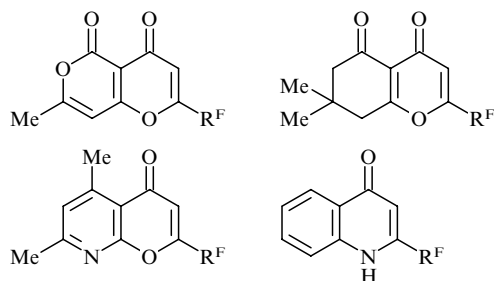
Fluorokhellins **112** were prepared by the reaction of khellinone **113** with $R^F\text{CO}_2\text{Et}$ in the presence of LiH followed by dehydration of the condensation products, which exist as furochromanones **A** in crystals and in $\text{DMSO}-d_6$ solutions. In CDCl_3 , these compounds (except for $R^F = \text{CF}_3$) are mixtures of tautomers **A**–**C**. Irrespective of length of the fluoroalkyl group, cyclic form **A** predominates (50%–78%), while the content of the diketone form **C** usually does not exceed 8%.¹³⁷



$R^F = \text{CF}_2\text{H}, \text{CF}_3, (\text{CF}_2)_2\text{H}, \text{C}_2\text{F}_5, \text{C}_3\text{F}_7, \text{C}_4\text{F}_9$.

The Claisen condensation is the most convenient and efficient method for the synthesis of 2- R^F -chromones as it is based on simple and readily available initial compounds. This reaction can proceed in the presence of sodium¹²⁸ or other condensing reagents such as sodium hydride¹³¹ or lithium hydride.¹³⁴ Ether¹³¹ and THF¹³⁴ are commonly used as solvents. Due to the low solubility of phenolates, derivatives hydroxylated at the benzene ring are synthesised using hexamethylphosphorotriamide¹³⁸ or the Kostanecki–Robinson method. For example, 7-hydroxy-2-trifluoromethylchromone was prepared in 68% yield by heating 2,4-dihydroxyacetophenone with trifluoroacetic anhydride and sodium trifluoroacetate.¹⁴

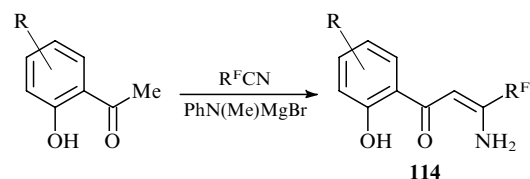
If a heterocyclic or another 2-hydroxyacetophenone derivative such as dehydroacetic acid, 2-acetyldimedone, 3-acetyl-4,6-dimethyl-2-pyridone and 2-aminoacetophenone is used as the methylene component in the condensation with $R^F\text{CO}_2\text{Et}$, the reaction gives chromone, 7-methyl-2-polyfluoroalkylpyrano[4,3-*b*]pyran-4,5-diones,¹³⁹ 7,7-dimethyl-2-polyfluoroalkyl-7,8-dihydro-6*H*-chromene-4,5-diones,¹⁴⁰ 8-aza-2-polyfluoroalkylchromones¹⁴¹ and 2-polyfluoroalkyl-4-pyridones.¹⁴²



$R^F = \text{CF}_2\text{H}, \text{CF}_3, (\text{CF}_2)_2\text{H}$.

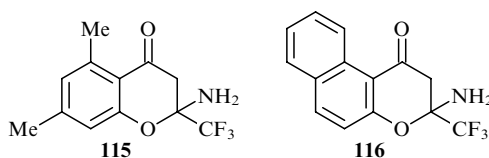
In addition to the Claisen condensation, other methods for the synthesis of 2- R^F -chromones have also been developed. For example, the reaction of 2-hydroxyacetophenones with $R^F\text{CN}$ in the presence of *N*-methylanilinomagnesium bromide affords aminovinyl ketones **114** with geminal arrangement of the amino group and the fluorinated substituent (yields 35%–60%). Unlike diketones **109**, these compounds usually exist in the open form as

Z-isomers having a coplanar *S*-*cis*-conformation stabilised by an intramolecular hydrogen bond.¹⁴³



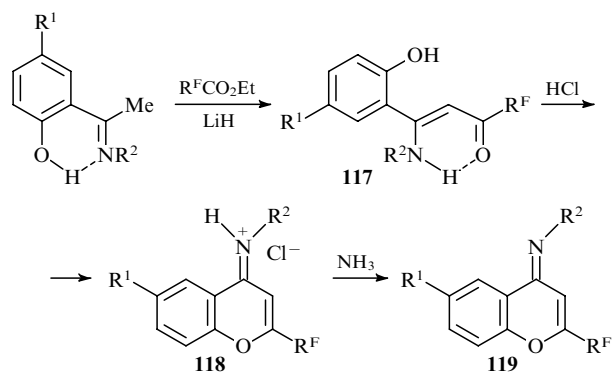
$R = \text{H}, \text{Me}, \text{MeO}, \text{Cl}; R^F = \text{CF}_2\text{H}, \text{CF}_3, (\text{CF}_2)_2\text{H}$.

However, the products of condensation of CF_3CN with sterically hindered 2-hydroxy-4,6-dimethylacetophenone and 1-acetyl-2-naphthol exist predominantly as 2-aminochroman-4-ones **115** and **116**. In these compounds, the aminoenone form is destabilised due to unfavourable interactions between the vinylic hydrogen atom and the *ortho*-substituent in the benzene ring.^{144, 145}



A similar ring–chain isomerism occurs also in the series of aliphatic hydroxyoxoenamines with a *gem*-dialkyl group in the α -position to the carbonyl group.^{146–148} In an acid medium, compounds **114**–**116** are converted almost quantitatively into 2- R^F -chromones **111**.

The condensation of ketimines prepared from 2-hydroxyacetophenones and primary amines with $R^F\text{CO}_2\text{Et}$ in the presence of LiH yields aminovinyl ketones **117** with γ -arrangement of the NHR and R^F groups, which exist only in the open form.^{149, 150} In an ethanol solution of HCl ($\sim 20^\circ\text{C}$, 2 h), these compounds cyclise to 2-polyfluoroalkyl-4*H*-chromene-4-iminium salts **118**, which can be neutralised with ammonia to form 2-polyfluoroalkyl-4*H*-chromene-4-imines **119**.

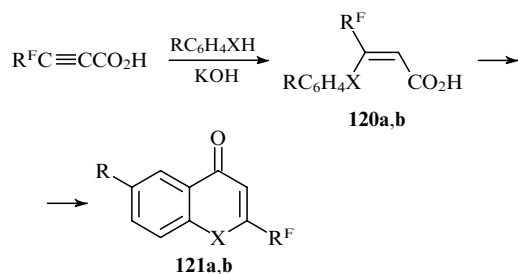


$R^1 = \text{H}, \text{Me}; R^2 = \text{CH}_2\text{Ph}, \text{Pr}^i, (\text{CH}_2)_2\text{OH}; R^F = \text{CF}_3, (\text{CF}_2)_2\text{H}$.

On treatment with aqueous acetic acid ($\sim 20^\circ\text{C}$, 12 h or 80°C , 1 h), compounds **117** and **119** are hydrolysed to chromanones **110**, which can be easily converted into chromones **111**. Chromeneimines **119** are of interest for synthesis by themselves, because they exist in an acid medium as highly reactive iminium cations **118**, which are more reactive than 2- R^F -chromones **111**.¹⁵¹

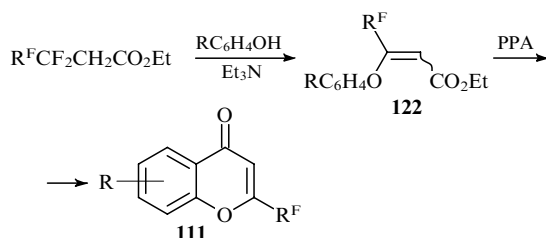
The reactions of polyfluoroalk-2-ynoic acids with a fivefold excess of ArOH and KOH in an aqueous solution are stereospecific and result in (*Z*)- β -polyfluoroalkyl- β -aryloxyacrylic acids **120a**. On treatment with concentrated H_2SO_4 at $\sim 20^\circ\text{C}$, compounds **120a** are converted into 2- R^F -chromones **121a** (yields 51%–76%).¹⁵² Due to the higher nucleophilicity of arenethiols, a similar reaction involving arenethiols can be carried out in aqueous ethanol at a reactant molar ratio of 1 : 1. The resulting arylthioacrylic acids **120b** also have the *Z*-configuration of the

double bond; on successive treatment with PCl_5 and AlCl_3 in benzene at $\sim 20^\circ\text{C}$, they produce 2- R^{F} -thiochromones **121b** (yields 68%–87%).¹⁵²



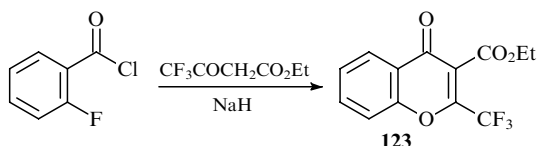
$\text{R}^{\text{F}} = \text{CF}_2\text{H}, \text{CF}_3, (\text{CF}_2)_3\text{H}$; $\text{R} = \text{H}, \text{Me}, \text{MeO}, \text{Cl}$; $\text{X} = \text{O}$ (a), S (b).

A similar approach to the synthesis of 2- R^{F} -chromones has been described in a study¹⁵³ in which ethyl 2,2-dihydropolyfluorocarboxylates were used as the starting substrates. They were made to react with phenols in the presence of Et_3N in MeCN at 60°C , which gave ethers **122**, most often, as mixtures of *Z*- and *E*-isomers. When heated with polyphosphoric acid (PPA) at 170°C , they were converted into chromones **111** in high yields.

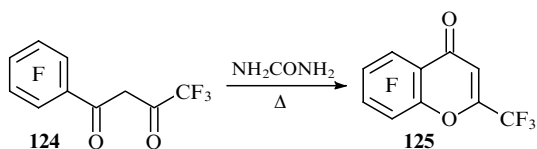


$\text{R}^{\text{F}} = \text{CF}_2\text{Cl}, (\text{CF}_2)_3\text{Cl}, (\text{CF}_2)_5\text{Cl}$; $\text{R} = \text{H}, \text{Me}, \text{Ph}, \text{Cl}, \text{Br}$.

The reaction of *o*-fluorobenzoyl chloride with β -ketoesters in the presence of NaH has been proposed as a method for the synthesis of 2-methylchromone-3-carboxylic acids and their esters;¹⁵⁴ in particular, this reaction proved to be suitable for the preparation of ethyl 2-trifluoromethylchromone-3-carboxylate (**123**).

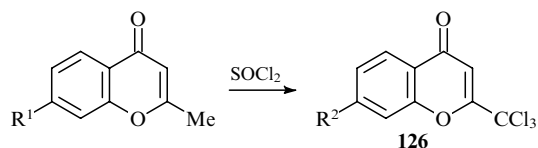


Heating compound **124**, containing an easily replaceable fluorine atom in the *ortho*-position to the carbonyl group, with urea results in 2-trifluoromethyl-5,6,7,8-tetrafluorochromone (**125**), instead of the expected pyrimidin-2(1*H*)-one derivative.¹⁵⁵



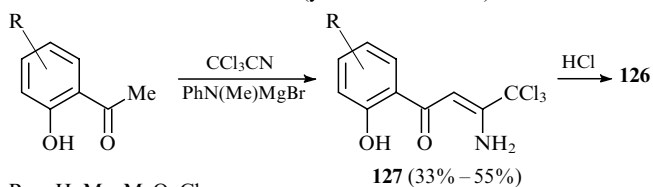
2. Synthesis of 2-trichloromethylchromones and halomethylchromones

Esters of trichloroacetic acid undergo haloform cleavage under the Claisen condensation conditions in the presence of sodium alkoxides giving rise to chloroform¹⁵⁶ and dichlorocarbene.¹⁵⁷ Apparently, this is the reason why the first 2-trichloromethylchromones **126** were obtained only in 1972 by the reaction of 2-methylchromone or 7-hydroxy-2-methylchromone with thionyl chloride proceeding as chlorination of the side methyl group.¹⁵⁸ Later, this method has found no use.



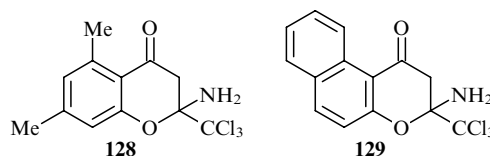
$\text{R}^1 = \text{H}, \text{OH}$; $\text{R}^2 = \text{H}, \text{Cl}$.

A simple and more general method for the synthesis of chromones **126** consists of condensation of 2-hydroxyacetophenones with CCl_3CN in the presence of *N*-methylanilinomagnesium bromide. This reaction affords aminovinyl ketones **127**, which are converted into chromones **126** on treatment with concentrated HCl at $\sim 20^\circ\text{C}$ (yields 77%–96%).^{143, 159}

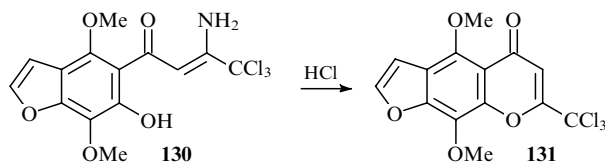


$\text{R} = \text{H}, \text{Me}, \text{MeO}, \text{Cl}$.

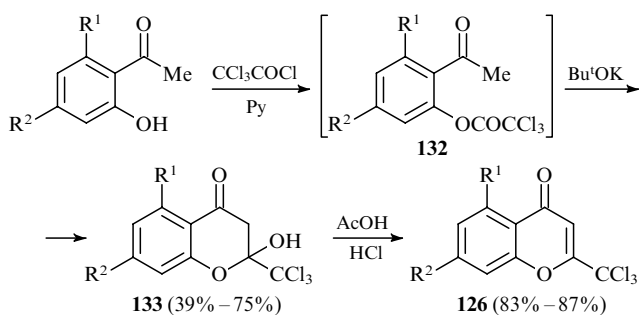
When sterically hindered ketones are used, the aminovinyl ketones formed initially cyclise spontaneously to yield 2-aminochromanones **128** and **129**.^{144, 145}



It is of interest that compound **130** exists only as the open form, despite the presence of the methoxy group in the *ortho*-position with respect to the carbonyl group. Acid hydrolysis of aminovinyl ketone **130**, prepared in 37% yield from 5-acetyl-6-hydroxy-4,7-dimethoxybenzo[*b*]furan (khellinone) and trichloroacetonitrile, gives 7-trichloromethylnorkhellin **131** in a yield of 87% (the overall yield over two steps was 32%).¹³⁶



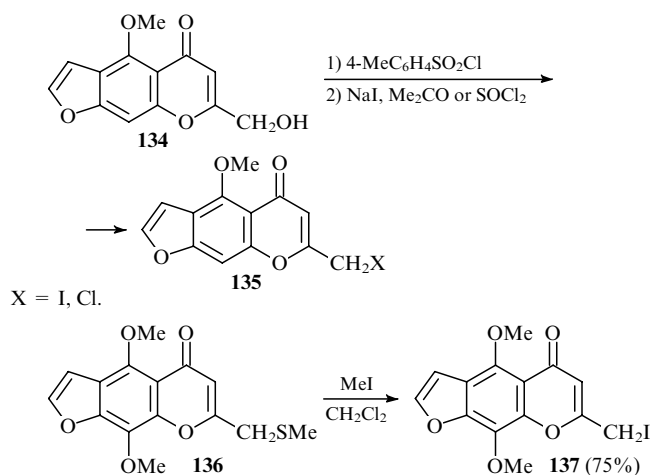
Recently,¹⁶⁰ we proposed a new method for the synthesis of chromones **126**, underlain by the Baker–Venkataraman rearrangement. When trichloroacetates **132** (prepared *in situ* by acylation of 2-hydroxyacetophenones with trichloroacetyl chloride) is treated with potassium *tert*-butoxide in THF at -30°C , 2-hydroxy-2-trichloromethylchroman-4-ones **133** are formed; they represent the cyclic form of the corresponding β -diketones. Refluxing of these compounds in AcOH in the presence of concentrated HCl results in the corresponding chromones. In the synthesis of trichlorokhellin **131** by this procedure, an overall yield of 64% was attained.¹⁶⁰



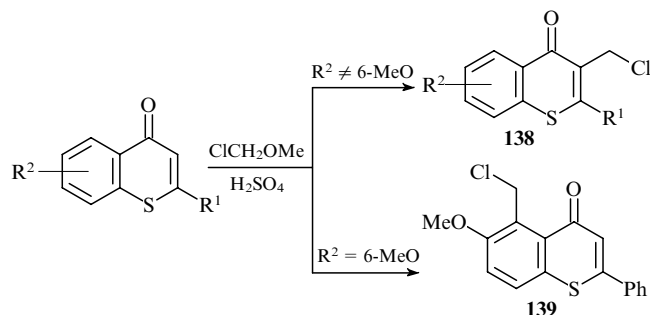
$\text{R}^1 = \text{R}^2 = \text{H}$; $\text{R}^1 = \text{MeO}, \text{R}^2 = \text{H}$; $\text{R}^1 = \text{R}^2 = \text{Me}$.

The Claisen condensation, which proceeds successfully with esters of polyfluorocarboxylic acids that contain ≥ 2 fluorine atoms, proves to be inapplicable to alkyl trichloroacetates or monohaloacetates. In the latter case, this is due to the easy replacement of the halogen atom under the action of nucleophilic species. Therefore, 2-halomethyl chromone derivatives are more difficult to prepare than 2-polyhaloalkylchromones. Only a few examples of synthesis of these compounds have been reported. For example, treatment of 2-ethoxymethyl-7-methoxychromone (obtained by condensation of 2-hydroxy-4-methoxyacetophenone with ethyl ethoxyacetate) with a mixture of HBr and AcOH yields 2-bromomethyl-7-methoxychromone.¹⁶¹ The bromination of 3-benzoyl-2-methylchromone with *N*-bromosuccinimide furnishes 3-benzoyl-2-bromomethylchromone.¹⁶²

A natural furochromone — khellol **134** — was used to prepare 7-iodomethyl-¹⁶³ and 7-chloromethylnorvisnagins **135**.¹⁶⁴ 7-Methylthiomethylnorkhellin (**136**), obtained by condensation of khellinone **113** with ethyl methylthioacetate in the presence of NaH or NaOMe, reacts with methyl iodide to give 7-iodomethyl-norkhellin **137**.¹⁶⁵



3-Halomethylchromones are prepared by the reaction of 3-hydroxymethylchromones with SOCl_2 , chloromethylation of chromones, or bromination of 3-methylchromones with *N*-bromosuccinimide.² When 2,3-dimethylthiochromone is treated according to Ziegler [NBS , $(\text{PhCOO})_2$, CCl_4], only the hydrogen atom of the 3-methyl group is substituted, which gives 3-bromo-2-(methyl)thiochromone (yield 74%).⁴⁹ The chloromethylation of 2-(methyl)thiochromone and thioflavones is carried out by treating these compounds with chloromethyl methyl ether in sulfuric acid. The reaction results in the formation of 3-(chloromethyl)thiochromones **138**; the only exception is 6-methoxythioflavone, which is converted into 5-chloromethyl derivative **139**.¹⁶⁶



$\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$; $\text{R}^1 = \text{Ph}$, $\text{R}^2 = 6\text{-Me}$, 6-MeO , 8-Me , $8\text{-CO}_2\text{Me}$.

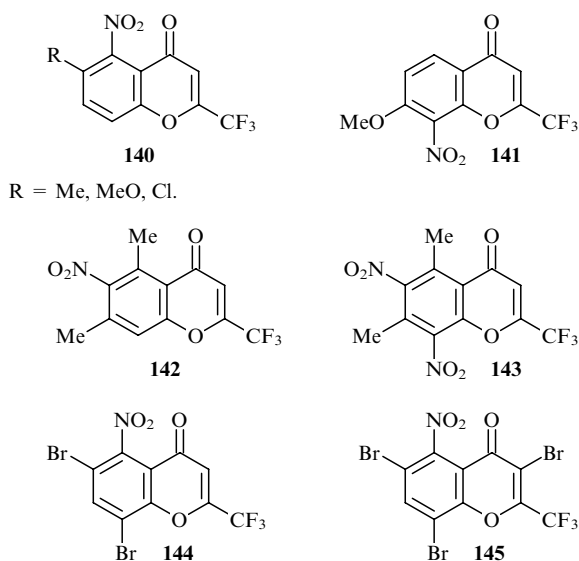
V. Chemical properties of 2-polyhaloalkyl- and halomethylchromones

1. Reactions of 2-polyfluoroalkylchromones

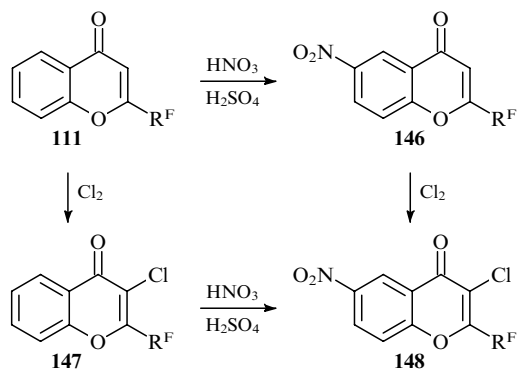
Unlike halochromones considered in Sections II and III, haloalkylchromones containing halogen atoms in the side chain have not received adequate attention. Transformations involving the active halogen atom in the halomethyl or haloacetyl substituent have been mainly considered. In recent years, a number of features of 2-polyfluoroalkyl- and 2-trichloromethylchromones important from the synthetic standpoint have been found; this allowed these compounds to be recommended as readily accessible highly reactive substrates for the synthesis of various heterocyclic derivatives including CF_3 -containing compounds with a potential biological activity.^{167, 168}

a. Nitration and halogenation

On heating with a mixture of nitric and sulfuric acids, 6- and 7-substituted 2-trifluoromethylchromones are nitrated into the 5- and 8-positions, which is in line with the directing effect of substituents, giving rise to compounds **140** and **141**.^{134, 169} The reaction of 5,7-dimethyl-2-polyfluoroalkylchromones with a nitric-sulfuric acid mixture gives 6-nitro derivatives **142** as intermediates, which can be isolated at $0-3^\circ\text{C}$ and converted into 6,8-dinitrochromones **143** at 75°C .^{169, 170} 6,8-Dibromo-2-trifluoromethylchromone is nitrated at 75°C at the 5-position to give chromone **144**. Under more rigorous conditions ($100-160^\circ\text{C}$), 6,8-dibromo-2-trifluoromethylchromone is unexpectedly converted into tribromochromone **145**, i.e., the nitration is accompanied by oxidative destruction giving molecular bromine, which brominates derivative **144** to give **145**.¹⁷¹

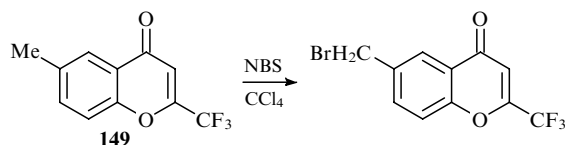


2- R^{F} -Chromones **111** unsubstituted in the benzene ring, like their non-fluorinated analogues,³² are smoothly nitrated at the 6-position yielding chromones **146**. When treated with chlorine in the light (CCl_4 , $\sim 60^\circ\text{C}$, 1 h), compounds **111** add a chlorine molecule at the double bond of the pyrone ring and, after elimination of HCl, they are converted into 3-chlorochromones **147**, which are readily nitrated at a high rate to give compounds **148**.^{150, 169, 172} Chloronitrochromones **148** are also formed upon chlorination of compounds **146** but this takes a longer time (8 h).^{150, 169, 172}



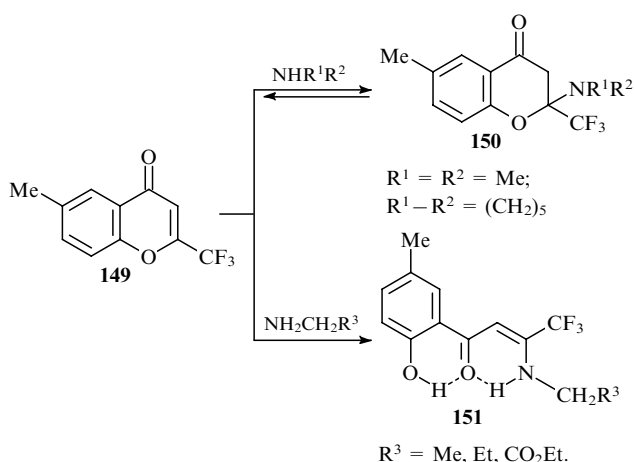
$R^F = \text{CF}_2\text{H}, \text{CF}_3, (\text{CF}_2)_2\text{H}$.

The bromination of 6-methyl-2-trifluoromethylchromone **149** with *N*-bromosuccinimide on refluxing in CCl_4 in the presence of azobis(isobutyronitrile) for 1.5 h is directed at the methyl group and results in 6-bromomethyl-2-trifluoromethylchromone (yield 49%).¹⁷³



b. Reactions with mono-, di- and triamines

In 1981, an attempt at using chromone **149** as a protective group in the peptide synthesis was made, which showed for the first time¹⁷³ that secondary amines (dimethylamine and piperidine) add reversibly to the C(2) atom without opening of the pyrone ring to give unstable compounds **150** (in the case of sterically hindered diethylamine, the reaction does not proceed). However, even mere mixing of chromone **149** with primary amines (ethyl- and propylamines) induces opening of the pyrone ring, characteristic of the chromone system, to give aminovinyl ketones **151**.^{174, 175}

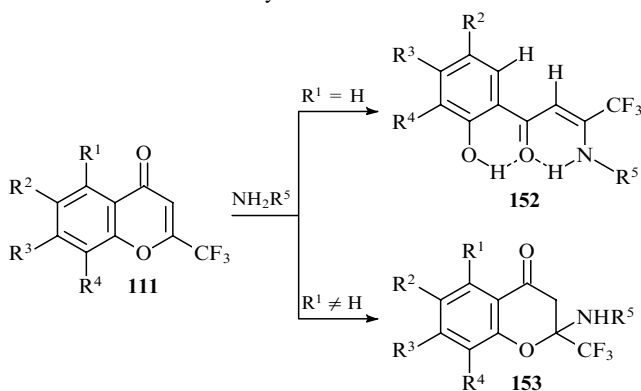


$R^3 = \text{Me}, \text{Et}, \text{CO}_2\text{Et}$.

A similar transformation takes place (although at a lower rate) when the chromone **149** is treated with ethyl glycinate in MeCN and DMF but the methyl ester of alanine does not react with this chromone for steric reasons.

Subsequently, the significance of the steric factor in the reactions of 2- CF_3 -chromones **111** ($R^F = \text{CF}_3$) with ammonia and primary amines was also demonstrated for other examples. The nature of the substituent at the 5-position of the chromone system influences the form of existence of the products of this reaction, which can be either ring or open. The attack by the amine on the C(2) atom of 2- CF_3 -chromones **111** for $R^1 = \text{H}$ is accompanied by opening of the pyrone ring and yields aminovinyl

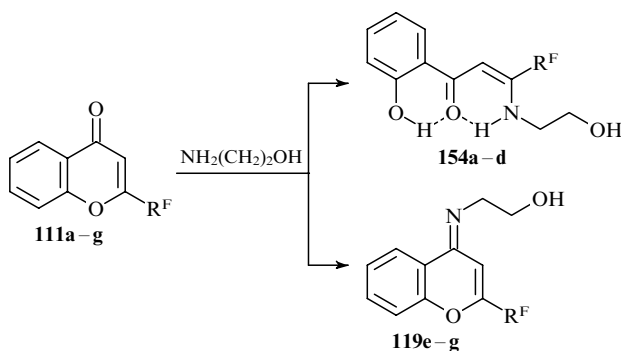
ketones **152**; when $R^1 \neq \text{H}$, the process stops after the nucleophilic addition of the amine, which gives 2-aminochromanones **153** stable on storage. This is due to destabilisation of the open form with $R^1 \neq \text{H}$ by the repulsion between the R^1 substituent located in the *ortho*-position to the oxo group and the vinylic hydrogen atom of the aminoenone system.¹⁷⁶



$R^1 = R^3 = \text{Me}, R^2 = R^4 = \text{H}; R^1 - R^2 = 5,6\text{-benzo}, R^3 = R^4 = \text{H};$
 $R^1 = R^2 = R^3 = R^4 = \text{H}; R^1 = R^2 = \text{H}, R^3 - R^4 = 7,8\text{-benzo};$
 $R^5 = \text{H}, \text{Me}, \text{Bn}$.

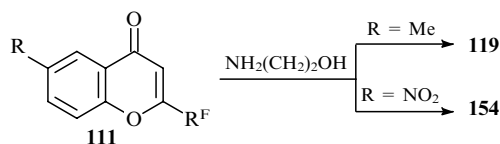
In spite of the presence of the methoxy group in the *peri*-position, fluorokhellins **112** also react with ammonia and primary amines mainly along the pathway of pyrone ring opening.^{177, 178}

A change in the direction of nucleophilic attack has been found in a study of the reaction between chromones **111a–g** unsubstituted in the benzene ring and 2-aminoethanol at $\sim 20^\circ\text{C}$. This amine easily reacts with compounds **111a–d** yielding aminovinyl ketones **154a–d**, which precipitate from the reaction mixture over a period of 10–15 min; on long storage, they are hydrolysed to give the starting chromones. Completion of the reaction between 2-aminoethanol and chromones **111e–g** requires more than 24 h. In this case, chromeneimines **119e–g** are formed as products of transformation of 2-aminoethanol involving the carbonyl group.¹⁷⁹ This behaviour of compounds **111e–g**, difficult to explain and unusual for a chromone system, may be related to a specific combination of steric and electronic effects of the R^F groups in these molecules.



$R^F = \text{CF}_3$ (a), CF_2H (b), $(\text{CF}_2)_2\text{OCF}_3$ (c), C_4F_9 (d),
 $(\text{CF}_2)_2\text{H}$ (e), C_2F_5 (f), C_3F_7 (g).

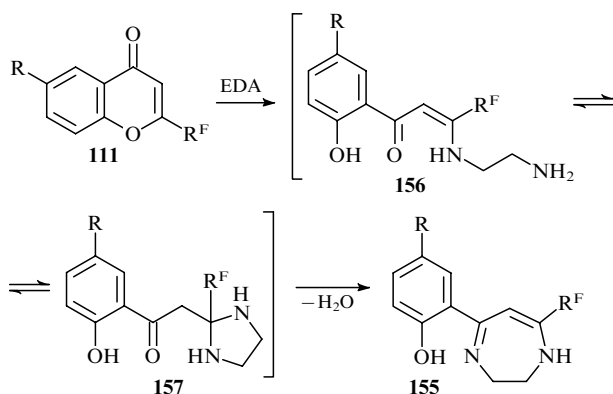
The reactivity of the C(2) and C(4) atoms in chromones **111** towards 2-aminoethanol depends on not only the length of the polyfluoroalkyl chain but also on the nature of the substituent at the 6-position. For example, aminoethanol reacts with 6-methyl-substituted chromone **111** at the C(4) atom (*i.e.*, at the carbonyl group) giving imine **119**, whereas its reaction with 6-nitro-substituted chromone **111** involves the C(2) atom and gives the corresponding aminovinyl ketone **154**, as the electron-withdrawing nitro group facilitates opening of the pyrone ring due to stabilisation of the leaving phenoxide anion.¹⁸⁰



R = NO₂, Me; R^F = (CF₂)₂H, C₂F₅.

6-Nitro-2-trifluoromethylchromone, unlike 2-methyl- and 2-trifluoromethylchromones, reacts with aniline to give aminovinyl ketone. The bulky *tert*-butylamine does not react with 2-CF₃-chromones, and morpholine adds to the C(2) atoms to form 2-morpholino-2-trifluoromethylchroman-4-ones stable during storage. The formation of these products is facilitated by the nitro group present in the benzene ring of 2-CF₃-chromones.^{134, 181}

Unlike non-fluorinated chromones, whose reactions with ethylenediamine give complex mixtures of products,¹⁸² the reactions of 2-R^F-chromones **111** with excess ethylenediamine (EDA) in an ethanol solution (~20 °C, 3 h) are more unambiguous and give rise to 5-(2-hydroxyaryl)-7-polyfluoroalkyl-2,3-dihydro-1*H*-1,4-diazepines **155** (75%–91%).¹⁸³ The reaction is accompanied by opening of the pyrone ring with the formation of aminovinyl ketones **156**, which occur in equilibrium with imidazolidines **157**[‡] and cyclise into the final dihydrodiazepines **155**.

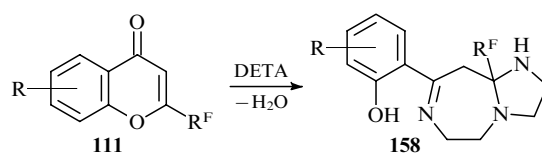


R = H, Me, MeO, Cl; R^F = CF₂H, CF₃, (CF₂)₂H.

Compounds **155** exist in CDCl₃ as the 1*H*-7-R^F-tautomers due to the formation of an intramolecular bond between the phenolic proton and the imine nitrogen atom of the heterocycle. This conclusion was based on the values of the ³J_{H,F} spin–spin coupling constants, which are 2.8–4.5 Hz for molecules with the HCF₂CF₂–C(X)=C fragments, where X = O, N.¹⁸⁴ The values ³J_{H,F} = 3.2–3.4 Hz have been found for dihydrodiazepines **155**; thus, they contain this type of fragment.^{183, 185}

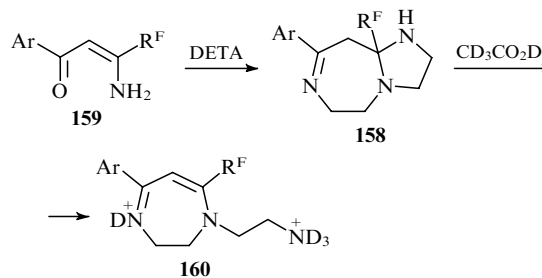
With diethylenetriamine (DETA), chromones **111** are converted into 5-(2-hydroxyaryl)-7-polyfluoroalkyl-1,4,8-triazabicyclo[5.3.0]dec-4-enes **158** (35%–91%), which represent the cyclic form of dihydrodiazepines containing a 2-aminoethyl group at the nitrogen atom located most closely to the fluorinated group. This reaction has virtually no limitations as regards the nature of the polyfluoroalkyl group or the nature and position of the substituent in the benzene ring. It is facilitated by the formation of a strong intramolecular hydrogen bond between the phenolic hydroxyl and the imine nitrogen atom (¹H NMR and X-ray diffraction data).^{186, 187} The first step is nucleophilic addition of the primary amino group to the C(2) atom accompanied by opening of the pyrone ring yielding *N*-substituted aminovinyl ketones, which further cyclise to triazabicyclic products **158** with participation of both electrophilic centres.

[‡] The cyclic products **157** formed in the reaction of ethylenediamine with 8-aza-5,7-dimethyl- and benzo[*h*]-2-trifluoromethylchromones have been isolated.



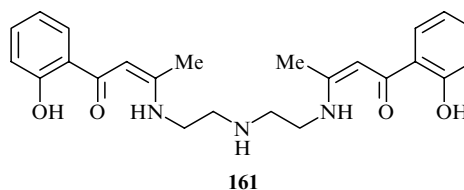
R = H, Me, MeO, Cl; R^F = CF₂H, CF₃, (CF₂)₂H, (CF₂)₂OCF₃, C₄F₉.

Note that similar products have been obtained from compounds **159** and diethylenetriamine. This reaction can be used to prepare bicyclic compounds **158** having no *o*-OH group in the aromatic ring. In the presence of CD₃CO₂D, the five-membered ring opens and compound **158** is transformed into dication **160**.^{188, 189}

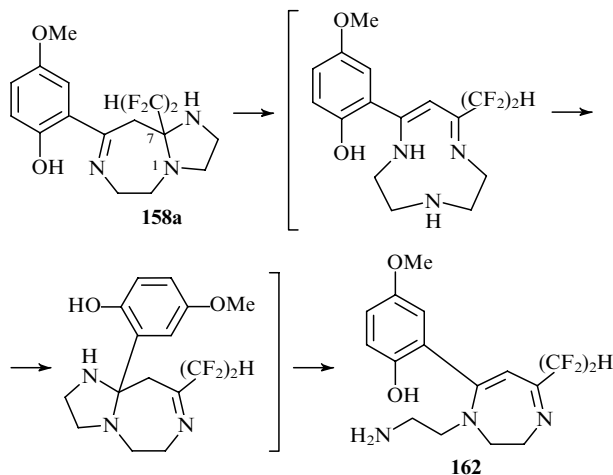


Ar = Ph, 4-MeC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 4-BrC₆H₄, 4-NO₂C₆H₄, 2-HOC₆H₄, 2-C₄H₃S, 2-C₄H₃O; R^F = CF₃, (CF₂)₂H.

It should be emphasised that the formation of bicyclic products **158** is typical only of 2-R^F-chromones and R^F-aminovinyl ketones, where the polyfluoroalkyl group substantially increases the reactivity of the carbon atom that carries this group. This reaction does not proceed for non-fluorinated analogues. For example, 2-methylchromone reacts with diethylenetriamine under conditions used to prepare compounds **158** to give bisaminoenone **161**.¹⁸⁷



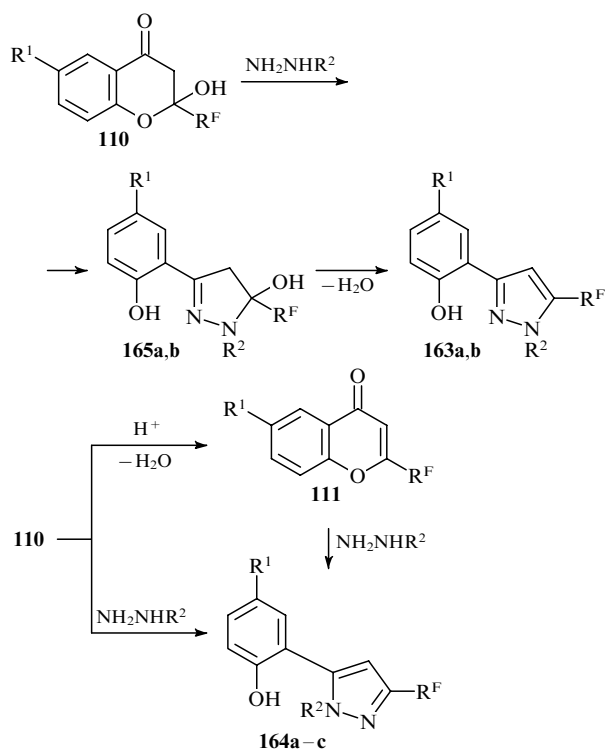
On keeping in ethanol for a week, compound **158a** [Ar = 2-HO-5-MeOC₆H₃, R^F = (CF₂)₂H] isomerises into dihydrodiazepine **162**; its structure was established by X-ray diffraction.^{187, 190} This unusual rearrangement may start with cleavage of the C(7)–N(1) bond, while the triazacyclodecadiene thus formed may be converted into **162** by intramolecular transamination.



Thus, the reaction of 2- R^F -chromones with amines usually starts with the attack by the amino group on the C(2) atom. In the case of secondary amines or in the presence of a substituent at the 5-position, the reaction can stop after 1,4-nucleophilic addition; however, in most cases, it is accompanied by pyrone ring opening giving the corresponding aminovinyl ketones, whose structural features and subsequent transformations provide a variety of products. An exception is the reaction of 2- R^F -chromones with 2-aminoethanol; with $R^F = (CF_2)_2H$, C_2F_5 and C_3F_7 , it gives chromeneimines **119**, pointing to the possibility of an attack by the amine on the carbonyl group.

c. Reactions with hydrazines, hydroxylamine and sodium azide

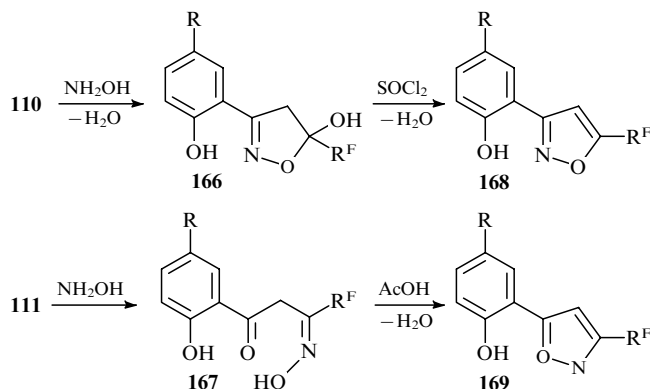
The reactions of chromanones **110** and chromones **111** with hydrazine hydrate resulted in the synthesis of 3(5)-(2-hydroxy-aryl)-5(3)-polyfluoroalkylpyrazoles that have a planar conformation and mainly exist as 1*H*-5- R^F -tautomers **163a** in $CDCl_3$ and as 1*H*-3- R^F -tautomers **164a** in DMSO. The reaction with phenylhydrazine allows one to synthesise regioisomeric 5- R^F -pyrazole **163b** from compounds **110** and 3- R^F -pyrazoles **164b** from compounds **111**. With methylhydrazine, only the 3- R^F -regioisomers **164c** are formed. Under mild conditions, the reaction of chromanones **110** with hydrazines can be arrested after the formation of dihydropyrazoles **165**.¹⁹¹



$R^1 = H, Me, MeO, Cl$; $R^2 = H$ (a), Ph (b), Me (c).

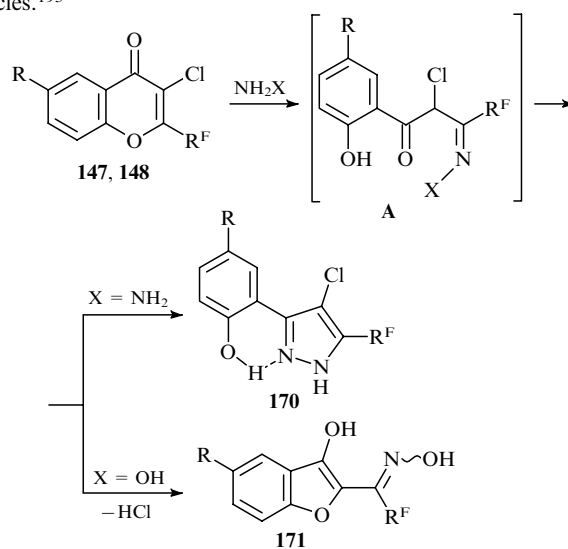
The products formed from chromanones **110** and hydroxylamine hydrochloride in the presence of AcONa are oximes existing in the ring isoxazoline form **166** owing to the high electrophilicity of the carbonyl carbon atom.¹³³ Under similar conditions, chromones **111** react at the C(2) atom rather than at the oxo group and give isomeric oximes **167**, which do not tend to cyclise, unlike the aliphatic analogues,¹⁹² and exist in the linear oxime form. The change in the direction of the nucleophilic attack on passing from compounds **110** to **111** makes it possible to synthesise regioisomeric 5- R^F -isoxazoles **168** (refluxing of isoxazolines **166** in toluene with $SOCl_2$) and 3- R^F -isoxazoles **169** (refluxing of oximes **167** in AcOH with HCl). By investigating isoxazoles **168** and **169** by ^1H , ^{19}F and ^{13}C NMR spectroscopy, a number of specific features were revealed, which make it possible to distinguish between these regioisomers.¹³³

Fluorokhellins **112** react with hydrazine and hydroxylamine in a similar way; they were used to prepare R^F -containing pyrazoles and regioisomeric isoxazoles of the benzofuran series.^{177, 178}



$R = H, Me$; $R^F = CF_2H, CF_3, (CF_2)_2H$.

3-Chlorochromones **147** and **148** are resinified even at $\sim 20^\circ C$ on treatment with hydrazine hydrate, while refluxing of these compounds in ethanol with hydrazine dihydrochloride for 4–48 h gives 4-chloropyrazoles **170** in good yields.¹⁷² In view of the chemical reactivity of the 3-halochromones considered above (see Section III.2), this transformation does not appear evident, because it is the first example of a reaction of 3-halochromone with a nucleophile with retention of the halogen atom in the reaction product. When chromones **147** and **148** are refluxed with hydroxylamine hydrochloride in ethanol in the presence of AcONa, contraction of the pyrone ring to the furan ring, typical of 2-unsubstituted 3-halochromones, takes place to give derivatives **171** (58%–91%). These products are of interest as regards subsequent transformations into various R^F -containing heterocycles.¹⁹³

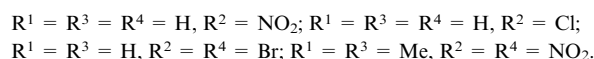
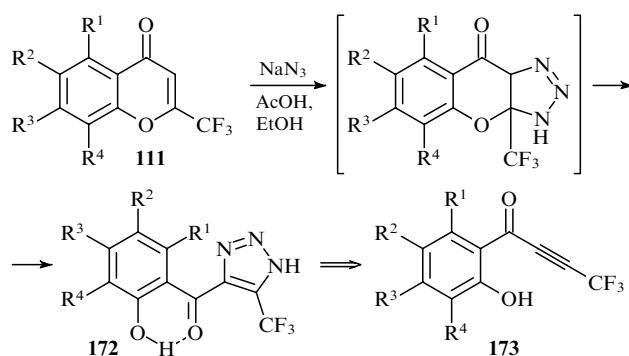


$R = H$ (**147**), NO_2 (**148**); $R^F = CF_2H, CF_3, (CF_2)_2H$.

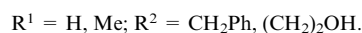
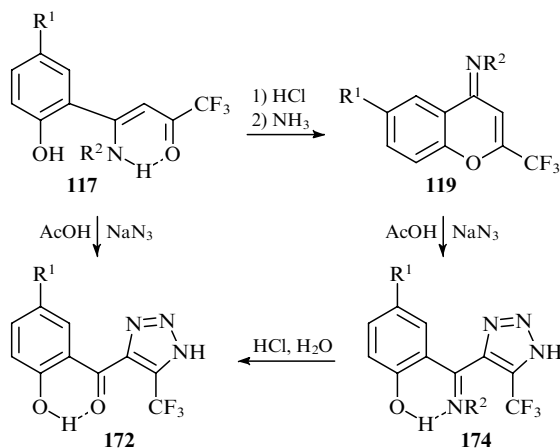
It has been suggested¹⁹³ that the reactions of chromones **147** and **148** with hydrazine and hydroxylamine involve intermediate **A** resulting from the attack of the NH_2 group on the C(2) atom with opening of the pyrone ring. This is followed by either an intramolecular A_N-E reaction between the $C=O$ and NH_2 groups (for $X = NH_2$) or nucleophilic substitution of the phenolic hydroxyl for the chlorine atom ($X = OH$). According to the IR, ^1H NMR and ^{19}F NMR data, the isomer and tautomer composition of oximes **171** depends on the number of fluorine atoms in the R^F -substituent, the nature of substituents in the benzene ring and the solvent nature. The nitro derivatives exist almost entirely, both in the solid state and in solution in $CDCl_3$ or

DMSO- d_6 , as the enol form represented by the *Z*-isomer when $R^F = CF_3$, $(CF_2)_2H$ and by a *Z*- and *E*-isomer mixture when $R^F = CF_2H$. When the nitro group is missing, a mixture of two stable keto-enol tautomers of oximes **171** is formed.¹⁹³

By the reaction of 2- CF_3 -chromones **111** with sodium azide (AcOH, EtOH, 80 °C, 4–10 h), salicyloyltriazoles **172** were prepared (50%–86%); hence, the 2- CF_3 -chromones **111** can be considered as synthetic equivalents of trifluoropropynyl ketones **173**, which are difficult to prepare.¹⁵¹ This reaction is a novel transformation involving the chromone system. It should be noted that on replacement of the CF_3 group by H, CF_2H , $(CF_2)_2H$ or CCl_3 , the reaction does not take place and without an electron-withdrawing group at the 6-position, the reaction slows down to such an extent that 2-trifluoromethylchromone is recovered unchanged after a 10-hour contact with NaN_3 under the conditions described above.¹⁵¹

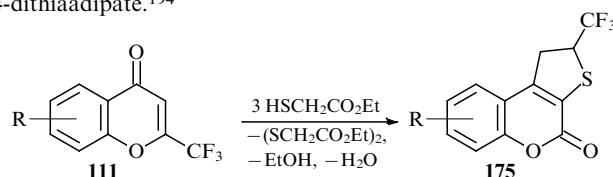


The reactivity of the pyrone ring with respect to NaN_3 can be increased by replacement of the $C=O$ group by the $C=NR$ group. It was shown¹⁵¹ that the presence of an electron-withdrawing group in the benzene ring is not obligatory for chromoneimines **119**, and they easily react with NaN_3 in the presence of AcOH to give aryltriazolylketone imines **174**. This is due to the fact that, being rather strong bases, compounds **119** are protonated at the imine nitrogen atom even in the presence of AcOH,¹⁷⁹ thus generating iminium cations, which participate in the reaction. Hydrolysis of imines **174** affords triazoles **172**, which could not be synthesised from the corresponding 2- CF_3 -chromones. Since the transformations **117** $\rightarrow$ **119** and **119** $\rightarrow$ **172** proceed *via* common iminium intermediate **118**, it comes as no surprise that aminovinyl ketones **117** are converted under these conditions into triazoles **172** as easily as chromoneimines **119**.

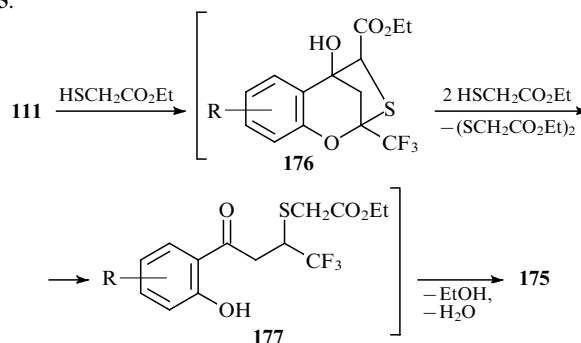


d. Reactions with alkyl sulfanylacetaes

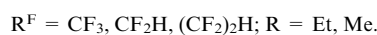
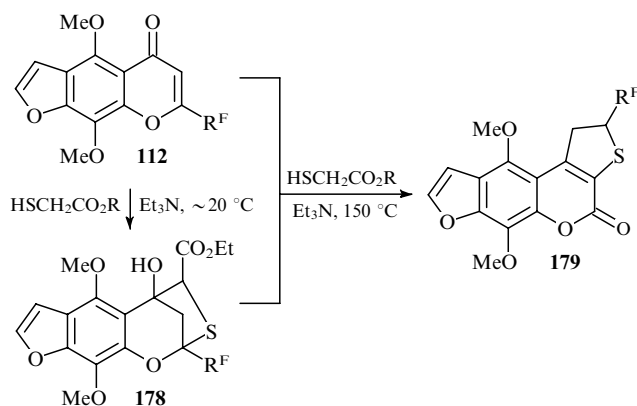
One of the most unexpected and interesting reactions of 2- CF_3 -chromones **111** is the reaction with ethyl sulfanylacetaes in the presence of Et_3N , which results in 1,2-dihydro-2-trifluoromethyl-4*H*-thieno[2,3-*c*]chromen-4-ones **175** (66%–93%) and diethyl 3,4-dithiaadipate.¹⁹⁴



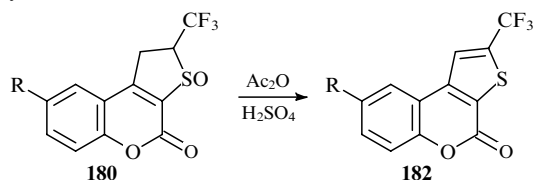
The formation of these products is indicative of the redox pattern of the given transformation. The nature and the positions of substituents in the benzene ring do not affect significantly the course of the reaction; however, as in the case of sodium azide, this reaction can be accomplished only with 2- CF_3 -chromones. The reaction mechanism is not entirely clear but, most likely, as in the case of 3,3-dialkyl-6-trifluoromethyl-2,3-dihydro-4-pyrones,¹⁹⁵ the reaction starts with the formation of the benzo derivative of 2-oxa-7-thiabicyclo[3.2.1]octane **176**. The subsequent reductive opening of the pyrone ring in **176** induced by ethyl sulfanylacetaes leads to ether **177**, which cyclises yielding dihydrothienocoumarin **175**.



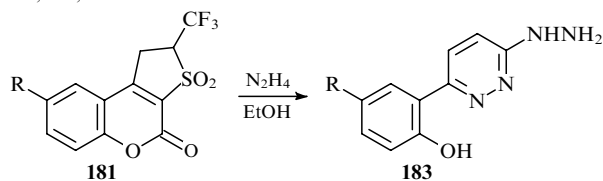
Interestingly, the reaction of alkyl sulfanylacetaes with fluoro-khellins **112**, although they are closely related to chromones, stops after the formation of products **178** (66%–85%), represented by a single diastereomer with *cis*-arrangement of substituents in the thiolane fragment (X-ray diffraction data).^{150, 196} Only under rigorous conditions (sealed tube, 150 °C), were 7- CF_3 - and 7- CF_2H -norkhellins **112** converted into dihydrothienopsoralens **179**, which can also be synthesised from compounds **178**. This proves that compounds **178** are intermediates.¹⁹⁶



Selective oxidation of dihydrothienocoumarins **175** gives rise to highly reactive substrates, namely, sulfoxides **180** (NO_2 , CHCl_3) and sulfones **181** (H_2O_2 , AcOH). Under Pummerer rearrangement conditions, sulfoxides **180** produce thienocoumarins **182**,¹⁵⁰ and sulfones **181** are transformed into 3-hydrazino-6-(2-hydroxyaryl)pyridazines **183** under the action of hydrazine.¹⁹⁷ Previously, these pharmaceutically valuable products providing the basis for a series of 3-hydrazinopyridazine drugs,¹⁹⁸ were synthesised in seven steps starting from phenols and succinic anhydride.¹⁹⁹

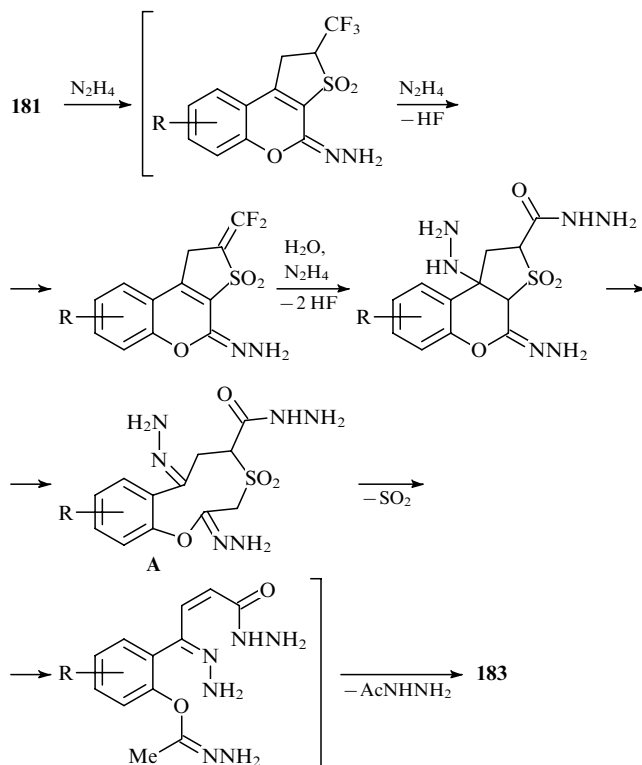


R = H, Me, Cl.



R = H, Me, MeO, NO_2 , NH_2 .

The reaction of 8-nitosulfone with hydrazine has been used to elucidate the mechanism of the unusual transformation of sulfones **181** into pyridazines **183**. The reaction was arrested after an intermediate step that gave intermediate **A**. On the basis of spectroscopic data, the isolated intermediate **A** was identified as having a benzocyclononene structure, which allowed the researchers to propose a possible reaction pathway. It was suggested¹⁹⁷ that this reaction starts with the attack of the keto group of sulfone **181** by the hydrazine molecule, resulting in the replacement of the carbonyl oxygen atom by a hydrazone group. The subsequent hydrazinolysis and hydrolysis of the CF_3 -group to CONHNH_2 , the addition of a hydrazine molecule to the activated double bond and cleavage of the shared bond in the bicyclic structure furnish intermediate **A**. Further transformation of this intermediate

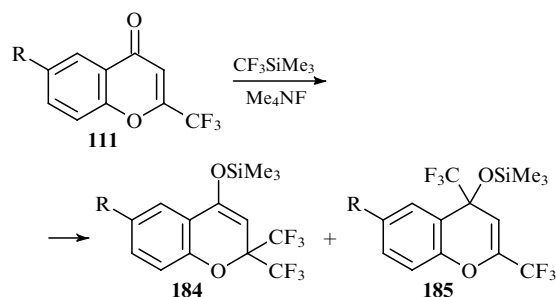


involves elimination of SO_2 yielding the hydrazine derivative of β -aroylacrylic acid, which is then converted into pyridazine **183** upon an intramolecular cyclisation.

This reaction can find wide application, as it represents a new approach to the synthesis of 3-hydrazinopyridazines from readily available compounds, namely, 2-hydroxyacetophenones and ethyl trifluoroacetate.

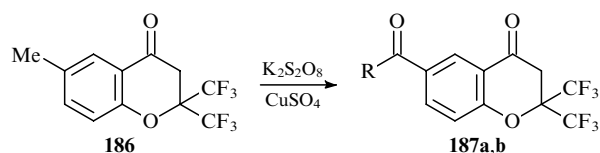
e. Reactions with C-nucleophiles

Nucleophilic trifluoromethylation of organic compounds is complicated by appreciable instability of the free trifluoromethyl anion, which tends to decompose giving the fluoride anion and difluorocarbene. By using trimethyl(trifluoromethyl)silane (Ruppert's reagent) in the presence of fluoride anions, one can avoid decomposition and accomplish direct insertion of the CF_3 group into the organic substrate. Ruppert's reagent easily reacts with both saturated and α,β -unsaturated carbonyl compounds according to the 1,2-nucleophilic addition pattern yielding the corresponding trifluoromethylated alcohols.^{200–202} The reaction of $\text{R}^{\text{F}}\text{SiMe}_3$ with 2- R^{F} -chromones is the first example of preparative 1,4-trifluoromethylation of the α,β -enone system.^{203,204} ^{19}F NMR monitoring of this system showed that in the presence of the nucleophilic initiator Me_4NF (THF, 0°C , 4 h), chromones **111** react almost quantitatively and with high regioselectivity with CF_3SiMe_3 along the 1,4-addition route to give trimethylsilyl ethers **184** (the contents of 1,2-addition products **185** in the reaction mixture does not exceed 10%–12%). When the reaction mixture is treated with dilute HCl, only 1,4-addition products **184** are hydrolysed giving 2,2-bis(trifluoromethyl)chroman-4-ones.



R = H, Me.

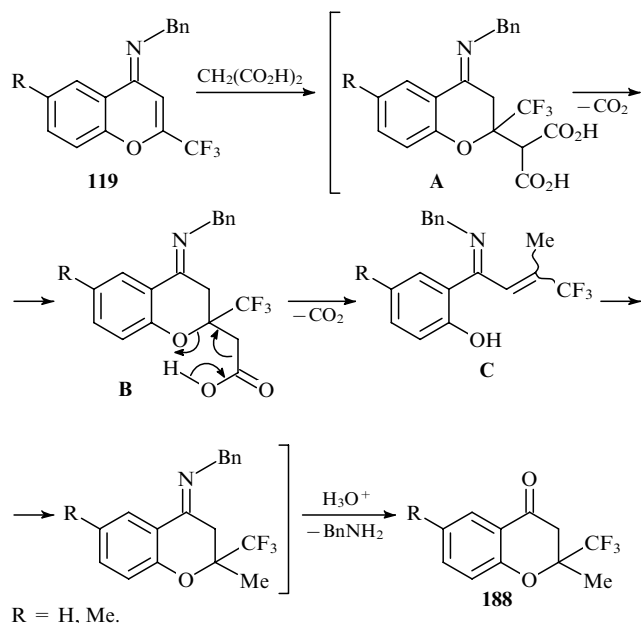
This reaction has been used²⁰⁴ to prepare fluorinated analogues of naturally abundant chromanones with the *gem*-dimethyl group at the 2-position. Oxidation of the 6-Me group of chromanone **186** with a mixture of $\text{K}_2\text{S}_2\text{O}_8$ and CuSO_4 in aqueous acetonitrile provided the synthesis of aldehyde **187a** — an analogue of natural lactarochromal (a metabolite of the fungi *Lactarius deliciosus*²⁰⁵) in which both methyl groups have been replaced by trifluoromethyl groups. Apart from hexafluorolactarochromal **187a**, the corresponding acid **187b** was obtained, which is also a fluorinated analogue of the natural acid isolated from the plant *Chrysothamnus viscidiflorus*.



R = H (a), OH (b).

A fairly unexpected reaction has been reported.²⁰⁶ By refluxing equimolar amounts of *N*-benzyl-2-trifluoromethylchromene-4-imines **119** and malonic acid in dioxane, 2-methyl-2-trifluoromethylchroman-4-ones **188** were obtained in ~60% yields. In this transformation, malonic acid functions as a methylating agent. Presumably,²⁰⁶ the first step of the reaction is mutual activation of the starting compounds; in particular, malonic acid protonates the chromeneimine to give the iminium

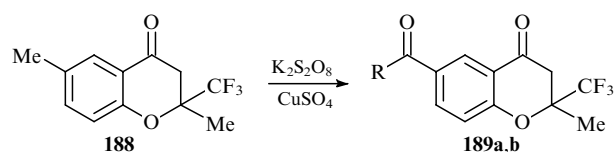
cation, which results in a higher electrophilicity of the C(2) atom, while chromeneimine, which is a rather strong base, deprotonates the activated CH₂ group of the acid, thus increasing its nucleophilicity. This mutual activation is crowned with the addition of malonic acid at the C(2) atom to form intermediate **A**, whose decarboxylation gives acid **B**. The ease of decarboxylation of the second CO₂H group is attributed to opening of the pyrone ring in intermediate **B**. As a result, intermediate **C** is produced. The subsequent cyclisation and hydrolysis of intermediate **C** in the presence of HCl afford chromanones **188**.



R = H, Me.

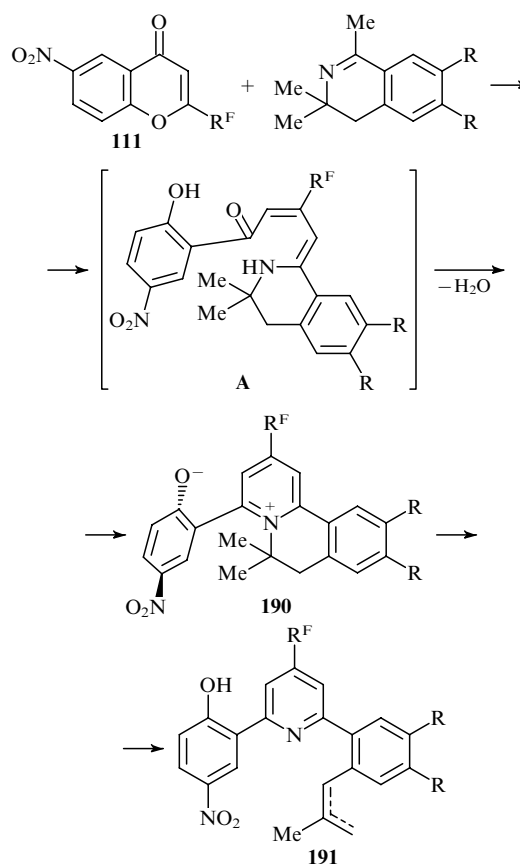
Methylmalonic and phenylacetic acids do not react with chromeneimines under similar conditions. Malonic acid does not methylate 2-CF₃ chromones in the presence of pyridine.

Oxidation of the 6-Me group in chromanone **188** by K₂S₂O₈ has yielded aldehyde **189a**, an analogue of lactarochromal in which, unlike aldehyde **187a**, only one of the methyl groups is replaced by the trifluoromethyl group. In addition to trifluoro-lactarochromal **189a**, the corresponding carboxylic acid **189b** was also isolated.²⁰⁶



R = H (a), OH (b).

The reaction of 6-nitro-2-R^F-chromones **111** with 1,3,3-trimethyl-3,4-dihydroisoquinolines (THF, 20 °C, 4 days) affords coloured (from orange to dark red) chiral zwitter-ions **190** in 50%–80% yields; the structure of these products was confirmed by X-ray diffraction analysis.^{150, 207} This reaction is typical only of 6-nitro derivatives, it involves an attack of the C(2) atom of chromone by the enamine tautomer of dihydroisoquinoline followed by cyclisation involving the carbonyl group with elimination of a water molecule. According to the ¹H NMR spectra of these compounds, the protons of the CH₂ group attached to the heterocyclic fragment are diastereotopic and account for an AB system with J_{AB} = 16.5 Hz. This attests to hindered rotation around the bond that connects the phenolate residue and the heterocycle and to the existence of the zwitterions **190** as atropoisomers. On heating or in the presence of sulfuric acid, the steric strain in the molecule is removed due to cleavage of the Me₂C–N bond, resulting in the formation of isomers **191**, differing in the position of the double bond in the alkenyl substituent.

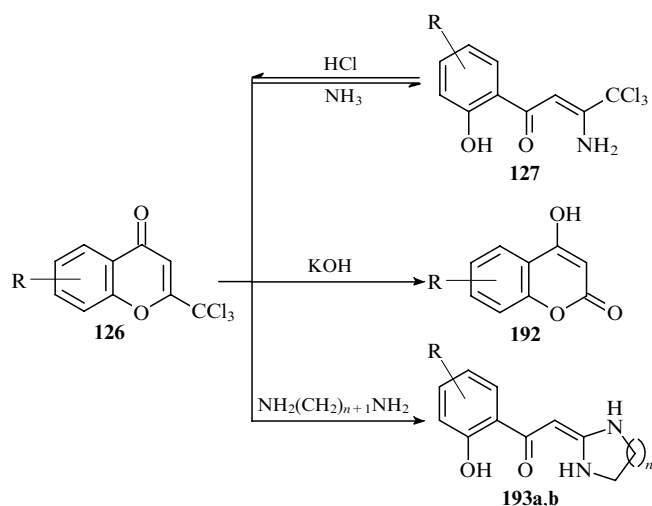


R^F = CF₃, CF₂H, (CF₂)₂H; R = H, Me, OMe.

Thus, as distinct from highly reactive 5,5,5-trifluoropent-3-en-2-one studied previously, which easily adds a variety of nucleophilic species to the C=C bond,²⁰⁸ 2-R^F-chromones considered in this Section incorporate, apart from a similar fragment, a good leaving group at C(2), which increases appreciably the synthetic value of these compounds. Modification of 2-R^F-chromones by introducing electron-withdrawing substituents and/or a halogen atom into the 3-position of the benzene ring not only increases the reactivity of these compounds with respect to nucleophiles but also alters the route of some reactions. The replacement of the C=O group by a C=NR group further extends the synthetic potential of the chromone system. It is also noteworthy that the trifluoromethyl group occupies a special place among polyfluorinated substituents, because the most interesting and peculiar transformations with N-, S- and C-nucleophiles, such as addition of morpholine and reactions with sodium azide, ethyl sulfanylacetate and malonic acid can be carried out only for 2-CF₃-chromones and their derivatives.

2. The properties of 2-trichloromethylchromones and halomethylchromones

The trichloromethyl group is known to be a synthetic equivalent of the carboxy group to which it is transformed upon hydrolysis. For example, refluxing of 5-trichloromethylisoxazole with water or alcohols in the presence of sulfuric acid affords isoxazole-5-carboxylic acid and its esters in high yields.²⁰⁹ However, the 2-trichloromethyl group in chromones cannot be hydrolysed in an acid medium, while on treatment with a methanol solution of KOH, this group is replaced by a hydroxy group, which results in the formation of 4-hydroxycoumarins **192**. On treatment with an alcohol solution of ammonia, the pyrone ring in 2-CCl₃-chromones **126** is opened, giving rise to aminoenones **127**, which are hydrolysed in hydrochloric acid giving again chromones **126**.¹⁵⁹



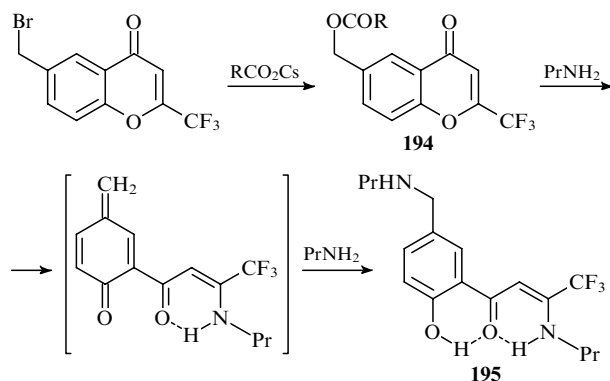
$\text{R} = \text{H, Me, MeO, Cl; } n = 1 \text{ (193a), } 2 \text{ (193b)}.$

The 2- CCl_3 -chromones **126** react with ethylene- and trimethylenediamines differently from 2- R^{F} -chromones. This reaction is a new convenient method for the synthesis of 2-phenacylideneimidazolidines **193a** and -hexahydropyrimidines **193b** ($\sim 20^\circ\text{C}$, 3–5 h, yield 50%–95%),^{210, 211} which have been prepared formerly by cyclocondensation of diamines with α -oxoketene dithioacetals.²¹² The reaction involves the intermediate formation of aminoenones with a 2-aminoethyl or 3-aminopropyl group at the nitrogen atom. Cyclisation of these aminoenones is accompanied by elimination of the CCl_3 group, which leads to products **193a,b**, existing in DMSO- d_6 and CDCl_3 solutions as keto-amine tautomers.^{210–212} The conjugation of the lone electron pairs of the nitrogen atoms with the carbonyl group markedly increases the electron density on the *exo*-methylene carbon atom of enediamines **193a,b**; as a consequence, this atom is the first to be attacked by electrophiles and 1,3-dipoles. The subsequent involvement of nitrogen or the carbonyl group in the reaction makes these substances valuable substrates for the synthesis of new heterocyclic systems that are difficult to obtain by other methods.^{213, 214}

7-Trichloromethylnorkhellin **131** reacts with ethylene- and trimethylene-diamines in a similar way, giving rise to enediamines of the benzofuran series. The reaction of compound **131** with a methanol solution of KOH gives a new khellin derivative, 7-methoxynorkhellin,¹⁷⁷ instead of the expected 4-hydroxyisopimpinellin.²¹⁵

Thus, the high reactivity of 2-trichloromethylchromones, which is manifested as easy opening of the pyrone ring with simultaneous replacement of the CCl_3 group under the action of aliphatic diamines, makes these compounds useful substrates for the preparation of partially hydrogenated heterocycles, which are of synthetic interest by themselves.

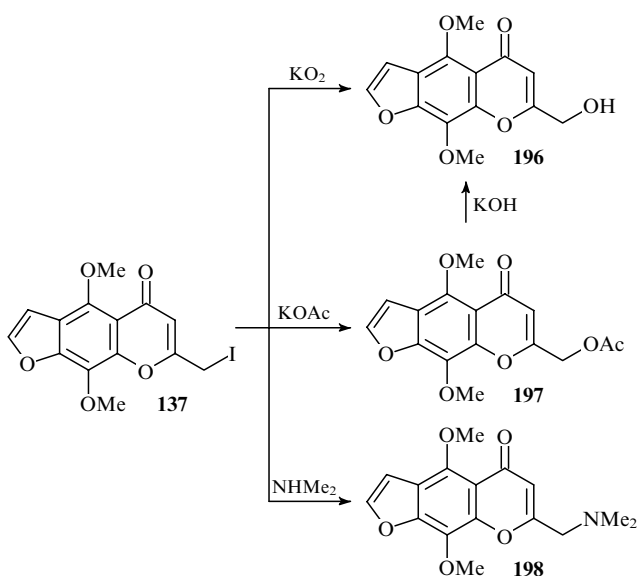
The reactivity of halomethyl derivatives of chromones is similar to that of benzyl halides, which was reflected in a series of publications. For example, 6-bromomethyl-2-trifluoromethylchromone reacts with caesium salts of α -amino acids (DMF,



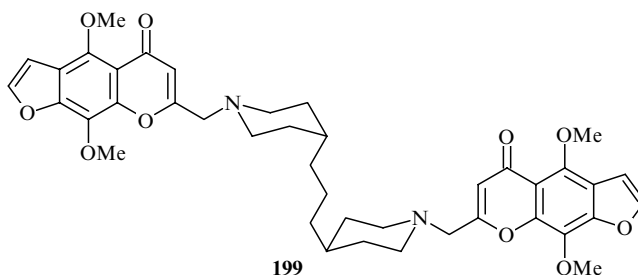
25°C , 4 h) to give esters **194**, which have been proposed as protective groups for the carboxy function in the peptide synthesis.¹⁷³ The easy replacement of the carboxylate group in **194** on treatment with propylamine during the synthesis of aminovinyl ketones **195** was attributed¹⁷³ to the formation of the quinone-methide intermediate.

The bromine atom in ethyl 3-bromomethylchromone-2-carboxylate is readily replaced by an amino-, cyano- or acetate group, or can be involved in intramolecular cyclisation giving 1*H*-furo[3,4-*b*]chromene-3,9-dione.⁵³

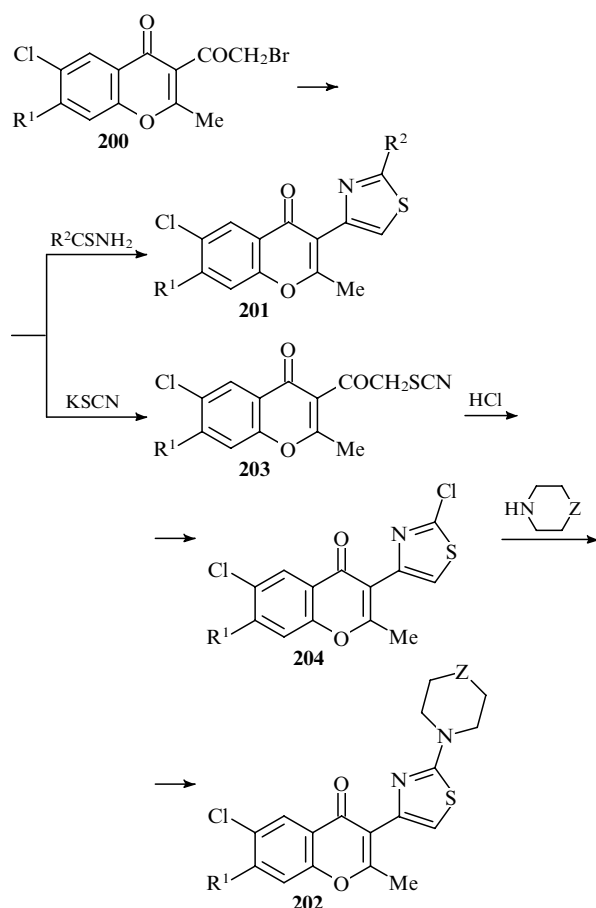
The reduction of 7-iodo- and 7-chloromethylnorvisnagins **135** by zinc dust in AcOH smoothly leads to visnagin.^{163, 164} Ammiol **196** — the natural furochromone least abundant of the furochromones isolated from the plant *Ammi visnaga* L., — has been prepared from 7-iodomethylnorkhellin **137** via intermediate acetate **197** in a high final yield. Upon oxidation by potassium peroxide, 7-iodomethylnorkhellin **137** is directly converted into ammiol **196**, but the yield is low (27%). On treatment with dimethylamine, **137** is transformed into the amino-substituted khellin **198**.¹⁶⁵



The reaction of iodokhellin **137** with 4,4'-trimethylenedipiperidine in MeCN in the presence of K_2CO_3 affords bisaminofurochromone **199**, which is a potential antiatherosclerotic agent.²¹⁶



Bromoacetyl derivatives of chromones have found use in the synthesis of biologically active compounds. The condensation of 3-bromoacetyl-2-methylchromones **200** with thioamides and thiourea results in 3-(thiazol-4-yl)-2-methylchromone hydrobromides, which were converted into free bases **201** (69%–85%) by treatment with an aqueous solution of NH_3 .^{217, 218} The reaction of chromone **200** with potassium thiocyanate allows one to obtain 3-thiazolylchromones **202**, which contain a residue of a cyclic secondary amine in the thiazole ring and exhibit a high anti-inflammatory activity.²¹⁹ The last-mentioned reaction involves the intermediate formation of compounds **203** and 3-(2-chloro-4-thiazolyl)-2-methylchromones **204**.



$R^1 = \text{H, Me}; R^2 = \text{Ar, NH}_2, \text{NHAr, Het}; Z = \text{O, NH}.$

VI. Conclusion

Analysis of the published data demonstrates that of the diverse halogen-containing chromones, 3-halo- and 2-polyhaloalkylchromones, as well as chromones with the perfluorinated benzene ring have now been studied most comprehensively.¹⁸ Data on 2-halo-chromones are quite scarce and data on 3-polyhaloalkylchromones are totally missing. The introduction of a halogen atom into the 3-position of the chromone system changes crucially the reactivity of the pyrone ring with respect to nucleophiles and stipulates the broad synthetic potential of 2-unsubstituted 3-halochromones. The diversity of properties of these compounds is due to the fact that, being actually highly reactive geminally activated haloalkenes¹⁰¹ with a good leaving group at the β -carbon atom, they acquire the ability to undergo additional reactions related to opening and transformation of the γ -pyrone ring. In addition, 3-halochromones are valuable substrates in homo- and cross-coupling reactions catalysed by transition metal complexes. These reactions have been used to prepare various 3-substituted chromones, 3,3'-bischromones and isoflavones.

Strangely enough, but, despite the ready accessibility of 2-polyfluoroalkylchromones, these compounds have long remained out of sight of chemists engaged in synthesis, and their systematic study has started only in recent years. Nevertheless, it is already clear that 2- R^F -chromones and, in particular, fluorinated analogues of a natural furochromone, khellin **2a**, are valuable substrates for the synthesis of diverse fluorine-containing heterocycles with a potential biological activity. Indeed, a polyfluoroalkyl group present at the C(2) atom entails dramatic changes in the reactivity of the pyrone ring, which is manifested as a bunch of new transformations (this is especially pronounced for the CF_3 group) absolutely uncharacteristic of 2-alkylchromones. It is of interest that 2- R^F -chromones substantially differ in reactivity from 2- CCl_3 -chromones, which tend to give off the trichloro-

methyl group on treatment with nucleophiles. In view of the fact that 20% to 30% of modern pharmaceuticals and 30% to 40% of agrochemical preparations contain at least one fluorine atom in the molecule,²²⁰ the research dealing with modification and study of the reactivity of 2- R^F -chromones and their derivatives aimed at extending the synthetic scope of the chromone system appear to be a topical and promising line for the future research into fluorine-containing heterocyclic compounds and search for new biologically active substances.

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Sulfide hydrodesulfurisation catalysts: structure of the active component and mechanism of the catalytic action

A N Startsev, I I Zakharov

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Abstract. A new phenomenon in heterogeneous catalysis, namely, oxidative addition of hydrogen to active metal atoms (Ni, Co) within sulfide hydrodesulfurisation catalysts, is considered. The possibility of hydrogen occlusion into the MoS₂ matrix of the active components of these catalysts is demonstrated. The electronic structure of Ni(IV) and Co(III) active sites with d⁶ electronic configuration is analysed. The concerted mechanism of thiophene hydrogenolysis on a bimetallic active site is considered and substantiated. The concept of the governing role of the metal–sulfur bond energy in catalysis by metal sulfides is analysed critically. The bibliography includes 198 references.

I. Introduction

Hydrotreating of oil fractions is the largest-scale process in the petroleum refining industry. Over 80 million barrels of oil (about 12.7 million m³) are processed in the world daily; the average sulfur content in this oil being 1.0 mass %–1.3 mass %.¹ In the last decade, the requirements for the quality of motor and jet fuels have increased considerably due to deterioration of the environmental conditions. According to the EC Directive of 11.05.2001, the total content of sulfur in diesel fuel should not exceed 50 ppm by 2005, whereas the content of aromatic compounds should not exceed 10 vol.%. The existing industrial hydrotreating catalysts only ensure a decrease in the sulfur content to ~ 500 ppm in diesel fuel; the required level can be achieved by either increasing the process temperature by 38 °C,² or decreasing considerably the liquid hourly space velocity of the feed stock, or, finally, enhancing considerably the activities of catalysts. The latter variant is the most cost-effective because the contribution of the catalyst cost to the production cost of the hydrotreating product is less than 0.5%. Therefore, world leading laboratories pay much attention to the development of new-generation catalysts for the deep hydrotreating of oil fractions. This can be illustrated by the fact that the range of hydrotreating catalysts includes more than 200 trade names.³

In this review, we will not dwell on the methods for catalysts' preparation, their chemical compositions, porous structures, kinetic studies of the hydrotreating process, *etc.* The issues of catalytic hydrotreatment of oil fractions are probably considered in most detail in the monograph by Topsøe *et al.*;⁴ the problems of deep hydrotreating, in the review by Vasudevan and Fierro;⁵ specific features of hydrogenolysis of polyaromatic sulfur-containing compounds, in the paper by Whitehurst *et al.*;⁶ and certain technological problems are analysed in the paper by Furimsky.⁷

The main purpose of this review is to analyse the fundamental aspects of hydrogenolysis of the C–S bond on sulfide hydrotreating catalysts. A decade has passed since the publication of the previous review on this subject.⁸ Considerable progress in understanding the mechanism of action of sulfide catalysts at the molecular level has been made during this period. Generally speaking, establishing the mechanism of heterogeneous catalysis and the nature of chemical interaction of reactants with solid catalyst surfaces is a very difficult task. This originates from the following reasons:

- as a rule, several types of compounds differing in composition and structure are present on a catalyst surface; as a result, chemical transformations occur in various directions and pathways to give diverse intermediates and side products in the gas phase;

- the degree of surface coverage by adsorbed molecules can vary over a very broad range, which complicates kinetic studies;

- in the overwhelming majority of cases, the structures of active sites on solid catalysts are unknown; therefore, certain theoretical models of the active component have to be used, based on analogies with the known structures [in this sense, sulfide hydrotreating catalysts present a rare exception: the geometric structures of their active components have been studied rather thoroughly (see below)];

- until now, there has been a lack of sufficiently sensitive physical methods (similar to multinuclear NMR in homogeneous catalysis) that would enable *in situ* studies of adsorption and chemical transformations of molecules on a surface;

- as a rule, heterogeneous catalytic reactions occur under drastic conditions (at high temperatures and pressures) where the reaction medium can affect the structure of the active component.

It is only the chemical and phase compositions of a catalyst that are usually known, and the structure of the active component is determined using a number of physical, chemical and kinetic methods in order to obtain responses of the catalytic system to various external impacts. Subsequently, correlations between the catalyst's activity and selectivity, on the one hand, and some

A N Startsev, I I Zakharov G K Borekov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, Prosp. Acad. Lavrent'eva 5, 630090 Novosibirsk, Russian Federation. Fax (7-383) 234 30 56. Tel. (7-383) 234 33 14. E-mail: startsev@catalysis.nsk.su (A N Startsev). Tel. (7-383) 234 10 64. E-mail: ivan@catalysis.nsk.su (I I Zakharov)

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specific parameter, on the other, are plotted and general features of a given chemical reaction are revealed.

There are two independent and mutually exclusive concepts of the mechanism of hydrodesulfurisation which are being developed simultaneously. In one of them it is assumed that the decisive role in the mechanism of catalysis by metal sulfides belongs to the bond energy of surface sulfur atoms with the solid catalyst. The other one, which is being developed at the G K Boreskov Institute of Catalysis, is based on the concept of the common nature of heterogeneous, homogeneous and enzyme catalysis as a natural phenomenon. The present review is devoted to the consideration of these concepts.

II. The structure of the active component of sulfide catalysts of hydrodesulfurisation

1. The geometric structure of the active component

Industrial catalytic hydrotreating of oil fractions began in the middle of the 1950s because of the necessity of preparation of gasoline fractions for the reforming process. In turn, reforming served as a source of inexpensive hydrogen required for hydrotreating. Hydrotreating was initially performed on a composition of sulfide compounds of two metal pairs, *viz.*, Mo(W)–Ni(Co). These catalysts were used in coal liquefaction which was developed in Germany in the middle of the 1930s. Until now, they remain unsurpassed and possess the best combination of operational properties,⁹ *viz.*, activity, stability, resistance against poisons, cost, *etc.*, though intense searches for new catalytic systems were carried out throughout all these years.

The accumulation of experimental data on the general regularities of hydrogenolysis of the C–S bond on these catalysts favoured the appearance in the 1950s–1960s of the first model of the structure of the active component;¹⁰ it was called the ‘monolayer’ model.¹¹ Later, this model was improved^{12,13} taking into account the inevitable sulfidation of the catalyst under the working conditions.

In parallel with the monolayer model, other models based on concepts of the sulfide forms of the MoS₂ and WS₂ catalysts appeared and were developed; these include intercalation models^{14–16} and models with spatially separated MoS₂ and Co₉S₈ clusters.¹⁷ A special place is occupied by models of surface complexes and boundary grains proposed by Phillips and Fote.¹⁸

The appearance in the 1960s of new methods for the study of highly dispersed species in supported catalysts opened prospects for more detailed studies of the active component of hydrodesulfurisation catalysts. This led to new models suggesting that bimetallic sulfides are the active components.^{19,20} The model known as ‘synergism upon contact’ was transformed into the ‘long-range control’ model.²¹ We believe that the most attractive model is that proposed by Ratnasamy and Sivasanker.²² It assumes that ‘promoter’ atoms, *viz.*, Co or Ni, are added to free valence bonds of the S atoms at the MoS₂ edge plane. However, this viewpoint did not receive convincing experimental confirmation; therefore, other models were created later (in the 1980s) based on the concept of a single MoS₂ slab[†] with Co ions incorporated at the edge plane.

Probably, the model of ‘Co–Mo–S phase’ developed by Topsøe *et al.*⁴ was recognised as the best; it assumed the localisation of Co ions at the edge plane of a single MoS₂ slab. This model was based on results of a Mössbauer emission spectroscopic study of catalysts, which was later confirmed by EXAFS data. Subsequently, this model was developed by other authors.^{23–27} The similarity of the structures of MoS₂ and the

Co–Mo–S phase is undoubted, but there are at least three viewpoints on the localisation of the Co(Ni) ions. For example, Nieman *et al.*²⁸ assume that Co or Ni atoms have a square-planar coordination of sulfur atoms located at the (10 $\bar{1}$ 0) edge of a single MoS₂ slab. Bouwens *et al.*²⁹ believe that a square-pyramidal surrounding of five sulfur atoms at the edges of a single MoS₂ slab is characteristic of Co, whereas Ledoux *et al.*³⁰ proposed distorted tetrahedral and octahedral coordinations for them (which followed from data obtained by ⁵⁹Co NMR).

An essentially similar model called ‘SBMS’ (sulfide bimetallic species) has been developed at the G K Boreskov Institute of Catalysis.^{8,31–35} Using modern physicochemical methods for studies of solid catalyst surfaces, it was shown that an SBMS consists of a single MoS₂(WS₂) slab with Ni(Co) atoms at its (10 $\bar{1}$ 0) edge plane. Figure 1 shows the structure of an SBMS active complex with an occluded hydrogen atom. The Ni(Co) atoms are coordinated to four sulfur atoms of the MoS₂ matrix, while the fifth coordination site is occupied by an adsorbed H₂S molecule. In such a case, the Ni(Co) atom is located in the centre of a square pyramid of sulfur atoms (the distance from the base plane to the Ni(Co) atom is 0.5 Å). The occluded hydrogen atom is located in the centre of an ‘empty’ trigonal prism of the MoS₂ sulfide matrix at a distance of 1.5 Å under the Ni(Co) atom.

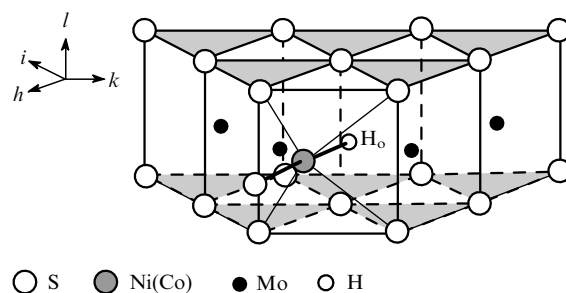


Figure 1. Structure of the active component of sulfide hydrodesulfurisation catalysts with an occluded hydrogen atom.

The bases of the trigonal prisms made of sulfur atoms, in the centres of which molybdenum atoms are located, are cross-hatched.

The SBMS model differs from other similar models in a number of points which we believe to be fundamental; they are listed below.

1. The necessary and sufficient structural element in SBMS consists of a single slab of MoS₂ (or some other disulfide that crystallises according to the molybdenite structural type) with ions of a transition metal (nickel, cobalt or any other metal that can interact with the sulfide matrix) situated at its edge plane. These ions are the catalyst active sites. This structure is also found in bimetallic sulfides ‘Ni–W–S’, ‘Cu–W–S’, ‘Ni–Nb–S’, ‘Ni–Re–S’, *etc.*, whose matrices crystallise according to the molybdenite (MoS₂) structural type.³¹

2. Hydrogen occluded during the catalyst sulfidation step is the second essential element of SBMS. It is hydrogen that defines the electronic structure of the active metal atom. The SBMS model does not make distinction between the square-planar and square-pyramidal coordination of active metal ions; these two states are transformed into each other once occluded hydrogen and adsorbed hydrogen sulfide have been eliminated.

3. The bimetallic sulfide species is an electrically neutral macromolecule.

4. The SBMS sizes on the surfaces of various supports in the most active catalysts do not exceed 10–20 Å, which means that no separate phase of this compound exists (in the crystallographic sense). Only the MoS₂ or WS₂ phase is detected by diffraction methods.

[†] A single MoS₂ slab is a sandwich in which a layer of molybdenum atoms is arranged between two layers of sulfur atoms, so that a molybdenum atom is located in the centre of a trigonal prism of sulfur atoms and every second prism remains ‘empty’.

The SBMS model was developed using highly active sulfide catalysts obtained by the synthesis of the corresponding metal-complex precursors on supports of differing nature (Al_2O_3 , SiO_2 , a new carbon material Sibunit) followed by their conversion to the sulfide form.^{36,37} The catalysts prepared by this method had uniform chemical compositions. This made it possible to obtain more reliable information about the structure of the active component and about the electronic state of the constituent metal ions. The following methods were used to study the structure of the active component: high-resolution transmission electron microscopy (HRTEM),³⁸ X-ray photoelectron spectroscopy (XPS),³⁹ X-ray radial atomic distribution,⁴⁰ EXAFS.⁴¹ In all the cases (except XPS, as explained below), the results obtained are in good agreement with the available literature data; therefore, we have the right to state that synthesis of catalysts from metal-complex precursors provides the same structure of the active component as that in catalysts prepared by traditional methods. On the other hand, the higher activity of the catalysts obtained from metal-complex precursors in comparison with those prepared by traditional methods demonstrates the superiority of systems with uniform composition of surface compounds. It can be expected that in this case all the supported metal is involved in the active component and participates in the catalytic reaction.

2. The electronic structure of the active component

The electronic structure of the transition metal atom (or ion) is a key factor determining the catalytic activity of sulfide catalysts. It is the metal electronic structure and the ligands surrounding it that determine its ability to adsorb a substrate molecule. However, the electronic structure of metal atoms in the active component of sulfide catalysts has not been considered in the literature. This stems from the complexity of the system in question and the absence of adequate models describing the state of active metal atoms.

X-Ray photoelectron spectroscopy is a main method for the study of the electronic state of metals in supported catalysts. Numerous XPS studies of complex compounds of metals with organic and inorganic ligands showed⁴² that the binding energy (E_b) of electrons on the central atom levels is a complex function of the metal oxidation state, coordination state and the nature of atoms involved in the first coordination sphere. The metal-metal chemical bond can also contribute significantly to this dependence. Nevertheless, E_b can characterise the metal oxidation state or its formal charge provided that the first coordination sphere of the metal is the same. However, studies of solid catalysts inevitably involve a number of experimental difficulties in the determination of this magnitude, as described in sufficient detail in reviews.^{43,44}

XPS was also used to study the electronic state of metals in sulfide catalysts.^{45–49} Different types of catalytic systems were studied, including bulk catalysts and catalysts on oxide (Al_2O_3 , SiO_2) and carbon (Sibunit) supports, at different steps of genesis. While the results regarding the state of Mo (or W) ions are in most cases consistent with data on bulk MoS_2 and WS_2 samples, the state of Co (or Ni) ions is a matter of discussion.⁴ This is primarily due to the non-uniform composition of surface compounds which results in broadening of XPS spectral lines.

Shortly after we started studies on sulfide catalysts prepared from organometallic precursors, we obtained quite an unexpected result:³⁹ the $\text{Ni}2p_{3/2}$ line turned out to be shifted by 1 eV towards higher binding energies in comparison with the similar line of highly dispersed nickel sulfide, which suggested an increase in the oxidation state of the Ni atom. Later, this result was reproduced with remarkable permanency for many systems, including both bulk systems⁵⁰ and those supported on alumina.⁵¹ Opponents asked a reasonable question: considering that nickel (or cobalt) should be reduced to lower oxidation states at high temperatures in a hydrogen environment, how is it possible that you observe the opposite phenomenon?

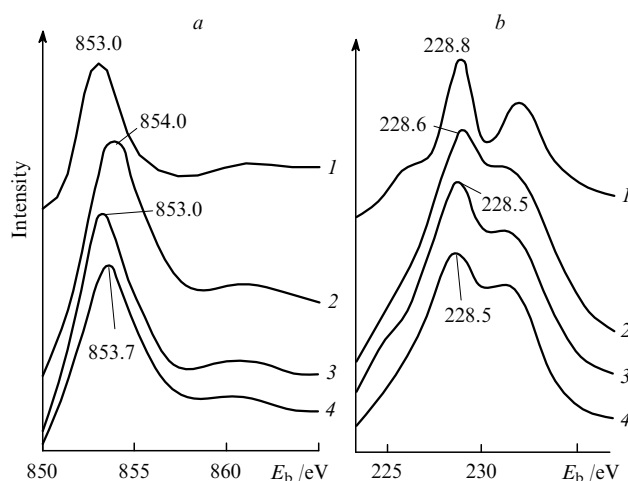


Figure 2. Electronic states of $\text{Ni}2p_{3/2}$ (a) and $\text{Mo}3d$ (b) atoms within the active component of sulfide catalysts $(\text{Ni},\text{Mo})\text{S}_x/\text{Al}_2\text{O}_3$ according to XPS data.^{52,53}

(1) Highly dispersed $\text{NiS}/\text{Al}_2\text{O}_3$ catalyst (a) and $\text{MoS}_2 + \text{Al}_2\text{O}_3$ mechanical mixture (b); (2) $(\text{Ni},\text{Mo})\text{S}_x/\text{Al}_2\text{O}_3$ catalyst sulfided *ex situ* in a stream of H_2S at 400 °C; (3) sample 2 preheated *in vacuo* at 300 °C to a residual pressure of 5×10^{-9} Torr; (4) sample 3 sulfided *in situ* in an $\text{H}_2 + \text{H}_2\text{S}$ mixture at 300 °C.

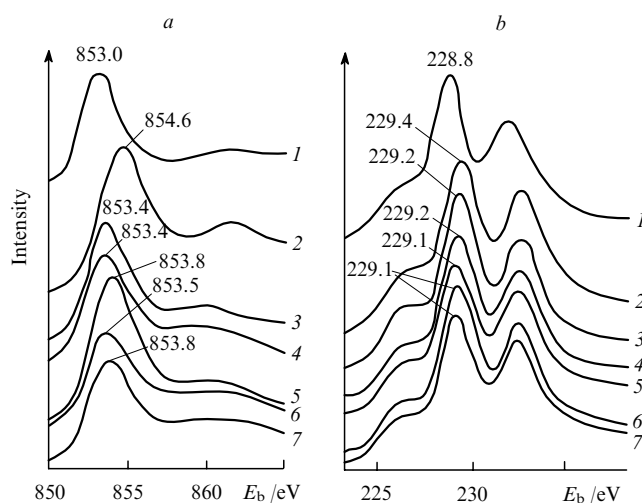


Figure 3. Electronic states of $\text{Ni}2p_{3/2}$ (a) and $\text{Mo}3d$ (b) atoms within the active component of sulfide catalysts $(\text{Ni},\text{Mo})\text{S}_x/\text{Sibunit}$ according to XPS data.^{52,53}

(1) Highly dispersed $\text{NiS}/\text{Sibunit}$ catalyst (a) and mechanical mixture $\text{MoS}_2 + \text{Sibunit}$ (b); (2) $(\text{Ni},\text{Mo})\text{S}_x/\text{Sibunit}$ catalyst sulfided *ex situ* in a stream of H_2S at 400 °C; (3) sample 2 preheated *in vacuo* at 300 °C to a residual pressure of 5×10^{-9} Torr; (4) sample 3 treated with hydrogen at 300 °C; (5) sample 4 sulfided *in situ* in an $\text{H}_2 + \text{H}_2\text{S}$ mixture at 300 °C; (6) sample 5 preheated *in vacuo* at 400 °C to a residual pressure of 5×10^{-9} Torr; (7) sample 6 sulfided *in situ* in an $\text{H}_2 + \text{H}_2\text{S}$ mixture at 300 °C.

We undertook a special study to answer this question using *in situ* XPS for sulfide (Ni,Mo) -catalysts[‡] supported on alumina and Sibunit.^{52,53} Catalysts sulfided *ex situ* were placed in the chamber of an XPS spectrometer without contact with air. The $\text{Mo}3d$ line in the spectra of $(\text{Ni},\text{Mo})\text{S}_x/\text{Al}_2\text{O}_3$ sulfide catalysts is a narrow, poorly resolved doublet. The E_b ($\text{Mo}3d_{5/2}$) value matches similar values for bulk and highly dispersed MoS_2 (Fig. 2). In the spectra of bimetallic sulfide catalysts supported on Sibunit, this line is represented by a narrow, well-resolved doublet (Fig. 3) shifted

[‡] The catalysts were obtained using metal complex precursors.

towards higher E_b values (in comparison with similar values for the bulk and highly dispersed MoS_2) due to epitaxial interaction of the active component with the surface of the conducting carbon material. It should be noted that the position of this line in the spectra of both catalysts did not change upon their thermal treatment in the spectrometer chamber (see Figs 2 and 3).

The situation with the Ni2p line is quite different. In the spectra of catalysts supported on alumina (see Fig. 2), the Ni2p_{3/2} line is rather narrow and is shifted by 1 eV towards higher E_b values in comparison with the spectrum of highly dispersed NiS. This shift is even more significant in the spectra of catalysts supported on Sibunit (see Fig. 3). After thermal treatment of sulfide catalysts in high vacuum at 300–400 °C, the Ni2p_{3/2} line shifts back towards lower binding energies so that its new position corresponds to a formal charge of 2+ on the nickel atom in highly dispersed NiS. If the sample is sulfided again in the spectrometer chamber, this line is shifted back to higher E_b values (see Figs 2 and 3). The reversible shift of the Ni2p line (see Fig. 3) implies that reduction reverts the catalyst to its original state.

When studying solid catalysts by XPS, the changes in the binding energies of electrons on inner levels of the atom of interest are often related to the impossibility of relaxation of the energy accumulated in dispersed species upon their photoionisation (see e.g., Refs 54 and 55). However, at least four counterarguments can be offered against this interpretation of results for the given catalytic system.

1. The NiS species in catalysts supported on Al_2O_3 are no larger than 10 Å (see Ref. 56). Thermal treatment of such catalysts in the chamber of an XPS spectrometer first in high vacuum and then in hydrogen actually reduces the sulfide species to the metal. It is very important that heating of reduced catalysts in an $\text{H}_2 + \text{H}_2\text{S}$ mixture does not result in the re-formation of sulfide species.⁵³

2. Thermal treatment of sulfide catalysts in the spectrometer chamber under various conditions does not change the position of the Mo3d line, whereas the position of the Ni2p line changes significantly and reversibly. Had the relaxation effect existed, similar changes in E_b would be expected for both metals.

3. An increase in E_b is also observed for bulk catalysts Ni– MoS_2 (Ni– WS_2),⁵⁰ in which the nickel atoms are situated at the edge planes of the bulk disulfide.

4. The carbon support Sibunit is a conducting material, which excludes ‘charging’ of a sample under ionising irradiation.

These arguments allow us to state that the reversible change in the E_b of electrons on the inner levels of nickel cannot be explained by any physical effect of irradiation on the object being studied. It should be interpreted as a chemical phenomenon, namely, the increase in the binding energy of electrons on the inner levels of nickel (or cobalt) should be ascribed to an unusually high oxidation state of nickel within the active component of sulfide hydrosulfurisation catalysts.

Let us try to explain why our data disagree with those obtained by other authors who studied similar systems. First, as noted above, sulfide catalysts synthesised from metal-complex precursors are characterised by high uniformity of the composition of surface species; as a result, the XPS lines become rather narrow. Second, these effects are not observed if sulfide catalysts have been exposed to air for a long time, as it is quite obvious that oxidation processes can occur in this case. It should be noted that results obtained by other researchers in experiments that took all the possible unfavourable effects into account (see, e.g., Ref. 57) are in good agreement with our data.

The possibility of existence of Ni(IV) ions with the d^6 electronic configuration was confirmed by *ab initio* theoretical studies of the $\text{Ni}(\text{S}_2\text{C}_2\text{H}_2)_2$ and $\text{Ni}(\text{S}_2\text{C}_2\text{H}_2)_2(\text{H}_2\text{S})$ complexes.^{58–60} The results obtained show that the square planar complex $\text{Ni}^{\text{II}}(\text{S}_2\text{C}_2\text{H}_2)_2$ with the d^8 electronic configuration⁶¹ is converted to a square-pyramidal Ni(IV) complex with the d^6 configuration upon adsorption of an H_2S molecule on the fifth coordination position. This is accompanied by the displacement of the nickel

atom by 0.35 Å from the plane of the four sulfur atoms. Similar conversion occurs upon adsorption of H_2S on active Ni sites within the active component. In this case, the electron density is transferred from nickel atoms to the neighbouring sulfur atoms bound to nickel, rather than to the molybdenum atom. It should be noted that this conclusion agrees with the XPS data (see Figs 2 and 3).

To explain the unusually high oxidation state of Ni, we assumed the possibility of the oxidative addition of hydrogen to a nickel ion within the active component.^{52, 62, 63} *Ab initio* calculations confirmed that the oxidative addition of hydrogen accompanied by the formation of Ni(IV) with the d^6 electronic configuration is thermodynamically favourable. It is assumed that a hydrogen molecule adds to a Ni(II) ion in a dissociative way to give a ‘surface’ hydrogen atom (H_s) and an ‘occluded’ hydrogen atom (H_o). The latter is localised in the matrix of the active component under the nickel atom, in the centre of an ‘empty’ trigonal prism formed by six sulfur atoms (see Fig. 1).

The concept of the oxidative addition of hydrogen to the nickel atom within the active component allows us to explain the XPS data presented above. In fact, *ex situ* evacuation of a sulfided sample at elevated temperature should remove occluded hydrogen due to reductive elimination to give Ni(II). Treatment with an $\text{H}_2 + \text{H}_2\text{S}$ mixture results in the oxidative addition of hydrogen; as a result, the Ni2p line is displaced towards higher binding energies. Prolonged exposure of samples to air can result in the oxidation of occluded hydrogen.

The first compound containing Ni(IV) ions was obtained more than 90 years ago.⁶⁴ It was the heteropolymolybdate anion $[\text{NiMo}_9\text{O}_{32}]^{6-}$. It is important for the existence of nickel in the high oxidation state that the number and electronegativity of the ligands surrounding the nickel atom be sufficiently high. The Ni(IV) cation in the complex mentioned above is located in a pseudo-octahedral coordination of oxygen atoms and has a d^6 electronic configuration. All the known Ni(IV) complexes are diamagnetic and tend to have an octahedral coordination.^{65, 66} Of other Ni(IV) compounds, the following inorganic compounds deserve mentioning: K_2NiF_6 , BaNiO_3 , NiO_2 , NaNiO_6 , NiAs_2 , etc. (see Ref. 67).

3. Substantiation of the possibility of oxidative addition of hydrogen in heterogeneous catalysis

Since at present there are no direct experimental methods for studying the nature of transient species formed upon adsorption of the starting reagents on the sites of heterogeneous catalysts, we will refer to analogies in the structures and mechanisms of action of homogeneous catalysts in order to explain the possibility of oxidative addition of hydrogen to these sites, although the conditions of the corresponding processes (temperature, pressure, presence of a solvent) differ considerably. Our approach is based on the concept of the common nature of the homogeneous, heterogeneous and enzyme catalysis.^{68–71}

The oxidative addition of hydrogen to square-planar Ir(I) complexes was discovered over 40 years ago⁷² and is now one of the key reactions in homogeneous catalysis.⁷³ In particular, it is well known that this reaction is the first step in the formation of active sites on catalysts for alkene hydrogenation.⁷⁴ In such a case, hydrogen acts as a unique molecule that simultaneously displays both reducing and oxidising properties under the same catalytic reaction conditions.

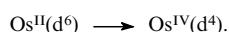
The oxidative addition of hydrogen is a particular case of the addition of neutral molecules XY to transition metal compounds with free coordination centres. The molecule XY is reduced in this reaction to give two anionic ligands X^- and Y^- , whereas the metal is oxidised. One of the examples best known is the oxidative addition of hydrocarbons $\text{R}-\text{H}$ to complexes of M(0) metals discovered by Shilov;^{75, 76} this reaction is accompanied by an increase in the formal oxidation state of the metal by two units and formation of alkyl hydride complexes. Since alkyl and hydride

ligands are very strong reducing agents, stable reaction products contain metals in low oxidation states only.

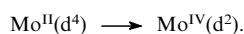
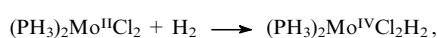
Numerous examples of the oxidative addition of hydrogen to various transition metals are currently known.⁷³ Two types of oxidative addition of hydrogen, *viz.*, two- and single-electron addition, are distinguished. In the study mentioned above,⁷² the oxidative addition of hydrogen resulted in the formal transformation of Ir(I) (d^8 electronic configuration) into Ir(III) (d^6 configuration):



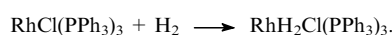
The addition of hydrogen to metals in higher oxidation states, *e.g.*, to Os(II), is also known:⁷⁷



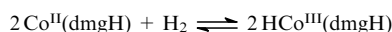
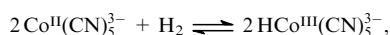
The oxidative addition of hydrogen can also involve Group VI metals, *e.g.*, Mo(II):⁷⁸



A typical example of the two-electron hydrogen addition to square-planar complexes is the synthesis of the Wilkinson catalysts:⁷⁹



It is important to note that the oxidative addition occurs readily if the coordination sphere of the metal comprises donor molecules such as PPh_3 , PBu_3 and the like. In the reactions considered above, the formal oxidation state of the metal and its coordination number increase by two units. Examples of the single-electron oxidative addition of hydrogen, *e.g.*, to Co(II) [$\text{Co}^{\text{II}}(d^7) \longrightarrow \text{Co}^{\text{III}}(d^6)$], are also known.^{80, 81}

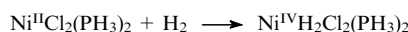


dmg is dimethylglyoxime.

The latter reaction is typical of square-planar complexes that have a pronounced tendency towards oxidative addition.

Because the possibility of oxidative addition of hydrogen to an active metal atom within the active component of sulfide catalysts was only shown by non-empirical quantum-chemical methods, it was desirable to confirm the validity of this conclusion for known structures. The square-planar complex $\text{NiCl}_2(\text{PH}_3)_2$ with the d^8 electronic configuration of the central atom was selected for this purpose.⁶² The calculation details are described in our publications.^{58–60, 62, 63}

In this kind of theoretical calculations, the change in the system free energy upon formation of a new chemical compound is the main validity criterion. For example, a theoretical study⁸² showed that the oxidative addition of hydrogen to the structural analogues $\text{PtCl}_2(\text{PH}_3)_2$ and $\text{PdCl}_2(\text{PH}_3)_2$ results in an energy decrease (ΔE) by -32.2 and -67.8 kJ mol⁻¹, respectively. In the reaction



the ΔE value was found to be -52.4 kJ mol⁻¹ (see Refs 61 and 62). The geometric structure of the complex obtained was optimised totally; the interatomic distances and bond angles are shown in Fig. 4.

The electronic state of nickel on transition from a square-planar $\text{Ni}^{\text{II}}(d^8)$ complex to an octahedral $\text{Ni}^{\text{IV}}(d^6)$ complex is shown in a correlation diagram (Fig. 5). As follows from the calculations, the oxidative addition of hydrogen results in a considerable destabilisation of the nickel d_{z^2} orbital, whereas the

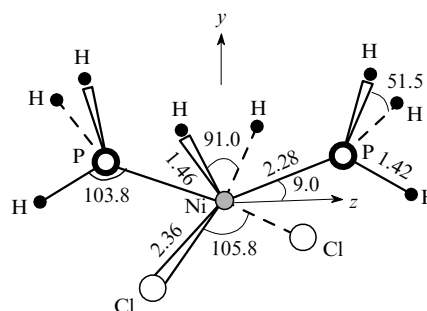


Figure 4. Geometric structure of the d^6 complex $\text{Ni}^{\text{IV}}\text{H}_2\text{Cl}_2(\text{PH}_3)_2$ totally optimised at the MP2 level (C_{2v} symmetry).⁶³ The bond lengths and angles are specified in angstroms and degrees, respectively.

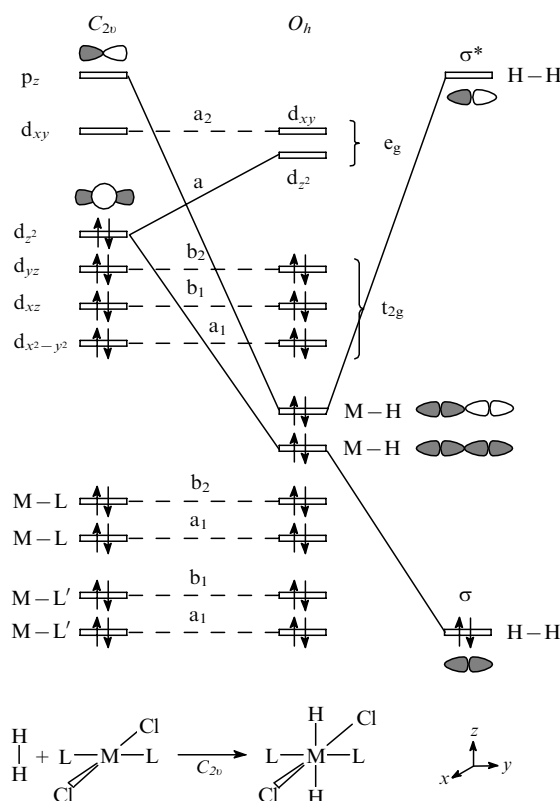


Figure 5. Correlation diagram of oxidative addition of hydrogen to the square-planar complex $\text{Ni}^{\text{II}}\text{Cl}_2(\text{PH}_3)_2$ in the d^8 electronic configuration.⁶⁵ The coordinate of the $\text{H}_2 + \text{M}(d^8)\text{L}_2\text{Cl}_2 \rightarrow \text{M}(d^6)\text{L}_2\text{Cl}_2\text{H}_2$ reaction maintains the C_{2v} symmetry.

$4p$ orbital stabilises due to the formation of a Ni–H bond. Thus, the d_{xy} and d_{z^2} orbitals become formally vacant, whereas the electron density on the Ni4s and Ni4p orbitals increases. The binding energy of electrons on the Ni2p level was calculated using this correlation diagram.⁶³ It was found to be 1.5 eV lower for Ni(II) than for Ni(IV). This result agrees very well with experimental results for nickel metal complexes⁸³ and with X-ray photoelectron spectra of sulfide catalysts.^{39, 50–53, 57}

Such a good agreement allowed us to use the same quantum-chemical methods for the analysis of the electronic states of nickel and cobalt within the active component of sulfide catalysts.

Calculations were carried out for the $\text{Ni}(\text{Co})\text{Mo}_2\text{S}_{10}\text{H}_{10}$ cluster, which has the following characteristic features:^{63, 84}

(1) this cluster is a fragment of the active component's structure, the interatomic distances in which were found experimentally by EXAFS;^{85–87}

(2) the Ni(Co) atom is located at the vertex of a square pyramid formed by four sulfur atoms; the pyramid height is 0.5 Å^{85–87} (Figs 6 and 7);

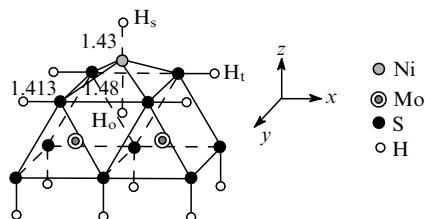


Figure 6. Quantum-chemical model of the $\text{NiMo}_2\text{S}_{10}\text{H}_{10}$ cluster after oxidative addition of a hydrogen molecule to a nickel atom (the bond lengths are indicated in Å).⁶³

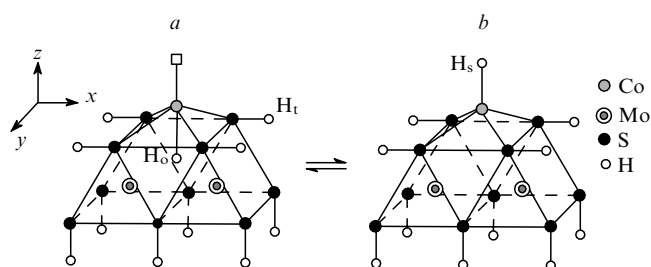


Figure 7. Quantum-chemical model of an $(\text{H})\text{CoMo}_2\text{S}_{10}\text{H}_{10}$ cluster [the active site is Co(III) in the d^6 electronic configuration] in Co/MoS₂ catalyst with occluded (a) and adsorbed (b) hydrogen.

□ — vacant coordination site.

(3) the stoichiometry of this cluster differs from MoS₂, but the calculated charges on Mo and S are ‘stoichiometric’ due to the compensation of the free valence bonds of sulfur atoms by terminal hydrogen atoms.⁸⁸

Non-empirical calculations were carried out using the Gaussian 92 quantum-chemical computational complex⁸⁹ at the Hartree–Fock method (HF), the Müller–Plesset perturbation theory (MP2) and the density functional theory (DFT) levels.

Dissociative adsorption of a hydrogen molecule on nickel atoms within the active component results in the formation of a complex containing an adsorbed (H_s) and an occluded (H_o) hydrogen atom (see Fig. 6) and in a considerable decrease in the calculated energy of the system ($\Delta E = -192.9 \text{ kJ mol}^{-1}$). The optimised interatomic distances $\text{Ni}-\text{H}_s$ and $\text{Ni}-\text{H}_o$ are 1.43 and 1.48 Å, respectively. The calculated formal charges on these atoms suggest that surface hydrogen H_s is more ‘acidic’ ($q = +0.16$) than occluded hydrogen H_o ($q = -0.42$). The oxidative addition of a hydrogen molecule results in a considerable increase in the formal charge on nickel (from +0.45 to +0.79) due to the covalent binding of nickel ions to the sulfur ions in the pyramid base. Two important circumstances should be emphasised in this connection:

(1) the electron density is partially transferred from the nickel atoms to the sulfur atoms bound to them rather than to the molybdenum atoms as one could expect; this result is in good agreement with XPS data (see the previous section);

(2) the d_{z^2} and d_{xy} orbitals of nickel (in the coordinate system used in Fig. 6) become formally ‘vacant’, and, as shown below, it is these orbitals that participate in the adsorption of donor molecules.

A similar situation is observed in the oxidative addition of hydrogen to Co(II) ions within the active component (see Fig. 7). Zakharov and Startsev⁸⁴ calculated the thermodynamic probability of the formation of surface and occluded hydrogen. *Ab initio* calculations showed that the total decrease in the free energy is

approximately the same in both cases shown in Fig. 7; therefore, it can be stated with a high degree of certainty that if hydrogen adsorption is possible, then its occlusion into the active component matrix should occur with the same probability. The optimised interatomic distances $\text{Co}-\text{H}_o$ and $\text{Co}-\text{H}_s$ are 1.52 and 1.42 Å, respectively.

It follows from *ab initio* calculations that an important role in the stabilisation of the electronic state of Ni(IV) and Co(III) within the active component belongs to the hydrogen sulfide molecule adsorbed on the active metal atom. The interaction scheme of the orbitals of a donor H_2S molecule with vacant orbitals of Co(III) is presented in Fig. 8 [this scheme also applies to Ni(IV)]. The calculated heats of adsorption of hydrogen sulfide on Ni and Co sites are 82.6 and 69.6 kJ mol^{-1} , respectively,^{67,84} whereas the heat of adsorption of hydrogen sulfide on Ni(II) is as small as 36.0 kJ mol^{-1} (see Ref. 67). Due to the difference in the heats of adsorption of the H_2S molecule on Ni(II) and Ni(IV) sites, the equilibrium bond lengths $\text{Ni}^{\text{II}}-\text{S}$ and $\text{Ni}^{\text{IV}}-\text{S}$ are different (2.77 and 2.60 Å, respectively).⁶⁷

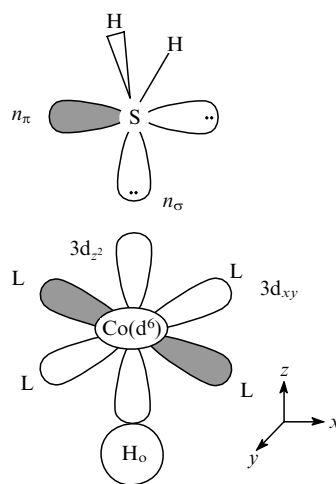


Figure 8. Scheme of interaction of n_σ and n_π orbitals of a hydrogen sulfide molecule with $3d_{z^2}$ and $3d_{xy}$ orbitals of the Co(III) atom in the d^6 electronic configuration.

4. Experimental proof of the existence of occluded hydrogen

Since direct experimental proof of the existence of occluded hydrogen is absent in the literature, let us try to analyse numerous data available on the $\text{MoS}_2 + \text{H}_2$ system in order to obtain information about the state of hydrogen in this system. We will pay attention to whether or not particular experimental data are consistent with the concept of the existence of occluded hydrogen.

The considerable adsorption of hydrogen by bulk molybdenum disulfide was probably first noted by Badger *et al.*⁹⁰ At 140 °C and 1 atm, the quantity of hydrogen retained by the sample is 0.37 mol of H_2 per mol of MoS_2 , which is much higher than that corresponding to the monolayer coverage. It was shown^{91–94} that the quantity of hydrogen adsorbed by bulk MoS_2 and WS_2 at 300–400 °C is at least three times higher than that in the case of monolayer coverage (the latter was measured using the adsorption of N_2 and CO_2). If MoS_2 is supported on alumina, the quantity of adsorbed hydrogen increases considerably.^{95–98} Since the layered packing of molybdenum disulfide is irregular in this case, Jalowiecki *et al.*^{96,97} assumed that spillover of hydrogen from MoS_2 to the surface of the support occurs. The latter serves as a ‘reservoir for hydrogen storage’.⁹⁷ Some other aspects of hydrogen sorption by bulk and supported molybdenum sulfide were described in a review by Moyes.⁹⁹

However, the existence of 'excessive' hydrogen in sulfide catalysts can also be explained from a different standpoint. Let us consider the strength of hydrogen binding to catalysts, which can easily be evaluated from the temperature at which hydrogen appears in the gas phase during the temperature-programmed heating (TPH) of catalysts. Erofeev and Kaletchits^{100, 101} were the first to discover strongly bound hydrogen which was desorbed from Co–Mo sulfide catalysts at temperatures above 400 °C. Hoodless *et al.*¹⁰² showed the presence of both weakly and strongly bound hydrogen in bulk MoS₂ (the total hydrogen content corresponded to the formula H_{0.027}MoS₂). If cobalt was introduced in a MoS₂ sample, the peak of hydrogen evolution shifted towards higher temperatures; at the optimum catalyst composition, the maximum hydrogen desorption was observed at 600 °C (the hydrogen content in the catalysts corresponded to the formula H_{0.015}Co_{0.8}MoS₂). Similar results were later obtained by other authors.^{103–107}

We undertook a study of the forms of hydrogen desorption from sulfide catalysts in the TPH mode (Fig. 9).¹⁰⁸ The catalysts were prepared by supporting metal-complex precursors on alumina followed by sulfidation of the samples in a stream of H₂S at

400 °C. There are two regions in which hydrogen is removed from all the catalysts studied: a low-temperature region (desorption temperatures up to 500 °C) and a high-temperature region. Weakly bound hydrogen is removed in the low-temperature region, whereas strongly bound hydrogen is removed in the high-temperature region. After removal of hydrogen from the catalysts in the TPH mode at temperatures up to 750 °C, the samples were again sulfided portionwise with H₂S at 400 °C and re-desorption was carried out in the TPH mode (see Fig. 9, curves 2). It was found that re-sulfided samples did not contain strongly bound hydrogen.

We believe that the strongly bound hydrogen is the hydrogen occluded in the sulfide matrix. In fact, every second trigonal prism built of sulfur atoms in the structure of molybdenum disulfide (see Figs 1 and 10) is 'empty'. If we subtract the ionic radius of S^{2–} (1.58 Å) from the interatomic distance Mo–S (2.41 Å), we obtain the radius of the 'empty' space (0.83 Å), which is slightly longer than the H–H distance in the hydrogen molecule (0.74 Å). Thus, the introduction of a hydrogen atom or even a hydrogen molecule into this space will not distort the structure of molybdenum disulfide. *Ab initio* calculations of the active component structure with an occluded hydrogen atom showed^{62, 84} that the optimised interatomic distances Ni–H_o (1.48 Å) and Co–H_o (1.52 Å) correspond to covalent binding. It is easy to show that these 'optimised' distances coincide with those calculated from the geometric structure of molybdenum disulfide.

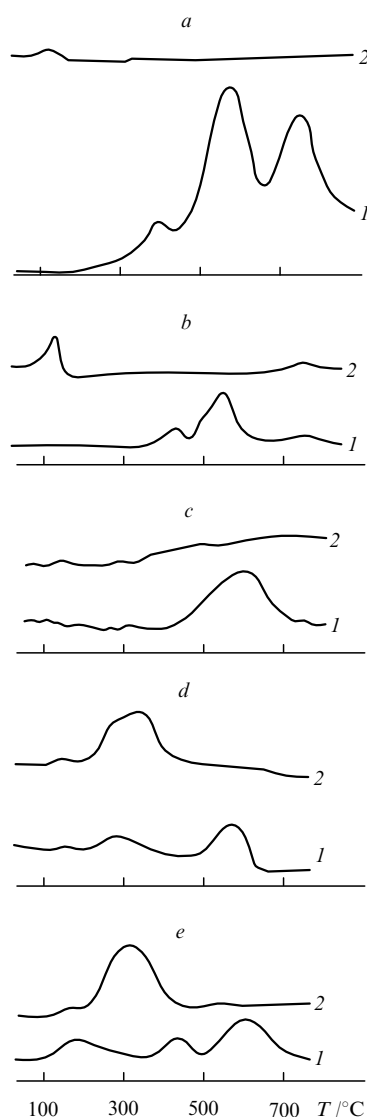


Figure 9. Desorption of hydrogen from sulfide catalysts.¹⁰⁸ (1) Catalysts sulfided *in situ* in a stream of H₂S at 400 °C; (2) the same samples sulfided after TPH with portions of H₂S at 400 °C. Catalysts: (a) 3.0 Co/Al₂O₃, (b) 3.0 Ni/Al₂O₃, (c) 7.1 Mo/Al₂O₃, (d) 1.6 Co + 7.5 Mo/Al₂O₃, (e) 1.6 Ni + 7.1 Mo/Al₂O₃.

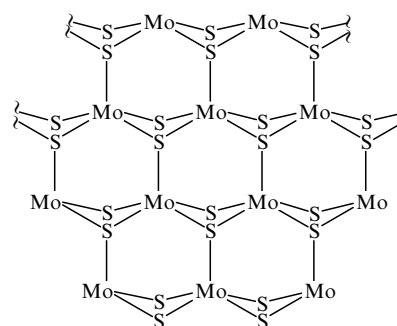


Figure 10. An electrically neutral (MoS₂)_x macromolecule.

The term 'occluded hydrogen'[§] in relation to sulfide catalysts was introduced because of the necessity to emphasise its specific role in the formation and functioning of the active component. Let us note the most important properties of occluded hydrogen:

- (1) strong bonding to the active component matrix (occluded hydrogen is removed only at temperatures much higher than those of typical catalytic reactions);
- (2) localisation only on specific sites of the active component matrix [unlike dissolved (absorbed) hydrogen];
- (3) interaction with surface metal atoms, owing to which occluded hydrogen favours the creation of an 'active' electronic configuration of these atoms (it is this configuration that determines the catalytic and adsorption properties of the active component);
- (4) oxidative properties (occluded hydrogen appears due to the oxidative addition of hydrogen to an active metal atom at the step of formation of the active component and therefore plays the role of an oxidant).

Hexagonal layered disulfide H_{0.76}NbS₂, which crystallises in the molybdenite structural type (Table 1), is one of the few

[§] Occlusio (Latin) means locking, hiding; occlude (English) — to close, seal. In metallurgy, the term 'occlusion' means dissolution of gases in solid or molten metals. In chemistry, there are synonyms for this word: absorption and dissolution.

Table 1. Crystallographic data on the structure of hexagonal NbS₂ with and without occluded hydrogen. The corresponding parameters of hexagonal single-crystal MoS₂ are shown for comparison.

System	Space group	Unit cell parameters /Å		Volume /Å ³	Bond lengths /Å				Ref.
		<i>a</i> = <i>b</i>	<i>c</i>		M–H	S–H	M–S	M–M	
NbS ₂	<i>P6₃/mmc</i> (<i>D</i> _{6h} ⁴)	3.320(1)	11.945(4)	114.02	—	—	2.467	3.320	109
H _{0.76} NbS ₂	<i>P6₃/mmc</i>	3.34(7)	12.39(5)	119.7	1.928(6)	2.51(1)	2.51(1)	3.34(7)	110
MoS ₂	<i>P6₃/mmc</i> (<i>D</i> _{6h} ⁴)	3.1602(1)	12.294(4)	—	—	—	2.42	3.16	111

systems where the presence of occluded hydrogen has been proved experimentally.^{109–111} The neutron diffraction method was used to study the structure of a single crystal of this disulfide and to determine the hydrogen atom coordinates.¹¹⁰ The latter indicate that this atom is situated in the centre of an ‘empty’ trigonal prism formed by six sulfur atoms. It was found that the hydrogen atom is located in the centre of the triangle formed by niobium atoms (the Nb–H distances are ~1.93 Å). One can see from Table 1 that the structure of niobium disulfide¹⁰⁹ undergoes minor changes upon hydrogen occlusion: the unit cell volume and the interatomic distances Nb–S and Nb–Nb increase slightly. This proves that atomic hydrogen introduced in the centre of an ‘empty’ trigonal prism does not distort the structure of the disulfide. Similar results, albeit with less unambiguous conclusions, were previously obtained by the same research group¹¹² for the H_xTaS₂ system.

Let us compare the vibration frequencies of occluded hydrogen calculated by non-empirical methods with literature data

obtained by different spectroscopic methods (Table 2). The stretching vibrations of the S–H bonds in H_xMoS₂ lie in the region 2450–2650 cm^{−1} (see Ref. 113), which corresponds to the similar parameters for pure compounds containing thiol groups.¹¹⁴ Inelastic neutron scattering (INS) spectra of a H_{0.5}TaS₂ sample contained¹¹² a band at 744 cm^{−1}, which was assigned to the deformation vibrations of the Ta–S–H group. It was concluded that this compound was non-stoichiometric covalent tantalum hydrosulfide. However, the absence of bands of the stretching vibrations of the S–H bonds casts doubt on the validity of this assignment. A similar band was found by Wright and co-workers¹¹⁰ in the spectra of an H_{0.76}NbS₂ sample. Of the three possible variants of assigning this band, deformation vibrations of the Nb–H bond in the direction parallel to axis *c* were preferred. The INS method was later used to study the H_xMoS₂ and H_xWS₂ systems.^{91–94} The absence of structural data for these systems made Wright and co-workers be very careful when

Table 2. Fundamental vibration frequencies of hydrogen in sulfide catalysts and their assignments (literature data).

Catalyst	Spectroscopic method ^a	Hydrogen adsorption conditions	Vibration frequencies /cm ^{−1}	Assignment	Ref.
H _x MoS ₂	IR	200 °C	2516 (broad)	—	113
		200 °C with subsequent evacuation	2649	—	
		at 300 °C	2532	<i>ν</i> _{S–H} ^b	
			2454	—	
H _{0.5} TaS ₂	INS	electrochemical reduction	744	<i>δ</i> _{Ta–S–H} ^c	112
H _{0.76} NbS ₂	INS	the same	2600	—	110
			1544	—	
			744	<i>δ</i> _{Nb₃–H}	
H _x WS ₂	INS	400 °C	2659	<i>ν</i> _{S–H}	94
			2470	<i>ν</i> _{S–H}	
			694	<i>δ</i> _{S–H}	
H _{0.067} MoS ₂	INS	300 °C, 0.9 atm	1977	—	91
			1348	—	
			847	—	
			662	—	
H _x MoS ₂	INS	room temperature, 1 atm	872	<i>δ</i> _{Mo–S–H} , <i>δ</i> _{Mo–H}	92
			662	<i>δ</i> _{S–H}	
		room temperature, 70 atm ^d	872	<i>δ</i> _{Mo–S–H} , <i>δ</i> _{Mo–H}	
			662	<i>δ</i> _{S–H}	
			~400	?	
H _x MoS ₂ /Al ₂ O ₃	INS	300 °C, 0.9 atm	960	—	91
			686	—	
			400	—	
H _x NiMoS ₂	INS	adsorption at 1–30 atm, desorption <i>in vacuo</i> at 200–400 °C	1895	<i>ν</i> _{Ni–H}	115
			795	?	
			650	<i>δ</i> _{S–H}	
H _x CoMoS ₂	CNS	H ₂ + H ₂ S, then H ₂ at 800 °C	1392 ± 26	—	116

^a INS is inelastic neutron scattering, CNS is Compton neutron scattering. ^b The vibration frequencies of the S–H bond in gaseous H₂S, thiophene and thiols are 2668, 2550 and 2550–2650 cm^{−1}, respectively (see Ref. 114). ^c The stretching vibration bands of the S–H bonds are absent. ^d The results obtained were interpreted as evidence of activated adsorption and formation of intercalated hydrogen.

assigning the observed absorption bands. However, they noted the following facts: (1) treatment of sulfide catalysts with hydrogen at 300–400 °C resulted in the appearance of bands corresponding to the stretching vibrations of the S–H bonds, whereas these bonds were not observed at low temperatures; (2) the bands at ~ 870 and ~ 660 cm^{-1} were observed in the spectra of samples which did not contain bands corresponding to the stretching vibrations of the S–H bonds, hence they should be assigned to other types of vibration [e.g., the former band may be assigned to the deformation vibrations of the M–H bond, whereas the latter, to the deformation vibrations of the H–S₃ bond (vibrations of the hydrogen atom located in the centre of the triangle of S atoms) within the molybdenum disulfide matrix].

Anderson *et al.*¹¹⁷ employed the semiempirical molecular orbital method ASED-MO[¶] to calculate the vibration frequencies of hydrogen in the H_xMoS₂ matrix (Table 3). A comparison of data in Tables 2 and 3 shows that the band around ~ 870 cm^{-1} can be assigned to the deformation vibrations of occluded hydrogen located in the centre of the triangle of molybdenum atoms, and hence in the centre of the ‘empty’ trigonal prism of sulfur atoms. The calculated bond length Mo–H (1.82 Å) totally agrees with the structural characteristics of molybdenum disulfide, hence the results obtained may be considered rather reliable.

Table 3. Vibration frequencies of hydrogen in a MoS₂ matrix calculated by the ASED-MO method.¹¹⁷

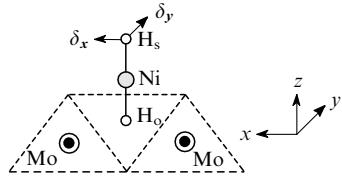
Bond type	Vibration frequency / cm^{-1}	
	stretching	deformation
H–S (basal)	2347	432
H–S (side)	2292	492, 583
H–S (angular)	2190	621
H–Mo ^{IV}	1901	519
H–Mo ^{II}	1948	224
H–Mo ₃ (see ^a)	–	865

^a Vertical vibrations of hydrogen in the centre of a triangle of molybdenum atoms.

Very few spectroscopic studies of hydrogen adsorption by bimetallic sulfide catalysts are known. In their meticulous study, Sandberg *et al.*¹¹⁵ carried out hydrogen adsorption at high pressure; subsequently, the samples were evacuated at 200–400 °C and studied using the INS method (see Table 2). Thus, the study was aimed at the ‘residual’, strongly bound hydrogen which is not removed at temperatures above the catalytic reaction temperature. The band at 650 cm^{-1} was assigned to the deformation vibrations of the S–H groups, although the spectra did not contain bands corresponding to the stretching vibrations of these groups and the preparation conditions of the samples favoured, most likely, the elimination of the SH groups from the surface. The broad band with a maximum at 795 cm^{-1} overlaps the band of stretching vibrations of the S–H bonds and the band of vibrations of hydrogen atoms in Raney nickel (950 cm^{-1}). The second broad band at 1895 cm^{-1} was assigned to the stretching vibrations of the Ni–H bond, although vibrations of hydride bonds in metal complexes have frequencies above 1970 cm^{-1} , and those in Raney nickel are equal to 2070 cm^{-1} .

In order to reveal the nature of hydrogen bonding in Ni–Mo sulfide catalysts, we calculated⁶² the frequencies of the stretching and deformation vibrations for adsorbed and occluded hydrogen atoms in the NiMo₂S₁₀H₁₀ structure (see Fig. 6). As one can see from Table 4, the band at 1895 cm^{-1} in the INS spectra

Table 4. Vibration frequencies and intensities of adsorbed and occluded hydrogen atoms in the active component of Ni–Mo sulfide catalysts calculated by non-empirical methods.⁶²



Vibration	Vibration frequency / cm^{-1}		Intensity (arb. units)
	calculated	found	
ν_z^s	1890.0	1895.0	174.0
ν_z^{as}	2010.0		124.5
$\delta_x(\text{H}_s)$	704.0		28.4
$\delta_y(\text{H}_s)$	834.0	795.0	45.8
$\delta_x(\text{H}_o)$	2062.0		339.2
$\delta_y(\text{H}_o)$	926.0		12.9

(see Ref. 115) is in good agreement with the deformation vibrations of the H_o–Ni–H_s fragment, whereas the band at 795 cm^{-1} can be assigned to the deformation vibrations of hydrogen adsorbed on nickel. Thus, the vibration frequencies of adsorbed and occluded hydrogen atoms that we have calculated are in better agreement with experimental data than the assignments made by Sandberg *et al.*¹¹⁵

Based on measurements of the mean kinetic energy of hydrogen in Co–Mo sulfide catalysts by Compton neutron scattering,¹¹⁶ the mean vibration frequency of hydrogen in these catalysts was calculated to be 1392 cm^{-1} (see Table 2). The arithmetic mean frequency of the stretching and deformation vibrations of the S–H bond was found to be 1270–1310 cm^{-1} . Based on this, Mitchell *et al.*¹¹⁶ concluded that hydrogen in these catalysts is bound to sulfur atoms because the M–H_s bond frequencies are much lower (~ 1100 cm^{-1}).

We calculated the vibration frequencies for adsorbed and occluded hydrogen on Co–Mo sulfide catalysts⁸⁴ in the coordinate system shown in Fig. 7. The following results were obtained: for Co–H_s, $\nu = 1972$ cm^{-1} and $\delta_x \approx \delta_y = 652$ cm^{-1} ; for Co–H_o, $\nu = 1696$ cm^{-1} , $\delta_x = 1764$ cm^{-1} and $\delta_y = 880$ cm^{-1} .

The calculated mean vibration frequency of adsorbed hydrogen in Co–H_s is 1092 cm^{-1} and that of occluded hydrogen in Co–H_o is 1447 cm^{-1} , which also agrees satisfactorily with the reported data.¹¹⁶

Thus, the spectral characteristics, considered in this section, of hydrogen in sulfide catalysts do not contradict the hypothesis of the existence of occluded hydrogen in these systems but even confirm it. To prove explicitly the existence of occluded hydrogen, it was necessary to perform directed experimental studies of sulfide catalysts with the same chemical composition and structure, either containing or not containing such hydrogen. The first steps in this direction have already been taken. For example, Shalagina *et al.*¹⁰⁸ were the first to obtain this type of sulfide catalysts.

III. The concerted mechanism of thiophene hydrogenolysis on sulfide catalysts

Synchronous (concerted) mechanisms play a key role in enzyme catalysis. Publications on homogeneous and heterogeneous catalysis in which the concerted mechanism of catalytic transformations is also assumed appear currently with increasing frequency.^{68–71} Numerous examples of concerted mechanisms in acid-base reactions were considered in a number of papers.^{68, 69, 71} Such catalytic transformations are possible if the acidic and basic sites of the catalyst act in a concerted way, provided that they are sufficiently close to each other and are oriented strictly in such a

[¶] Atom Superposition and Electron Delocalisation Molecular Orbital.

manner that the substrate coordination becomes favourable for catalysis. In such a case, the high rate of catalytic transformation is ensured by synchronous proton transfer along a system of chemical and hydrogen bonds in cyclic intermediate structures. There are also examples of concerted mechanisms in heterogeneous catalysis involving molecular oxygen.^{118–121} Concerted mechanisms are characterised by low activation energies (E_a) and high process selectivity.

Hydrogenolysis of thiophene on sulfide catalysts is the best-studied reaction involving a concerted mechanism.

The main regularities of thiophene hydrogenolysis on bimetallic sulfide catalysts have been considered in detail in a number of reviews;^{8,31–35} let us note just the most important specific features of this reaction.

1. Hydrogenolysis of thiophene on bimetallic sulfide catalysts is characterised by low activation energies, *viz.*, 42–63 kJ mol^{−1} in the temperature range 300–400 °C. Modification of catalysts with phosphorus or fluorine decreases the E_a value to 30 kJ mol^{−1}. Even for sulfide catalysts with non-optimum chemical composition (Ni–Nb, Ni–Re, Cu–W) where the reaction rates are low, the E_a values for different metal pairs also range within 38–63 kJ mol^{−1}.

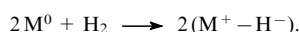
2. The thiophene hydrogenolysis on bimetallic sulfide catalysts with any chemical composition is characterised by high selectivity: four hydrogen molecules are added at once to one thiophene molecule, so, no products of partial hydrogenation of the thiophene ring (in particular, butadiene) appear in the gas phase. Butenes are the only real intermediates; the fraction of butenes in the resulting mixture with butane is the lower the higher the catalyst activity.

These two features serve as a weighty argument that the thiophene hydrogenolysis mechanism should be concerted. Below we describe the mechanism that we suggested for the activation of hydrogen and thiophene molecules and for the transfer of activated hydrogen to an adsorbed thiophene molecule.

1. The mechanism of activation of molecular hydrogen on sulfide catalysts

Hydrogen is the main ‘character’ in all processes of hydrotreatment of oil fractions; however, there are very few studies on the mechanism of its activation on sulfide catalysts. As a rule, the authors confine themselves to general guesswork without a theoretical substantiation of the interaction of hydrogen with sulfide catalyst surfaces. This happens because few appropriate physicochemical methods are available for *in situ* studies of the adsorption and activation of hydrogen on real catalysts and under real process conditions. On the other hand, the hydrogen activation mechanism has been studied rather thoroughly in homogeneous catalysis. Our subsequent consideration will be based on the concept that the nature of heterogeneous catalysis is the same as that of homogeneous catalysis.

The activation of molecular hydrogen can occur either as a result of its oxidative addition or homolytic and heterolytic cleavage.¹²² However, the homolytic activation of a hydrogen molecule on the surfaces of metallic catalysts can be regarded as a particular case of the hydrogen oxidative addition.⁷³ Each metal atom in the catalyst bulk is surrounded by neighbours on all sides, whereas surface atoms possess free coordination places; therefore, the adsorption of molecular hydrogen on the surface is accompanied by its dissociation (Fig. 11). The liberation of energy upon formation of two metal–hydrogen bonds serves as the driving force of the hydrogen addition to the metal. From the chemical viewpoint, this process can formally be represented as



The thermodynamic parameters of hydrogen activation on metals are listed in Table 5. The change in the free energy upon the homolytic (dissociative) adsorption of a hydrogen molecule on metals at room temperature is $-(25–109)$ kJ mol^{−1}. To estimate

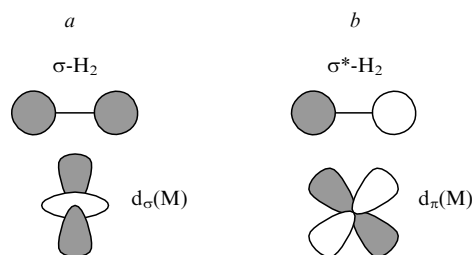


Figure 11. The scheme of interaction between molecular orbitals in the homolytic activation of hydrogen at a metal catalyst surface: (a) HOMO, (b) LUMO.

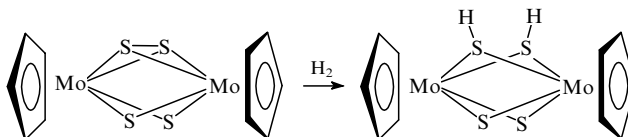
whether heterolytic dissociation of molecular hydrogen on sulfide catalysts is thermodynamically possible, we used the available thermochemical data.¹²³ As follows from Table 5, the change in free energy is $-(34–117)$ kJ mol^{−1} at temperatures within 300–400 °C typical of catalytic reactions. Thus, there is a reason to believe that the heterolytic activation of a hydrogen molecule on sulfide catalysts is as efficient as the homolytic activation on metals.

Table 5. Some thermodynamic parameters of the activation of a hydrogen molecule on metals and sulfides (a thermochemical estimate).

Parameter	Homolytic activation on metals ¹²²	Heterolytic activation on sulfide catalysts ¹²³
Bond energy, H–H /kJ mol ^{−1}	436	—
Bond energy, M–H /kJ mol ^{−1}	251–293	335–377
Bond energy, S–H /kJ mol ^{−1}	—	210–251
Enthalpy, ΔH° (experimental value) /kJ mol ^{−1}	−(67–151)	−(109–456)
Entropy, ΔS° (estimate) /J mol ^{−1} deg ^{−1}	−147	−126
$-T\Delta S^\circ$ /kJ mol ^{−1}	42 (at 300 K)	75 (at 600 K)
Free energy change, ΔG° /kJ mol ^{−1}	−(25–109)	−(34–117)

However, one should not reject the mechanism of homolytic activation of molecular hydrogen on sulfide catalysts involving terminal sulfur atoms. In fact, it is evident from Fig. 10 that the edges of a single slab of an electrically neutral MoS₂ macro-molecule are restricted by either (10 $\bar{1}$ 0) or (30 $\bar{3}$ 0) planes. In the former case, the edge is represented by coordinatively unsaturated sulfur atoms; in the latter case, by molybdenum atoms. Taking the principle of electric neutrality into account, it can be stated that free valence bonds of peripheral sulfur atoms can participate in the formation of pairwise S–S bonds, whereas the excess electron density will be delocalised on peripheral molybdenum atoms; these effects can result in the formal ‘reduction’ of Mo⁴⁺ into Mo²⁺. The presence of disulfide groups (S–S)^{2−} in bulk MoS₂ is indicated by the presence of a characteristic band at 529 cm^{−1} in the Raman spectra.¹²¹ The possibility of dissociative (homolytic) activation of hydrogen on terminal disulfide groups was also confirmed by quantum-chemical calculations (see below).

Binuclear molybdenum clusters (C₅H₅)Mo(μ-S)₂(μ-S₂) with bridging disulfide groups described by Rakowski DuBois^{124,125} can serve as good model compounds for studying the dissociative adsorption of the hydrogen molecule on terminal sulfur atoms.



Molecular hydrogen reacts with disulfide ligands of these complexes under very mild conditions.^{124, 125}

The possibility of dissociative adsorption of hydrogen on disulfide ligands was noted in other studies as well.^{121, 126} It should be emphasised that a specific role in the interaction with molecular hydrogen belongs to the S–S chemical bond in the disulfide group, since molecular hydrogen does not react with, *e.g.*, sulfur atoms sputtered onto the (110) plane of a molybdenum single crystal.^{123, 127}

Thus, molecular hydrogen can be activated on sulfide catalysts according to different mechanisms depending on the catalyst composition and the process conditions. The ease of its activation on sulfide catalysts is indicated by the fact that the isotope exchange $\text{H}_2\text{--D}_2$ occurs at 80–150 °C, *i.e.*, at much lower temperatures than the thiophene hydrogenolysis.^{128–131} Hence, hydrogen activation cannot limit the overall reaction rate under real hydrotreating conditions.

2. The concerted mechanism of thiophene hydrogenolysis

As noted above, the active component of sulfide hydrodesulfurisation catalysts is an electrically neutral macromolecule (MoS_2)_x with Ni(IV) or Co(III) ions in the d^6 electronic configuration situated at its edge. A fragment of this macromolecule in real scale with allowance for all interatomic distances and ionic radii is represented in Fig. 12. There is occluded hydrogen inside the macromolecule; the former reacts with nickel or cobalt surface atoms, creating the electronic configuration of the active metal atom required for adsorption and catalysis. Under catalysis conditions, the active site always contains an adsorbed hydrogen sulfide molecule; this favours stabilisation of the ‘active state’ of nickel or cobalt. Adsorption occurs due to efficient interaction between the vacant d_{z^2} and d_{xy} orbitals of the metal atom and the n_σ and n_π orbitals of hydrogen sulfide (see Fig. 8).

The catalytic cycle starts with the displacement of the hydrogen sulfide molecule from the coordination sphere of the active metal atom by a thiophene molecule; this occurs because the heat of adsorption of the latter is higher. The heats of adsorption of

Table 6. Heats of adsorption of hydrogen sulfide, thiophene and tetrahydrothiophene (THT) on active sites with different compositions.

Calculation method	Composition of the active component	Heat of adsorption /kJ mol ^{−1}			Ref.
		H ₂ S	thiophene	THT	
Method of interacting bonds (MIB)	Co–MoS ₂	48	89	147	132
	Ni–MoS ₂	51	92	151	
	Co–WS ₂	50	91	150	
	Ni–WS ₂	53	95	154	
Hartree–Fock method	Co–MoS ₂	69	77	112	84

sulfur-containing molecules on active sites with different compositions calculated by semiempirical and nonempirical methods are listed in Table 6.¹³² It has been shown¹³³ that electron density flows from a sulfur atom to a MoS₂ macromolecule if a thiophene molecule is η^1 -coordinated with a coordinatively unsaturated molybdenum atom at an edge plane of MoS₂. Obviously, this process can also occur if the thiophene molecule is coordinated with an active metal atom (Co, Ni). In such a case, an additional negative charge appears on the electrically neutral molecule of the active component. Since all valence bonds inside a macromolecule are saturated, the excess negative charge will be localised on the terminal sulfur atoms. In turn, this can become an additional driving force for the dissociative adsorption of the hydrogen molecule by the homolytic activation mechanism according to which electron density is transferred from sulfur atoms to the antibonding orbital of the hydrogen molecule (see the previous section).

The activated hydrogen is transferred through the system of chemical bonds created by bridging sulfur atoms to the adsorbed thiophene molecule, thus providing hydrogenation of the thiophene ring (see Fig. 12). This process results in the removal of π -conjugation from the aromatic thiophene ring and the buildup of additional electron density on the sulfur atom. The tetrahydrothiophene (THT) molecule, which is more basic than the thiophene molecule, remains strongly bound to the active site,¹³² whereas the excess electron density is transferred back to the macromolecule of the active component and concentrated on the terminal sulfur atoms. This excess negative charge becomes the driving force of dissociative hydrogen adsorption. The activated hydrogen formed due to dissociation is transferred back to the adsorbed THT molecule through the system of valence bonds. This results in the cleavage of C–S bonds, liberation of butane (butenes) to the gas phase and formation of adsorbed hydrogen sulfide. An adsorbed H₂S molecule, which is a weak ligand, can again be replaced by a thiophene molecule. The catalytic cycle is thus closed.

In order to understand why thiophene is adsorbed and THT is not desorbed during a catalytic cycle, Bulgakov and Startsev¹³² used the method of interacting bonds to calculate the heats of adsorption of these molecules on bimetallic sulfide catalysts with different chemical compositions (see Table 6). The low heats of H₂S adsorption imply the considerable reversibility of its adsorption under the catalysis conditions and confirm that adsorbed hydrogen sulfide can be replaced by thiophene. The high heat of THT adsorption completely agrees with the virtual irreversibility of adsorption of this molecule. This also means that the cleavage of C–S bonds and desorption of H₂S and hydrocarbons to the gas phase is the only way to complete the catalytic cycle. The only reason for the strong adsorption of THT on active sites is that the basicity of the sulfur atom in this molecule is higher than that in the thiophene molecule due to the removal of π -conjugation upon hydrogenation of the thiophene ring.

Direct experimental evidence of this mechanism was obtained by EXAFS in an *in situ* study of the adsorption of selenophene (a

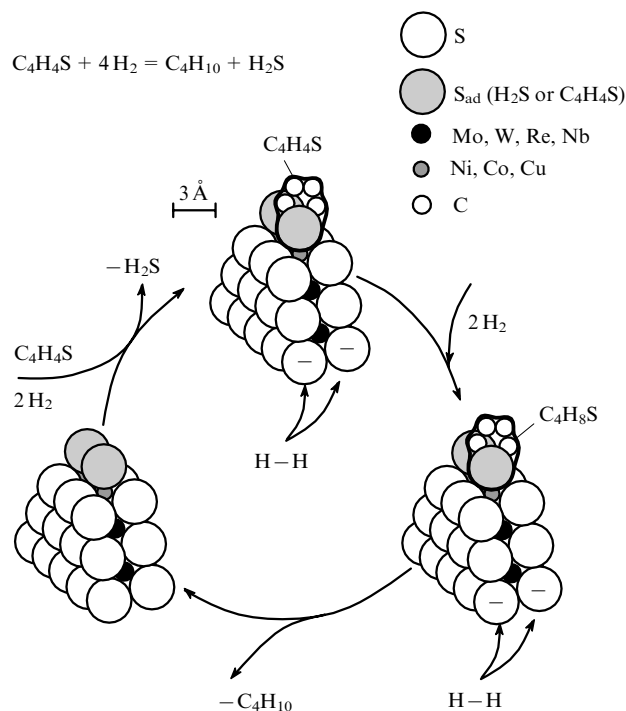


Figure 12. The catalytic cycle of thiophene hydrogenolysis on a bimetallic sulfide compound, *viz.*, the active component of hydrodesulfurisation catalysts [the ratios of interatomic distances and ionic (covalent) radii correspond to actual values].

structural analogue of thiophene) on (Ni,Mo)/Al₂O₃ sulfide catalysts of metal-complex origin.¹³⁴ It was shown that the adsorption of selenophene occurs on Ni atoms (the Ni–Se distance is 2.50 Å) but not on Mo atoms.

Thus, adoption of the hypothesis that the electric neutrality of such catalysts is violated and consideration of anionic vacancies as participants in the catalytic process are not required to describe the thiophene hydrogenolysis mechanism on bimetallic sulfide catalysts. The low activation energy, *i.e.*, high degree of compensation of the energy consumed for the cleavage of ‘old’ valence bonds in the thiophene molecule, results from the redistribution of the excess energy which is evolved upon the adsorption of thiophene and hydrogenation of its ring inside the macromolecule of the active component. The high rate of the catalytic process (synergism) is ensured by the fast transfer of electrons and protons along the closed system of valence bonds in a macromolecule of the active component with an optimum chemical composition.

Synergism is found in the catalytic systems Cr–WS₂ and Ni–NbS₂, whereas pronounced antagonism is found in the systems V–WS₂, Mn–WS₂, Cu–WS₂, Zn–WS₂ and Ni–ReS₂ (see Ref. 135). In order to explain this effect within the framework of the method of interacting bonds, the heats of thiophene adsorption on bimetallic sulfide catalysts with different compositions were calculated.¹³⁶ Good correlation between the heat of thiophene adsorption and the catalytic activity of bimetallic sulfides was observed (Fig. 13). The non-additive decrease in the activity may be due to the formation of either very strong (Ti, V, Mn, Zn) or very weak (Cu) M–S bonds. In the framework of the concerted mechanism considered here, this can mean (provided that the source of activated hydrogen is the same and the metal ion of the first transition row has the same environment) that high strength of M–S bonds prevents the displacement of H₂S adsorbed on an active site by thiophene, whereas the weakness of the M–S bond does not allow thiophene to remain on the active site for a period of time sufficient for completing the catalytic cycle. Certainly, the electronic factor should now be considered for understanding the deeper reasons for this phenomenon. In order to reveal the nature of the thiophene–metal bonding, it is necessary to study the electronic structure of the transition metal ion in the active component using quantum-chemical methods and taking into account the possibility of hydrogen occlusion into the matrix; revealing the deep reasons for synergism (or antagonism) requires that ‘cooperative’ electronic properties of the active component with a given chemical composition be established.

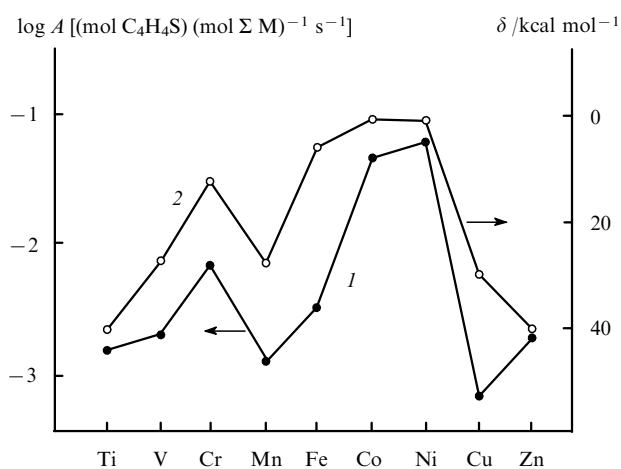


Figure 13. Dependences of activity (A) of catalysts in the hydrogenolysis of thiophene (curve 1) and deviations of the enthalpy of thiophene adsorption δ (assuming the heats of adsorption on nickel and cobalt as the optimum values) on the nature of the metal contained in the active component of bimetallic sulfide catalysts (curve 2).¹³⁶

It was noted at the beginning of this section that concerted mechanisms are mainly known for acid–base reactions. In fact, it is hard to expect that the concerted mechanism would be realised in redox catalytic reactions where the catalyst surface undergoes successive reductions–reoxidations on exposure to the reaction medium as is the case in, *e.g.*, the ‘classical’ version of the hydrogenolysis mechanism of the C–S bond, according to which the MoS₂ surface first undergoes reduction to give an anionic vacancy and then undergoes reoxidation by a thiophene molecule (see the next section).

The concerted mechanism of thiophene hydrogenolysis considered here cannot be attributed to redox reactions, as it does not explicitly assume reduction and reoxidation of the sulfide catalyst surface. It should formally be considered as an acid–base mechanism. In fact, Ni(IV) or Co(III) ions in the d^6 electronic configuration located at the edge plane of the MoS₂ matrix are Lewis acid sites; the unshared electron pair of the adsorbing molecule (a base, *e.g.*, thiophene) is transferred to the vacant d_{z^2} and d_{xy} molecular orbitals of these sites. On the other hand, the coordinatively unsaturated sulfur atoms located at the (0110) plane of the active component have an uncompensated valence bond and, as shown above, obtain an additional negative charge in the catalytic process. In other words, they act as a Lewis basic site that transfers electron density to the antibonding orbital of the hydrogen molecule which is being adsorbed, resulting in its dissociation. Thus, the electrically neutral macromolecule of the active component contains acid–base pairs; this is a prerequisite of the concerted mechanism. The electron density redistribution and the transfer of activated hydrogen to the thiophene molecule during the catalysis are not accompanied by changes in the formal oxidation states of the metals contained in the active component.

The concerted hydrogenolysis mechanism of the C–S bond on bimetallic sulfide catalysts, which has been proposed as an alternative to the generally accepted redox mechanism of this reaction, agrees completely with the concept of the common nature of heterogeneous, homogeneous and enzyme catalysis. The active component of sulfide catalysts is considered as an electrically neutral macromolecule containing acid–base pairs which serve as adsorption and activation sites for the reacting molecules. The high rate and selectivity of the catalytic process and the low activation energy are ensured by the synchronous activation of reacting molecules in the coordination sphere of the active component due to the fast transfer of electrons and protons along the closed system of valence bonds. This also ensures a high degree of compensation of the energy which has been spent for the cleavage of old bonds by the energy liberated in the exothermic steps of adsorption, hydrogenation and formation of new bonds.

IV. The concept of the determining role of the metal–sulfur bond energy in heterogeneous catalysis by metal sulfides

In the middle of the 1950s, G K Borekov proposed a hypothesis about the determining role of the bond energy of oxygen with the surface of oxide catalysts in oxidation reactions.¹³⁷ This concept was developed most consistently in the studies by V V Popovskii (see Ref. 138 and references cited therein). However, it was found already at that time that, in many cases, partial oxidation and deep oxidation obey different rules. Therefore, a concept appeared simultaneously about a conjoint mechanism of interaction of reactants with each other and with the solid catalyst.⁷⁰

Probably, the hypothesis on the participation of anionic vacancies of sulfide catalysts in the catalytic reaction was first put forward by Lipsch and Schuit,¹³⁹ although they did not give any experimental evidence for this mechanism.† Anionic vacancies

† It is this publication that was subsequently referred to most often to substantiate the role of anionic vacancies.

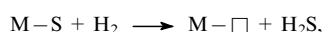
are formed on the surfaces of sulfide catalysts due to the reaction of the surface sulfur atoms with hydrogen at elevated temperatures, followed by removal of the sulfur atoms as hydrogen sulfide.

The following studies have been carried out in order to substantiate the concept of the determining role of the energy of bonding of sulfur atoms to surfaces of sulfide catalysts in their catalytic activity:

- (1) estimation of the strength of bonding of sulfur to sulfide catalyst surfaces under conditions of their temperature-programmed reduction in hydrogen;
- (2) determination of the mobility of surface sulfur atoms by measuring the isotope exchange rate between hydrogen sulfide from the gas phase and solid catalyst surfaces;
- (3) quantum-chemical calculations of the electronic structure of the active site.

1. The strength of bonding of sulfur to sulfide catalyst surfaces

The temperature-programmed heating of solid catalysts in different gases (or gas mixtures) is a relatively popular and informative method for the study of the nature of surface compounds and possible intermediates of catalytic reactions.¹⁴⁰ Correlations between the strength of bonding of surface sulfur atoms to the catalyst, on the one hand, and its catalytic activity, on the other hand, for sulfide catalysts are most commonly determined using temperature-programmed reduction (TPR) in hydrogen. Hydrogen reacts with surface sulfur atoms to remove them as hydrogen sulfide and to form anionic vacancies:



where $\square$ is an anionic vacancy. It is assumed *a priori* that the amount of removed hydrogen sulfide can serve as a quantitative measure of the number of vacancies formed on sulfide catalyst surfaces.

It has been shown in one of the first studies¹⁴¹ on the TPR of sulfide catalysts that the first maximum of the evolution of hydrogen sulfide from Ni–Mo and Co–Mo catalysts corresponds to 320 and 380 °C, respectively. A subsequent increase in the temperature is accompanied by the continuous evolution of H₂S. The continuous evolution of hydrogen sulfide from both mono- and bimetallic sulfide catalysts at temperatures above 300 °C found by Burch and Collins¹⁴² was used as the basis for drawing the conclusion that nickel does not affect the nature of surface sulfur compounds.

On the other hand, the temperature-programmed reduction of bulk molybdenum disulfide starts at higher temperatures, *viz.*, above 700 °C.¹⁴³ Non-stoichiometric sulfur (S_x) is found in catalysts supported on Al₂O₃; it can be adsorbed both on mono- and bimetallic sulfide catalyst surfaces. An analogy with the adsorption of oxygen on oxide catalysts is evident here. It is this non-stoichiometric sulfur that is readily hydrogenated with hydrogen at low temperatures, whereas the reduction of stoichiometric sulfides starts only at temperatures > 500 °C, which is much higher than typical temperatures of catalytic reactions. Similar results were obtained in a study of sulfide Ni–W catalysts.¹⁴⁴ A mechanism of the formation of non-stoichiometric sulfur was proposed by Mangnus *et al.*¹⁴⁵

No considerable difference between the TPR spectra of sulfide Co–Mo catalysts at low and high hydrogen pressures (1 and 31 atm, respectively) was found.¹⁴⁶ In both cases, low-temperature evolution of hydrogen sulfide was observed, which ceased at 200 °C. A further increase in temperature resulted in the evolution of an insignificant amount of H₂S; this amount increased at temperatures above 500 °C. Labruyere *et al.*¹⁴⁶ do not reject the possible formation of non-stoichiometric sulfur on catalyst surfaces due to the decomposition of hydrogen sulfide during their sulfidation; however, they do not rule out that other H₂S sources, *e.g.*, SH groups, can exist.

We will not analyse other works that deal with the TPR of sulfide catalysts, since poorly characterised samples and samples thermally treated under non-comparable conditions were studied in most of them. The corresponding references can be found in the monograph by Topsøe *et al.*⁴ and in studies cited above. Let us note just one short communication¹⁴⁷ describing an attempt to obtain direct experimental correlations between the M–S bond strength and the number of anionic vacancies, on the one hand, and the catalytic activity, on the other hand. However, the lack of sufficient information about the experimental conditions does not allow us to be sure that the conclusions are reliable.

2. The mobility of surface sulfur

Isotope exchange between molecular oxygen and oxygen in the solid oxide lattice (heteroexchange) was widely used for determining the mobility of surface oxygen in oxide catalysts.^{70, 137, 138} Sulfide catalysts were also studied using the heteroexchange between ³⁵S-labelled hydrogen sulfide and the sulfur atoms in MS₂ crystal lattices. Lukens *et al.*¹⁴⁸ were probably the first to show that the heteroexchange between H₂³⁵S and the surfaces of bulk or supported WS₂ occurs in toluene even at room temperature. These data were used to determine the specific surfaces of sulfide catalysts. In the gas phase, exchange occurs at 70 °C.¹⁴⁹

Radioactive hydrogen sulfide was detected^{150, 151} in thiophene hydrogenolysis products on sulfide catalysts containing radioactive sulfur. Analysis of pulse-mode kinetic curves allowed the conclusions to be drawn that catalyst sulfur atoms are involved in the reaction and that two types of sulfur atoms exist, *viz.*, those capable of fast and slow exchange.

Systematic studies on the conversion of radioactive dibenzothiophene ([³⁵S]DBT) on different catalysts^{152–154} made it possible to substantiate the hydrogenolysis mechanism of the C–S bond with involvement of anionic vacancies. The conclusions drawn were based on data on the appearance or disappearance of radioactive hydrogen sulfide in the hydrogenolysis products of [³⁵S]DBT upon periodic changes in the process conditions.

A study of the heteroexchange between H₂³⁵S and surfaces of sulfide catalysts at high hydrogen pressures (10–50 atm) showed^{155, 156} that the amount of ‘mobile’ sulfur does not depend on pressure but does depend on temperature. The ratio of the amount of ‘mobile’ sulfur to its total amount varied from 10% at 200 °C to 44% at 400 °C. A decrease in the hydrogen sulfide concentration in the gas phase decreased the exchange rate, but the amount of ‘mobile’ sulfur remained unchanged. It should be

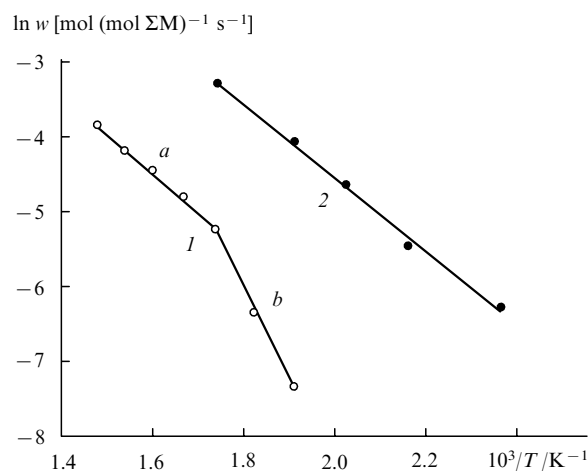


Figure 14. Temperature dependences of the rates of thiophene hydrogenolysis (1) and isotope heteroexchange of H₂³⁵S (2) on sulfide Ni–Mo catalysts.¹⁵⁷

The hydrogenolysis activation energy within segment *a* is 14 kcal mol^{–1} and that within segment *b* is 28 kcal mol^{–1}; the activation energy of heteroexchange is 10 kcal mol^{–1}.

stressed that exchange occurs with a measurable rate even at 200 °C, where the hydrogenolysis of the C–S bond is certainly impossible.

The heteroexchange of H_2^{35}S in highly dispersed sulfide catalysts of ‘organometallic origin’ occurs at temperatures ≤ 150 °C.¹⁵⁷ A comparison of the temperature dependences of heteroexchange and hydrogenolysis of thiophene (Fig. 14) shows that at moderate temperatures (250–300 °C), the heteroexchange rate is 2–5 orders of magnitude higher than that of the catalytic reaction. At lower temperatures, the hydrogenolysis of thiophene that requires high activation energy does not occur at all, whereas heteroexchange, which is characterised by low activation energy, occurs readily. It was concluded on this basis^{35,157} that the heteroexchange and hydrogenolysis on sulfide catalysts under conditions of the catalytic reaction occur simultaneously and independently following different unrelated mechanisms.

3. Quantum-chemical calculations

The hypothesis about the decisive role of the energy of bonding of sulfur to the catalyst surface dominates in the concept of the hydrogenolysis mechanism of the C–S bond on sulfide catalysts. Numerous attempts were made to substantiate this hypothesis from the standpoint that vacancies can be formed and involved in the coordination of sulfur-containing molecules, and also to explain the origin of the synergism discovered.

Duben¹⁵⁸ was probably the first to consider the electronic interaction of a thiophene molecule with a molybdenum ion. Although the active site model used (molybdenum in an oxygen environment) was inadequate, the expanded Hückel method made it possible to demonstrate the possibility of donor–acceptor interaction of a thiophene molecule and the vacant d_{z^2} orbital of a Mo^{4+} ion in the d^2 electronic configuration. Based on an estimate of the Mo–S bond strength, it was concluded that the Mo^{3+} active site in the d^3 electronic configuration is the most preferable for adsorption, as it ensures an energetically favourable possibility for the elimination of sulfur and regeneration of the active site.

A study of thiophene adsorption on a molybdenum cluster and on cobalt atoms in a hypothetical active site within the framework of the same expanded Hückel method showed,^{159,160} albeit indirectly, that two ways of thiophene adsorption are possible, *viz.*, either single-point adsorption on an anionic vacancy, or two- or four-point adsorption on cobalt atoms.

However, no studies on the electronic configuration of an active metal atom and its interaction with the substrate were carried out subsequently; instead, research mainly focused on the search for general regularities of catalytic properties as a function of the electronic structure of transition metal sulfides. It was found¹⁶¹ that the reactivities of sulfides of metals belonging to the second and third transition rows in the dibenzothiophene hydrogenolysis differed by 2–3 orders of magnitude. On the other hand, this difference is small for metals of the first transition row. The attraction of this kind of studies was that the regularities obtained could provide a universal key for unravelling the catalysis by metal sulfides as a general phenomenon, since similar dependences of activity on the nature of the catalyst have also been found for other systems, including metals and oxides.¹⁶² Binary transition metal sulfides have been well studied by physical and structural methods (see, *e.g.*, Refs 163 and 164 and references cited therein). The covalency of the metal–sulfur bond, which makes the dominant contribution to the electronic structure of the disulfide, is an important property of binary sulfides used as the basis in theoretical studies.^{165,166}

Calculations aimed at the determination of how the electronic structure of a transition metal depends on its position in the Periodic system and which electronic factor determines the catalytic activity have been performed in a series of studies.^{166–168} The energy levels and charge distribution in octahedral clusters MS_6^{n-} were analysed in a calculation by the scattered wave method (SCF- $X\alpha$). Metals of the first and second transition rows were

used as central atoms in these clusters; the formal oxidation state of sulfur was taken to be 2–, whereas the formal oxidation state of the metal corresponded to that found experimentally. It was found that the calculated covalency of the M–S bond did not correlate explicitly with the sulfide activity. On the other hand, a correlation was found between the number of d-electrons in the HOMO of the transition metal and the activity of its sulfide. Based on the analysis of the HOMO symmetry, it was concluded that not only the presence of a certain number of electrons in the HOMO but also its $2t_{2g}$ -symmetry are prerequisites for high activity. In view of this, a new parameter B was introduced, which specifies the strength of the given bond:

$$B = n_{\sigma}D_{\sigma} + n_{\pi}D_{\pi},$$

where the D_{σ} and D_{π} values determine the contribution of the metal d orbitals to the σ - and π -bonding orbitals of the molecule, whereas n_{σ} and n_{π} are the numbers of the σ - and π -bonding electrons, respectively. Thus the products $n_{\sigma}D_{\sigma}$ and $n_{\pi}D_{\pi}$ are measures of the relative contributions of the σ - and π -components to the M–S bond strength. However, the correlation still remained unsatisfactory; therefore, yet another parameter was introduced, *viz.*, the bond activity parameter A_2 :

$$A_2 = nB,$$

where n is the total number of electrons.

Although this resulted in a relatively good correlation between A_2 and catalytic activity,¹⁶⁶ the physical meaning of this parameter is vague.

This approach was used to explain the nature of synergism in bimetallic sulfide catalysts of hydrotreating. The $[\text{M}'\text{MoS}_9]^{n-}$ cluster, where M' is a metal of the first transition row, was used as the model. This cluster consists of two MoS_6 octahedra sharing three sulfur atoms at their base. The calculations show^{166,167} that if $\text{M}' = \text{Co}$ or Ni , the electrons from the $3d(e_g)$ orbital of the ‘promoter’ atom are transferred to a lower orbital of molybdenum, *viz.*, $4d(t_{2g})$, resulting in the formal reduction of molybdenum. If $\text{M}' = \text{Cu}$, the electron transfer occurs in the reverse direction. No electron transfer occurs in the case of Fe and Zn; for other metals of the first transition row, the situation is uncertain. Thus, the promoting effect is explained by the electron transfer from a promoter’s orbital to the antibonding orbital of molybdenum. Since these electrons are located on an antibonding orbital, the Mo–S bond strength decreases, which results in a decrease in parameter B and an increase in the catalytic activity. Thus, the role of a promoter is to increase or decrease the number of electrons on the antibonding orbital of molybdenum: the higher the electron density on the metal the higher the catalyst activity. Anionic vacancies play the role of active sites; their formation is facilitated when the Mo–S bond weakens.

However, the correlations found do not explain why a linear combination of calculated electronic parameters determines the catalytic properties of binary sulfides of transition metals. Therefore, Topsøe *et al.*^{4,169,170} carried out *ab initio* calculations of the energy-band structures of these catalysts. All calculations were based on the idea of the determining role of the M–S bond strength in the catalyst activity; therefore, the hypothesis was called the bond energy model (BEM). This model considers the hybridisation of the valence states of sulfur with the d-states of the transition metal and hybridisation of the states of sulfur with the s-states of the metal. Different terms were combined to calculate the total bond energy of sulfur in binary sulfides of transition metals. The M–S bond strength was in good correlation with the observed catalyst activity; it was therefore concluded that the activity of transition metal sulfides originates from the difference between the energy gain due to the hybridisation of the metal states with sulfur valence states and the energy loss due to the weakening of the metal–metal bond when sulfur atoms are located on the surface. This viewpoint differs fundamentally from that considered above as, according to it, the maximum catalyst activity is reached at some optimum M–S bond strength.

Thus, the hydrogenolysis rate of the C—S bond should be proportional to the concentration of anionic vacancies on the surface of sulfide catalysts, which depends on the composition of the reaction mixture and the M—S bond strength.

At the next stage of the BEM development, the possibility of the formation of vacancies on an edge plane of a single molybdenum disulfide slab was considered.¹⁷¹ It was shown within the framework of the density functional theory (DFT) that the elimination of a sulfur atom from the (30 $\bar{3}$ 0) MoS₂ edge plane (see Fig. 10) requires no less than 326 kJ mol⁻¹. Considerably less energy (46 kJ mol⁻¹) is required to eliminate sulfur from the (10 $\bar{1}$ 0) edge. It is noteworthy that the interatomic distances in a single molybdenum disulfide slab without anionic vacancies, calculated within the DFT method, differ noticeably from the corresponding distances in a single crystal. Byskov *et al.*¹⁷¹ explain this by the fact that only a relatively small part of the surface was considered in the calculations.

If part of the molybdenum atoms is replaced by cobalt atoms, the elimination of a sulfur atom bonded both to molybdenum and cobalt becomes thermodynamically favourable and gives an energy gain of 34 kJ mol⁻¹. On the other hand, the 'remaining' sulfur atom is very strongly bound to the matrix (222 kJ mol⁻¹). This fact agrees with the calculated Co—S bond lengths (2.34 Å in the former case and 2.24 Å in the latter).

Byskov *et al.*¹⁷² undertook an attempt to determine the geometric form of an active component with the maximum possible number of anionic vacancies, which they believe to be necessary to acquire the maximum catalyst activity. Since the possible number of anionic vacancies at the edge plane of a regular hexagon is quite limited (see Fig. 10), it was assumed that the geometric shape of the active component can be a dynamic function of the reaction conditions. It was found that the maximum concentration of active sites (anionic vacancies) per unit volume is provided by the triangular configuration of the active component. DFT calculations confirmed that the higher the structure defectiveness of the active component the lower the M—S bond strength and the higher the catalyst activity.

The study by Byskov *et al.*¹⁷¹ was based on studies of molybdenum sulfide nanoclusters by scanning tunnelling electron microscopy (STM).^{173,174} The nanoclusters were obtained by sputtering molybdenum atoms on the surface of an Au(111) single crystal in hydrogen sulfide at 127 °C followed by annealing at 400 °C (also in hydrogen sulfide). It was shown by STM that the sample contained islets, mainly triangular, with a mean side length of 30 Å; these are molybdenum sulfide nanoclusters whose basal plane (0001) is oriented parallel to the Au(111) plane. Analysis of nanocluster images obtained at atomic resolution made it possible to establish that the interatomic distances in it are 3.15 ± 0.05 Å, *i.e.*, they are the same as those in molybdenum disulfide. This served as the basis for the conclusion that this method gave a triangular MoS₂ nanocluster, whose edge planes are limited by single sulfur atoms located in irregular lattice positions. After treatment of the cluster with atomic hydrogen, pictures obtained at atomic resolution revealed point defects, *i.e.*, anionic vacancies. The authors claim that they were the first to observe the active site of a catalytic reaction.

Without doubt, these studies^{173,174} have been carried out on the highest experimental level and can be regarded as classical studies of solid surfaces. The results obtained in these studies had a certain resonance in scientific circles (see, *e.g.*, Ref. 175). However, let us try to consider the results described above from the viewpoint of the consistency of the picture obtained with real catalytic systems.

First, the unusual triangular shape of the species is doubtful: the most thermodynamically stable shape of any isolated system is a sphere¹⁷⁶ (or a circle for two-dimensional systems). It was confirmed experimentally that a regular hexagon is the most thermodynamically stable shape of a single molybdenum disulfide slab. The triangular shape of the species indicates that molybdenum disulfide nanoclusters possess an excess of internal energy.

The invariability of this shape after annealing at 400 °C in a hydrogen sulfide atmosphere is only possible in the case of strong epitaxial interaction of the nanocluster with the surface.

In fact, the Au(111) plane is a hexagonal closely packed structure with the Au—Au distance of 2.884 Å. It is well known¹⁷⁷ that epitaxial interaction of solids is only possible if the symmetry groups of the interacting bodies are the same and the interatomic distances are equal to within 10%. In this case, such a coincidence is in fact observed: molybdenum disulfide has a hexagonal densely packed structure with a lattice parameter of 3.16 Å, which differs from the lattice parameter of gold by less than 9%. If the symmetry of the crystal lattice differs from that of the nanocluster, single slabs of molybdenum disulfide are oriented orthogonally to the substrate surface on which they have been deposited by some method (see Ref. 111). This is explained by the absence of strong chemical interaction between the basal surface of molybdenum disulfide and the substrate surface. Therefore, stabilisation occurs due to the formation of chemical bonds between the atoms of the MoS₂ edge plane and the support atoms. For example, parallel orientation of slabs was observed in the MoS₂/Mo(111) system.¹⁷⁸

The second important criticism also corresponds to the shape of the nanocluster species. It is easy to show (see, *e.g.*, Ref. 179) that MoS₂ species of any shape that differs from the regular hexagon are non-stoichiometric; as a result, the macromolecule is no longer electrically neutral. If the species are triangular, sulfur atoms are present in a considerable excess, which inevitably results in a charged cluster [MoS_x]ⁿ⁻. Since epitaxial growth implies the electronic interaction of the substrate with the support, one should expect the electron density transfer from the surface atoms of the support to the triangular nanoclusters of MoS₂. Thus, a considerable excess of sulfur atoms is inconsistent with the conclusion drawn by the same authors^{173,174} regarding the 'inherent' defects of the molybdenum disulfide structure.

The third important issue is related to the discovery of defects (anionic vacancies) after treatment of a nanocluster with atomic hydrogen. As the authors state,^{173,174} a side of the triangle consists of sulfur atoms located in irregular positions of the nanocluster crystal lattice. It is these sulfur atoms that are eliminated upon the reaction of a cluster with atomic hydrogen. On the other hand, according to their calculations,¹⁷¹ elimination of these atoms requires an energy of 326 kJ mol⁻¹. This means that elimination of these atoms is impossible under catalysis conditions, and this defect can exist only in ultra-high vacuum.

Finally, there is the fourth important issue. The model suggested by Byskov *et al.*¹⁷¹ assumes the existence of 'inherent' defects, *viz.*, anionic vacancies.[‡] It is known (see, *e.g.*, Ref. 180) that the linear size of the active component in the most active catalysts is no higher than 10–15 Å. An electrically neutral (MoS₂)_x macromolecule of this size is shown in Fig. 10. On an alumina surface, the active component can have the form of filiform structures up to 50 Å long and several atomic layers high. This is the type of structure considered within the BEM approach. The number of 'inherent' defects in such a structure should be one per cobalt atom or one per two molybdenum atoms. It is easy to see that in this case a single filiform MoS₂ slab should be represented as Mo₂S₃, as the number of anionic vacancies should match the number of defects. Table 7 lists the interatomic distances in a Mo₂S₃ single crystal published by Jonge *et al.*¹⁸¹ and the interatomic distances calculated for a defective molybdenum disulfide structure.¹⁷¹ One can see that these interatomic distances agree well, which is not surprising: the elimination of a sulfur atom

‡ It should be noted that a strong deformation of the MoS₂ slab structure results in new interatomic distances, which favours weakening of the Mo—S bonds. The introduction of cobalt deforms the structure of a MoS₂ slab further. In the most active catalysts, the defectiveness reaches a maximum value, so that a vacancy appears at each cobalt atom.¹⁷²

Table 7. Interatomic distances in the structure of a Mo₂S₃ single crystal and in the defective structure of molybdenum disulfide.

Bond	Interatomic distances (Å) in	
	single crystal Mo ₂ S ₃ ¹⁸¹	defective structure ¹⁷¹
Mo–Mo	2.86	2.85
	3.208	3.12
	3.22	—
Mo–S	2.31–2.72	2.34–2.43

from the MoS₂ structure must inevitably be accompanied by the reduction of Mo(IV) into Mo(III). However, reduced forms of molybdenum disulfide have not been found in any XPS studies of sulfide catalysts. Furthermore, it was reported¹⁸¹ that Mo₂S₃ is crystallised in monoclinic system with space group *P*2₁/*m* (*C*_{2h}), which differs from the MoS₂ symmetry group (see Table 1). It is MoS₂ species that are always detected by high-resolution electron microscopy.

Thus, studies by Topsøe *et al.*^{169–174} contain an internal logical contradiction between the experimental results and theoretical calculations, which they invariably interpret in favour of the bond energy model they are developing, without consideration of the laws of thermodynamics and structural chemistry.

The bond energy concept was also used as the basis of a series of studies carried out by Raybaud *et al.*^{182–186} They used the *ab initio* DFT method to study the crystal structure and the electronic and energetic properties of over 30 transition metal sulfides.^{182, 184} The calculations took into account the actual crystal structure of each sulfide and the possibility of rearrangement (relaxation) of surface atoms in comparison with bulk atoms. The cohesion energy, *i.e.*, intermolecular bonding, was calculated in these studies, unlike in other works.^{169–174} As opposed to the standard heat of formation of sulfides, the cohesion energy is the atomisation energy of a compound. Thus, the energy of each particular bond is a fraction of the total intermolecular interaction energy. In the simplest case, the strength of the M–S bond can be determined as the intermolecular cohesion force divided by the number of valence bonds in a unit cell. The M–S bond strength calculated this way correlates very well with the activity of catalysts measured by Pecoraro and Chianelli.¹⁶¹ However, it should be noted that the bond energies found reflect the actual strength of the M–S bond in the sulfide and are totally unsuitable for kinetic equations for a catalytic reaction. In fact, the M–S bond strength is 210 kJ mol^{−1} in the most reactive sulfide, *viz.*, RuS₂, and 251 and 272 kJ mol^{−1}, respectively, in the less reactive sulfides MoS₂ and WS₂. On the other hand, it is well known that the activation energy of the catalytic hydrogenolysis of the C–S bond is 42–63 kJ mol^{−1} (see, *e.g.*, Ref. 8). If we assume that the elimination of a sulfur atom from the active site is the limiting step, the bond energy of sulfur with this site should not exceed the activation energy.

The DFT method was used to calculate the geometric structure of the surface of a single MoS₂ slab and the electronic structure of molybdenum at the edge plane of this slab.¹⁸³ According to the data obtained, the (3030) edge plane undergoes a noticeable rearrangement: the surface molybdenum atoms are shifted by 0.04 Å into the macromolecule, whereas the surface sulfur atoms are shifted by 0.6 Å in the opposite direction. In our opinion, this agrees very well with the structure of a real macromolecule affected by surface tension forces. Yet another important conclusion drawn by Raybaud *et al.*¹⁸³ is that a rearranged side of a macromolecule is stable at least up to 400 °C.

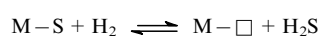
Finally, the localisation sites of cobalt in the MoS₂ structure were considered.¹⁸⁶ It was found that the replacement of molybdenum atoms by cobalt atoms inside a macromolecule and the coordination of cobalt to sulfur atoms at the (1010) edge plane are less energetically favourable than the replacement of molybdenum atoms at the (3030) edge plane of a single MoS₂ slab. The

optimised interatomic distances Co–S and Co–Mo, which are 2.21 and 2.84 Å, respectively, are in good agreement with the values found experimentally using EXAFS. Based on the concept of the determining role of the M–S bond strength in the catalyst activity, the enthalpy of adsorption of sulfur atoms on metal atoms at the edge plane of a MoS₂ slab was calculated. It should be emphasised that it was the adsorption on coordinatively unsaturated metal atoms that was considered, not the formation of anionic vacancies which was postulated in the previous works. It is believed that the adsorption of sulfur (probably H₂S, as indirectly follows from Ref. 186) involves two adjacent metal atoms simultaneously. The adsorption of sulfur on two cobalt atoms is a weakly isothermic process (the heat of adsorption is 3.8 kJ mol^{−1}). The heat of adsorption of sulfur on the Co–Mo pair increases to 9.6–28.9 kJ mol^{−1} and reaches a maximum value on the Mo–Mo pair (122 kJ mol^{−1}). On the other hand, the adsorption of sulfur on the Ni–Ni and Cu–Cu pairs is endothermic (−38 and −113 kJ mol^{−1}, respectively). The heats of adsorption of sulfur on single metal atoms were not reported in this work, which, as we believe, may be due to their negative values. We calculated the heats of adsorption of sulfur-containing molecules and found⁸⁴ that Ni(II) and Co(II) ions cannot adsorb donor molecules. Such adsorption becomes possible only if these atoms are bound to occluded hydrogen and the active metal is in the d⁶ state.

We are not going to analyse other theoretical studies in detail as this would require a separate review on this subject. Let us just note some remarkable results directly related to the subject of our paper. For example, it was shown¹⁸⁷ that no less than 5 eV is required to create an anionic vacancy in an end face of a molybdenum disulfide molecule. Smit and Johnson,¹⁸⁸ who considered the bond strength of the 3p orbitals of sulfur with the d orbitals of metals, attributed the greatest importance to the metal oxidation state: as a result of the electron density transfer from nickel or cobalt atoms to molybdenum, their oxidation states became higher than those in the binary sulfides. A similar electron density transfer from the Ni atom to MoS₂ was observed by Collman *et al.*¹²² They considered the adsorption of thiophene on coordinatively unsaturated atoms rather than on anionic vacancies (the adsorption of pyridine occurs similarly¹⁸⁹). The totally optimised hexagonal structure of an electrically neutral cluster Mo₂₇S₅₄ was calculated.^{190, 191} According to the calculations, the adsorption of thiophene occurs on the molybdenum atoms located in the vertices and edge planes of this cluster; anionic vacancies were not considered.

Thus, although many authors initially postulate that the M–S bond strength has a determining role in the activity of sulfide catalysts (*i.e.*, that anionic vacancies are involved in catalytic transformations), the majority of them eventually consider the interaction of sulfur-containing molecules with coordinatively unsaturated surface metal atoms. We believe that this is quite an objective reflection of the real situation that the active sites of heterogeneous catalysts participate in the catalytic process.

In conclusion, let us offer several additional arguments against the involvement of anionic vacancies in the catalytic cycle. A thermodynamic estimate of the possibility of formation of anionic vacancies in the MoS₂ and WS₂ structures by the interacting bonds method showed¹⁹² that the appearance of such bonds in a hydrogen atmosphere is unfavourable since the adsorption of hydrogen sulfide on a vacancy gives a much larger energy gain. Therefore, the equilibrium



is always shifted to the left under catalytic reaction conditions.

Direct experimental proof of the absence of correlation between the MoS₂ activity and the concentration of anionic vacancies was obtained in an *in situ* study of the electric conductivity of a MoS₂ single crystal under conditions of pulse-mode hydrogenolysis of butanethiol.^{193–195} A MoS₂ single crystal reduced in a stream of H₂ at 257 °C contained over 10¹⁸ electrons

per cm^3 , which corresponded to the concentration of anionic vacancies. After a portion of butanethiol was injected, the conductivity decreased abruptly and then increased without reaching its original value. The degree of butanethiol conversion did not exceed a few percent. Periodic injection of new portions of butanethiol decreased the conductivity (decreased the concentration of anionic vacancies) and increased the conversion. The conversion in the absence of n-type conductivity was $\sim 100\%$. Thus, an increase in the concentration of anionic vacancies during the reduction of MoS_2 results in a decrease in its reactivity in the hydrogenolysis of the C–S bond, whereas, on the contrary, a decrease in their concentration due to the surface upbuilding by sulfur from the gas phase is accompanied by an increase in the catalytic activity.

Doping of a MoS_2 single crystal with Co^{2+} ions results in p-type conductivity,^{193–195} the concentration of current carriers is almost independent of the thermal treatment conditions in an H_2 or He atmosphere and does not change during the catalytic reaction. The conversion of butanethiol under these conditions is close to 100%. On the one hand, it means that Co stabilises the MoS_2 structure and hinders its reduction. On the other hand, these data confirm again that the involvement of anionic vacancies in a catalytic reaction is not mandatory.

As noted above, sulfide catalysts are highly dispersed systems that operate steadily under real conditions at high temperatures (350–380 °C) and hydrogen pressures of 20–150 atm for long periods (months and years). The following calculations may be shown as an example. The hydrogenolysis rate of dibenzothiophene (the main contaminant in diesel fuel) at 400 °C is $\sim 3 \text{ (g S) (g Co)}^{-1} \text{ h}^{-1}$ (see, e.g., Ref. 165). Let us assume that the liquid hourly space velocity of diesel fuel containing 0.5% sulfur is $5 \text{ g (g Cat)}^{-1} \text{ h}^{-1}$ (where Cat stands for the catalyst). If the catalyst contains 3% of cobalt, it turns out that $0.8 \text{ (g S) (g Co)}^{-1} \text{ h}^{-1}$ passes through it. Thus, at 100% conversion of dibenzothiophene and under the condition that each cobalt atom has an anionic vacancy and can accelerate the reaction, three-fourths of the vacancies are not involved in the catalytic cycle at each time instant but are necessarily present on the surfaces of highly dispersed species. Hence, the active component is a highly defective structure which, nevertheless, works in a stable mode for a period of one year; each active site undergoes a reduction–reoxidation cycle more than 50 000 times during this period.

On the contrary, we believe that the site centre of sulfide catalysts is a thermodynamically stable system[§] with a minimum amount of structural defects.

A brief analysis of studies that dealt with the bond energy model shows that there is a trend to reconsider its fundamental postulate, namely, it is admitted more and more often that it is a coordinatively unsaturated metal atom rather than a point defect in the active component crystal structure that serves as an active site. This concept is consistent with that of the concerted mechanism of action of sulfide catalysts which is being developed at the Institute of Catalysis. Indeed, many experimental facts interpreted within the bond energy model can be explained in terms of the synchronous interaction of reacting molecules in the coordination sphere of a bimetallic active site. For example, the M–S bond strength is identical to the heat of adsorption of a sulfur-containing molecule on the active metal atom. Thus, the necessity of an ‘optimum bond strength’ becomes clear.¹³⁶ The fast heteroexchange of ^{35}S at low temperature^{148–157} should be considered as the intermolecular exchange of an adsorbed hydrogen sulfide molecule with the structure-building sulfur atoms of the active component. It is quite obvious that such exchange does not

require a considerable consumption of energy. The temperature-programmed heating of a sulfide catalyst in hydrogen or in an inert gas atmosphere results in the elimination of adsorbed hydrogen. This follows decisively from a study of the benzene hydrogenation on sulfide catalysts under non-steady-state conditions.^{196–198}

We hope that further progress in the study of the mechanism of action of sulfide catalysts will result in merging of the two alternative concepts into a unified theory of catalysis by metal sulfides.

V. Conclusion

Sulfide catalysts of hydrotreating of oil fractions constitute one of the best-studied and thoroughly characterised systems in heterogeneous catalysis. The success in the studies of these catalysts was considerably favoured by the specific structure of their active component, which is easily recognised among various supports and catalytically inactive surface compounds. However, we are still far from the understanding of the fundamentals of the nature of the catalytic action of sulfide catalysts. The generally accepted views that have been elaborated as a result of studies in areas bordering heterogeneous catalysis turned out to be unsuitable for describing many regularities of catalytic reactions on sulfide catalysts. However, the knowledge of the structure of the active component of these catalysts offers wide opportunities for the understanding of the fundamental bases of heterogeneous catalysis.

The concerted mechanism of action of sulfide catalysts described above is based on the principle of the common nature of heterogeneous, homogeneous and enzyme catalysis as a natural phenomenon. We believe that the active component of a solid catalyst is an electrically neutral macromolecule containing sites of adsorption and activation of substrate molecules. The chemical transformation of the substrate occurs in the coordination sphere of the active component without involvement of structure-forming atoms. Any point defects, including anionic vacancies, should be considered as a result of deviation of this system from the equilibrium state, which should have irreversible consequences, *viz.*, catalyst deactivation, poisoning of active sites, side processes, *etc.*

Below we formulate the main specific features of the concerted mechanism of thiophene hydrogenolysis on sulfide hydrodesulfurisation catalysts.

1. The chemical reaction occurs in the coordination sphere of the bimetallic sulfide active component without involvement of structure-forming atoms in the catalytic cycle.

2. The active sites of thiophene adsorption consist of Ni(IV) or Co(III) atoms in the d^6 electronic configuration. Adsorption occurs due to the interaction of the unshared electron pairs (n_σ and n_π) of sulfur atoms of a donor molecule with vacant d_{z^2} and d_{xy} orbitals of the active metal atom.

3. An indispensable part of the active site consists of an occluded hydrogen atom that appears in the active component due to oxidative addition of a hydrogen molecule to Ni(II) and Co(II) ions during the catalyst sulfidation. The occluded hydrogen is located in the matrix of a single MoS_2 slab in the centre of an ‘empty’ trigonal prism formed by sulfur atoms, under a nickel (cobalt) atom at a distance of 1.5 Å from it.

4. The activation of hydrogen occurs on paired sulfur atoms at the edge planes of a single $\text{MoS}_2(\text{WS}_2)$ slab. The driving force of this process is the presence of the S–S chemical bond at terminal sulfur atoms that border an electrically neutral macromolecule of the active component and act as the Lewis basic site. The excess electron density is transferred from these atoms to the antibonding orbital of a hydrogen molecule, which results in its homolytic dissociation.

5. The high rate of catalytic transformation is ensured by the fast transfer of electrons and protons along the system of chemical

§ Molybdenite, a natural mineral consisting of MoS_2 , is one such stable structure; furthermore, molybdenum disulfide is formed upon thermal decomposition of many molybdenum compounds with sulfur-containing ligands.¹¹¹

bonds within an electrically neutral macromolecule of the active component.

6. The low hydrogenolysis activation energy is explained by the high degree of compensation of the energy required for the cleavage of 'old' bonds in a thiophene molecule by the energy liberated in exothermic processes of adsorption and hydrogenation of the thiophene ring.

7. The concerted mechanism of thiophene hydrogenolysis on sulfide hydrosulfurisation catalysts corresponds to the class of acid–base heterogeneous catalytic reactions.

8. The concerted mechanism is also applicable to other sulfide catalysts that are crystallised in the molybdenite structural type.

Probably, concerted (synchronous) mechanisms of catalytic processes apply to a wider range of heterogeneous catalysts than was believed until recently. The main difficulties in finding such mechanisms are created by the non-uniform composition of the surface compounds and the possibility of their transformation on exposure to the reaction medium. This complicates considerably the analysis of kinetic regularities and makes it necessary to build complex kinetic models. Obviously, the solution to this problem should be searched for on the route to creating heterogeneous catalysts with homogeneous composition and with a known structure of the active component.

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Ferrocene-containing nucleic acids. Synthesis and electrochemical properties

T S Zatsepin, S Yu Andreev, T Hianik, T S Oretskaya

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Abstract. The published data on the synthesis of ferrocene-containing nucleic acid fragments are generalised. The known methods are systematised and their advantages and disadvantages are discussed. The use of nucleoside, nucleotide and oligonucleotide conjugates with ferrocene in the design of systems for electrochemical detection of nucleic acids is considered. The bibliography includes 121 references.

I. Introduction

Studies of nucleic acids (NA) and their complexes with proteins require the development of highly sensitive procedures for their identification and quantitation in analysed samples. The use of spectrophotometric, autoradiographic and electrochemical techniques for the analysis of nucleic acids envisages usually incorporation of appropriate reporter groups. Incorporation of reporter groups favours higher selectivity of analysis and allows detection of low concentrations of NA with a minimum effect on their structures and functions.

Labelling of NA with radioactive isotopes, ^{32}P in particular (see Ref. 1), has become a very popular procedure. Phosphorus isotopes are incorporated by enzymatic methods using labelled nucleoside 5'-triphosphates or nucleoside 3',5'-diphosphates. The efficiency of this reaction is very high for both short-chain and extended NA. However, manipulations with radioactive isotopes demand certain precautions. Other limitations of the method include short half-lives of ^{32}P , ^{35}S and ^{125}I and radiolysis of labelled NA.

The use of fluorescent labels has received the widest acceptance for the detection of nucleic acids.^{2,3} 5'-Triphosphates of nucleosides, 2'-deoxynucleosides and 2',3'-dideoxynucleosides containing various fluorescent labels are commercially available at present. The use of nucleoside triphosphate conjugates with biotin in enzymatic synthesis of NA enables detection and

selective isolation of target oligonucleotides due to the formation of stable biotin–avidin or biotin–streptavidin complexes immobilised on a polymeric substrate.⁴ Detection of nucleic acids by mass spectrometry [MALDI-MS (see Ref. 5) and ESI-MS (see Ref. 6)] is also being developed at a racing pace.

Electrochemical detection holds a tremendous potential in the analysis of nucleic acids. High sensitivity, low cost, the possibility of performing express analysis and, especially, simplicity of miniaturisation make electrochemical detection a promising tool in the design of DNA chips,⁷ in HPLC and capillary electrophoresis of NA.⁸

Synthesis of modified nucleosides, nucleotides and oligonucleotides containing various metal complexes is an approach to the design of electrochemical NA sensors.⁹ Conjugates of modified oligonucleotides with metal ions can also be used as chemical nucleases^{10,11} and in the studies of electron transfer in DNA.^{12–14} There are several methods for the synthesis of such compounds: (1) conjugation of a metal complex and an oligonucleotide containing a reactive group at the 5'- or 3'-end;^{15,16} (2) addition of metal ions to an oligonucleotide bonded to a chelating group;^{17,18} (3) synthesis of a nucleoside phosphoramidite derivative containing a metal complex^{19,20} and its subsequent incorporation into the oligonucleotide chain by automatic solid-phase synthesis. A recently published review²¹ is devoted to the synthesis of oligonucleotide complexes with platinum-group metals.

The present review deals with the methods of the synthesis and applications of ferrocene-containing nucleosides, nucleoside-5'-triphosphates and oligonucleotides. Nucleosides can be incorporated into NA *via* automated oligonucleotide synthesis and nucleoside-5'-triphosphates enzymatically respectively. Owing to their small size, high stability of oxidised and reduced forms, reversibility and high rates of redox reactions and accessibility, ferrocene derivatives represent promising starting compounds for the synthesis of metal-containing oligonucleotides.²²

Immobilisation of ferrocene-containing oligonucleotides on electrodes permits determination of the primary structure of NA[†] by hybridisation. An alternative approach to the study of nucleotide sequences entails the synthesis of ferrocene conjugates with various molecules capable of selective and effective binding to NA.²⁴ In some cases, ferrocene conjugates with intercalators are used for this purpose.^{25–27} However, the use of ferrocene-containing oligonucleotides ensures the highest specificity of binding

T S Zatsepin, S Yu Andreev, T S Oretskaya Department of Chemistry, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax (7-095) 939 31 81. Tel. (7-095) 939 31 48. E-mail: tsz@yandex.ru (T S Zatsepin), andreev@genebee.msu.ru (S Yu Andreev). Tel. (7-095) 939 54 11. E-mail: oretskaya@belozersky.msu.ru (T S Oretskaya)
T Hianik Comenius University, Mlynska Dolina F1, 84248 Bratislava, Slovak Republic. Fax (42-126) 542 67 74. Tel. (42-126) 029 56 83. E-mail: hianik@fmph.uniba.sk

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[†] It is known²³ that peptides containing a ferrocene moiety at the *N*-end are used for the studies of spatial structures by electrochemical methods and X-ray diffraction analysis. Unfortunately, no such studies of ferrocene-containing NA have been carried out so far.

to NA targets in comparison with other ferrocene derivatives suggested.

Electrochemical detection of NA on the electrode surface is a promising approach to the study of single nucleotide polymorphism (SNP), the most common type of genome mutations affecting one out of one thousand nucleotide units. It has been shown²⁸ that these mutations are responsible for certain genetic diseases. Direct sequencing studies have demonstrated²⁹ that the human genome contains about 1 420 000 SNP. Other popular procedures for recognition of SNP include the polymerase chain reaction (PCR) with nucleoside triphosphates bearing fluorescent labels³⁰ and the use of DNA chips.³¹

In addition, studies of SNP may include an analysis of single-³² and double-stranded³³ conformational polymorphism and hybridisation in solution followed by gel electrophoresis with denaturing gradient³⁴ or temperature gradient.[‡]

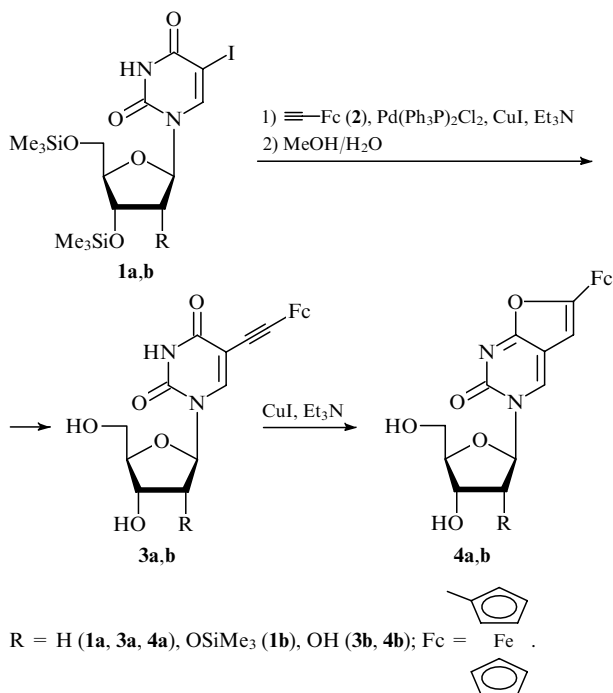
Thus, the methods for the synthesis of ferrocene-containing oligonucleotides and their applications described in this review present interest for specialists in the chemistry of nucleic acids and those engaged in the diagnostics of genetic diseases.

II. Synthesis of ferrocene-containing nucleic acid fragments

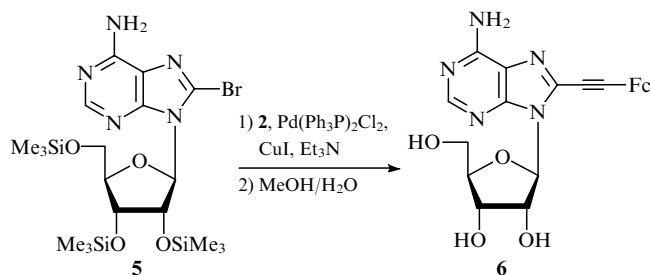
1. Synthesis of nucleic acid fragments containing ferrocene in a heterocyclic base

The first paper devoted to the synthesis of ferrocene-containing heterocyclic bases and nucleosides was published in 1991.³⁵ It described several synthetic strategies.

The first of them is based on the reaction of protected 5-iodo-2'-deoxyuridine (**1a**) or 5-iodouridine (**1b**) with ethynylferrocene **2** under conditions of the Sonogashira reaction,^{36,37} viz., stirring of the reactants in triethylamine in the presence of catalytic amounts of bis(triphenylphosphine)palladium dichloride and copper(I) iodide at 40 °C. The yields of the pyrimidine derivatives **3a,b** after removal of trimethylsilyl protective groups were as low as 10%–15%, since under the conditions used these compounds are partly converted into ferrocenylfuro-pyrimidones **4a,b**. The analogous reaction of 8-bromo-adenosine **5** yielded 70% of the ferrocenyl derivative **6**.³⁵

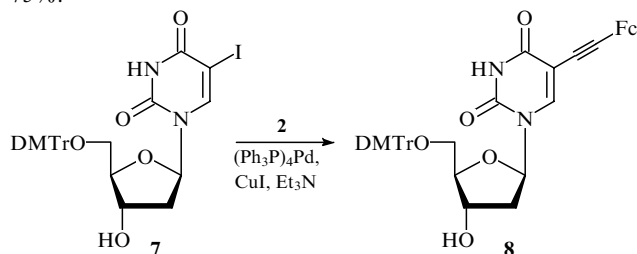


‡ R M Wartell, S Hosseini, S Powell, J Zhu *J. Chromatogr. A* **806** 169 (1998).



It has been shown³⁸ that the 5-(ferrocenylethynyl)uridine derivatives **3a,b** being incorporated into NA were converted into ferrocenylfuro-pyrimidones **4a,b** upon standard postsynthetic treatment of oligonucleotides with aqueous ammonia. The presence of furo-pyrimidone in the oligonucleotide chain reduces thermal stability of a DNA duplex.

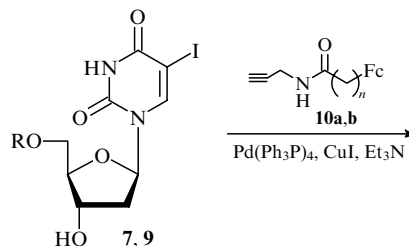
Later, Houlton *et al.*³⁹ used another palladium catalyst, viz., tetrakis(triphenylphosphine)palladium, and reduced the reaction temperature to room temperature. Such a change in the experimental conditions and the presence of a 5'-dimethoxytrityl protective group, which enhances the solubility of the starting nucleoside **7**, increase the yield of the substitution product **8** to 75%.

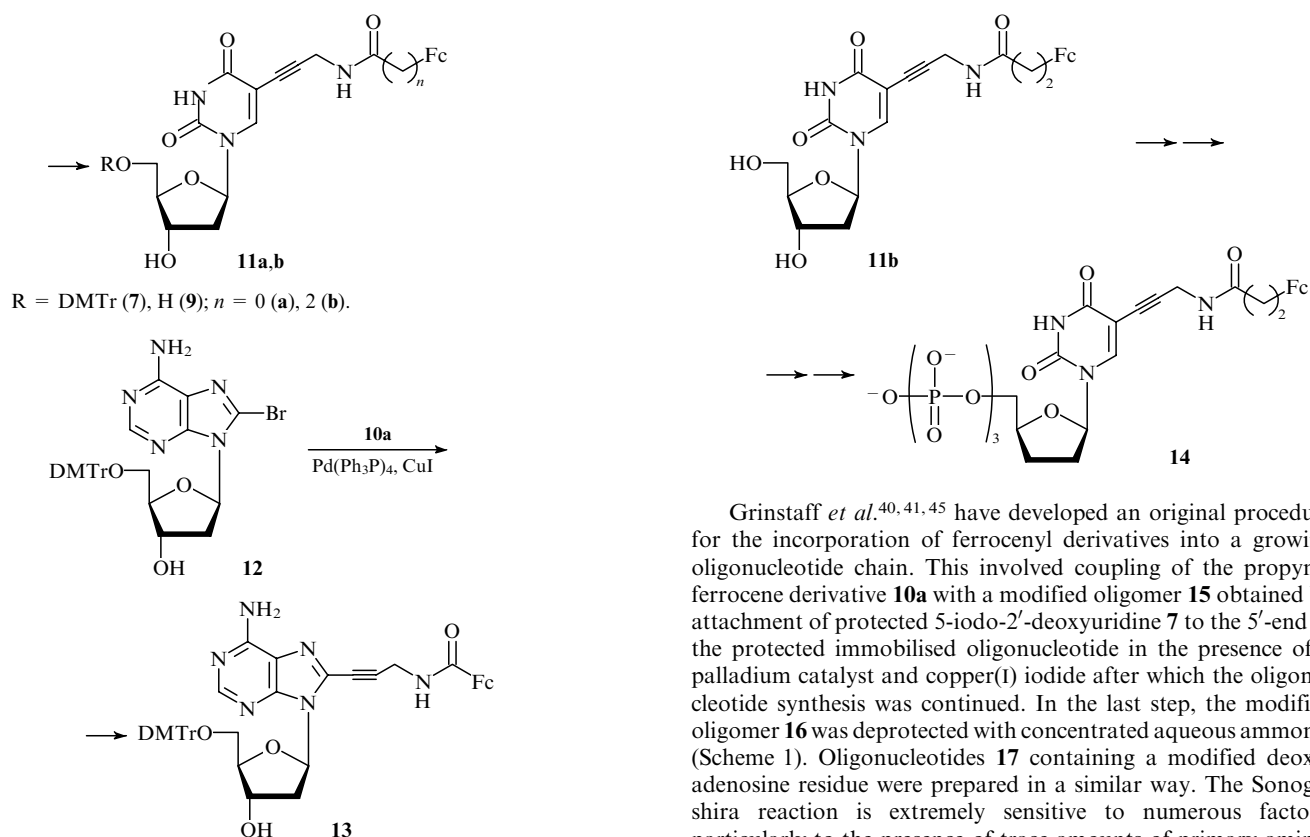


DMTr = $(4\text{-MeOC}_6\text{H}_4)_2\text{PhC}$.

Prior to the incorporation of the nucleoside **8** into the oligonucleotide chain, this was converted into a phosphoramidite derivative. The use of acetyl or phenoxyacetyl groups for the protection of exocyclic amino groups of heterocyclic bases in the oligonucleotide synthesis allowed postsynthetic deprotection of the target oligomers under milder conditions, viz., with 50 mM potassium carbonate in methanol instead of concentrated ammonia, which reduced the risk of cyclisation reactions. However, subsequent hydrolysis of the modified oligonucleotides with snake venom phosphodiesterase and alkaline phosphatase revealed that about 50% of ferrocene-containing nucleosides existed as ferrocenylfuro-pyrimidones. Storage of oligonucleotides in solution causes gradual oxidation of ferrocene with atmospheric oxygen and results in the formation of a ferrocenium cation as demonstrated by reversed-phase HPLC. Therefore, dithiothreitol was added to the solution to stabilise modified uridine residues.³⁹

At present, the Sonogashira reaction is still the most popular procedure for the introduction of a ferrocenyl unit into a heterocyclic base.^{38–43} Thus compounds **11a,b** were prepared starting from 5-iodo-2'-deoxyuridine **9** or its 5'-dimethoxytrityl derivative **7** and alkynyl derivatives of ferrocene **10a,b**. The reaction of compound **10a** with protected 8-bromo-2'-deoxyadenosine **12** yielded a modified nucleoside **13**.

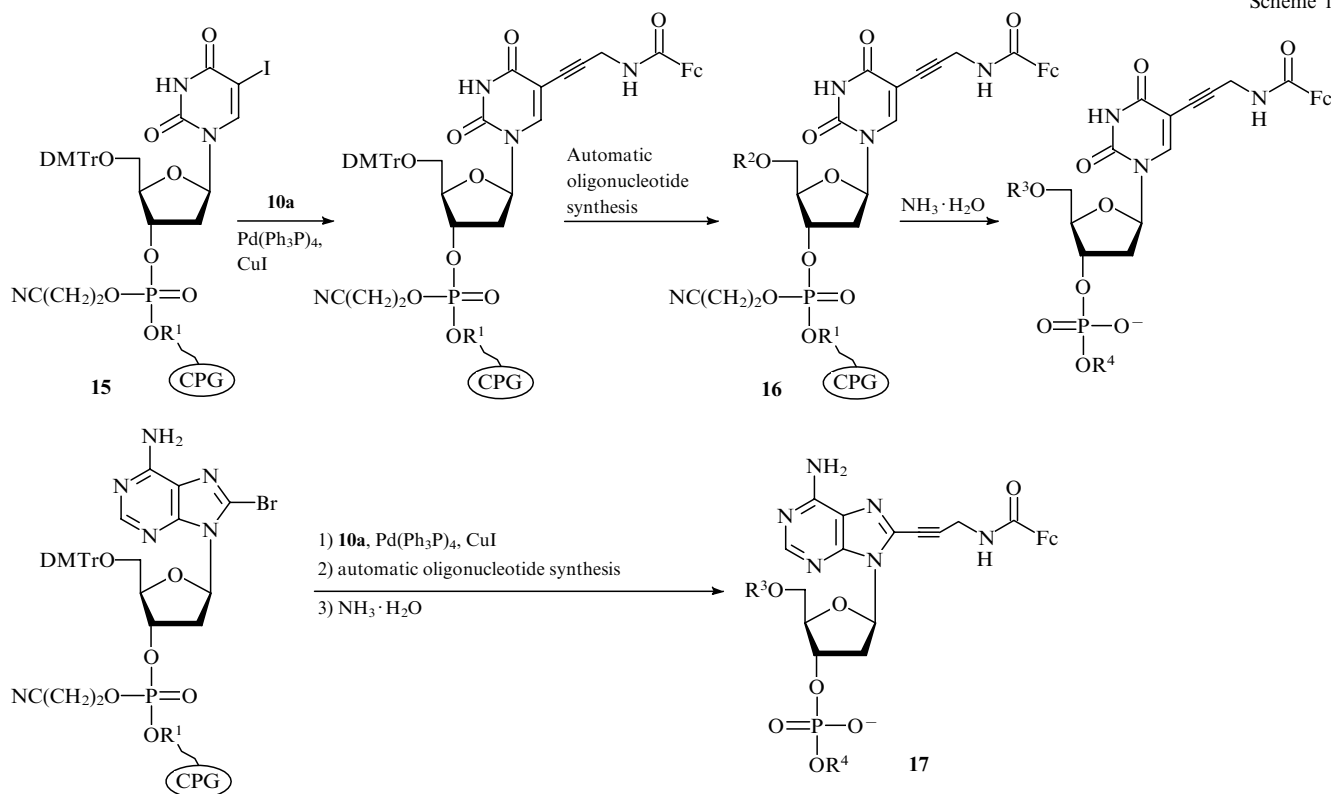




Modified 2'-deoxyuridine **11b** bearing a ferrocene derivative at C(5) was converted into 2',3'-dideoxy-5'-triphosphate **14** and attached to the 3'-end of an oligonucleotide using terminal deoxynucleotidyl transferase.⁴² Compound **14** and its analogues can be used for DNA sequencing according to Sanger⁴⁴ with electrochemical detection.

Grinstaff *et al.*^{40, 41, 45} have developed an original procedure for the incorporation of ferrocenyl derivatives into a growing oligonucleotide chain. This involved coupling of the propynyl ferrocene derivative **10a** with a modified oligomer **15** obtained by attachment of protected 5-iodo-2'-deoxyuridine **7** to the 5'-end of the protected immobilised oligonucleotide in the presence of a palladium catalyst and copper(I) iodide after which the oligonucleotide synthesis was continued. In the last step, the modified oligomer **16** was deprotected with concentrated aqueous ammonia (Scheme 1). Oligonucleotides **17** containing a modified deoxyadenosine residue were prepared in a similar way. The Sonogashira reaction is extremely sensitive to numerous factors, particularly to the presence of trace amounts of primary amines and water; therefore, the yields of the oligonucleotides were 20%–50%. It is of note that the yield of the target product **16** decreased to 8% when coupling of the ferrocene derivative **10a** was carried out after termination of the oligonucleotide synthesis. This can be attributed to steric hindrances created by the 5'-terminal fragment of the immobilised oligonucleotide. The yields of

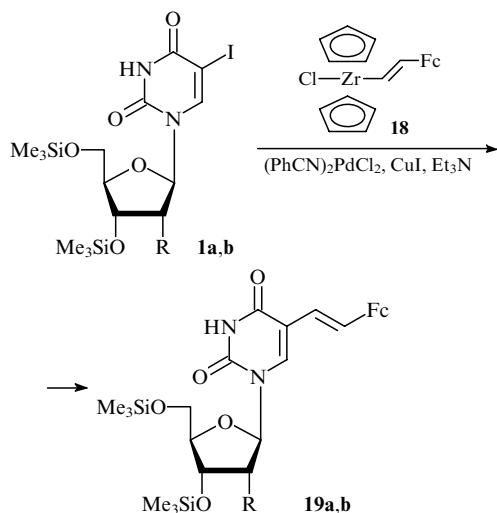
Scheme 1



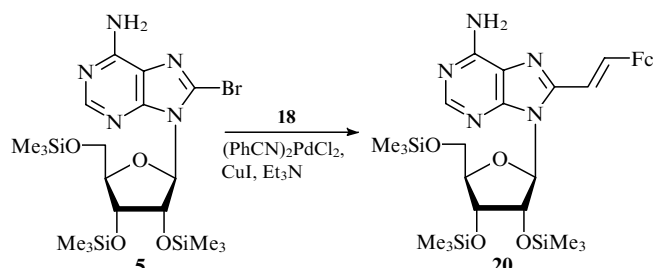
R^1, R^2 are fragments of a protected oligonucleotide chain; R^3, R^4 are fragments of an oligonucleotide chain; CPG, controlled pore glass.

the modified oligomers after incorporation of the ferrocene-containing nucleosides **11a** and **13** into the oligonucleotide chain were 10%–15%. The presence of a ferrocenyl-2'-deoxyadenosine derivative in the oligonucleotide chain induces greater destabilisation of a DNA duplex in comparison with its 2'-deoxyuridine analogue.

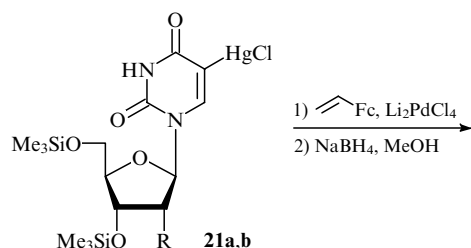
The second approach³⁵ to the synthesis of NA fragments containing a ferrocene residue in the heterocyclic base includes condensation of the halogenonucleosides **1a,b** and **5** with the organometallic vinylferrocene derivative **18**. The yields of the products **19a,b** and **20** were 15%–20%, which is significantly lower in comparison with the Sonogashira synthesis.



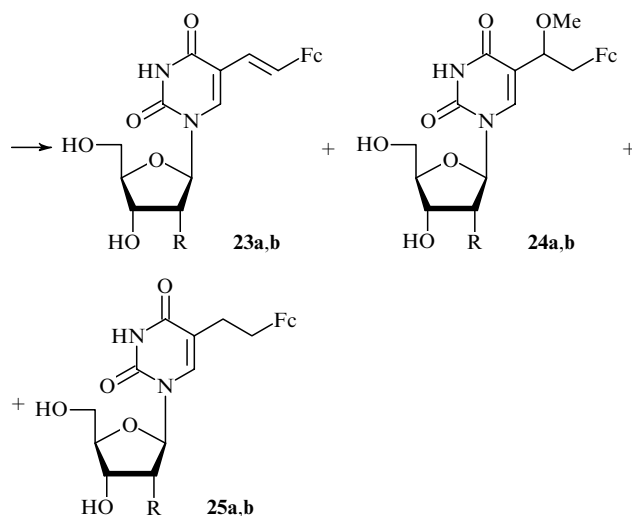
R = H (a), OSiMe₃ (b).



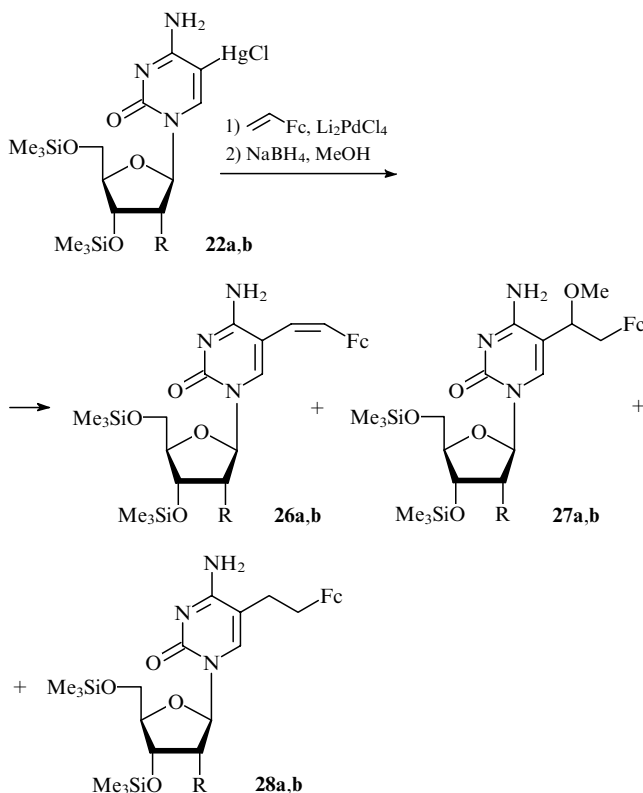
The third variant of the synthesis of NA fragments modified with ferrocene at the heterocyclic base³⁵ consists of cross-coupling of 5-chloromercurioorganic derivatives of uridine **21a,b** and cytosine **22a–c** with vinylferrocene in the presence of lithium tetrachloropalladate and subsequent treatment with sodium borohydride in methanol. This represents a modification of the Heck reaction.^{46,47} Methanol present in the reaction mixture interacts with the exocyclic double bond of the modified nucleoside, whereas sodium borohydride partly reduces it. Thus, the reaction of the uridine derivatives **21a,b** affords, along with the cross-coupling products **23a,b**, compounds **24a,b** and **25a,b** as well. Reaction of the cytosine derivatives **22a,b** with vinylferrocene gave the corresponding ferrocene-containing nucleosides **26–28**. In both cases, the total yields of the modified nucleosides were



15%–30%. The conditions favouring the predominant formation of one of the reaction products were selected.³⁵



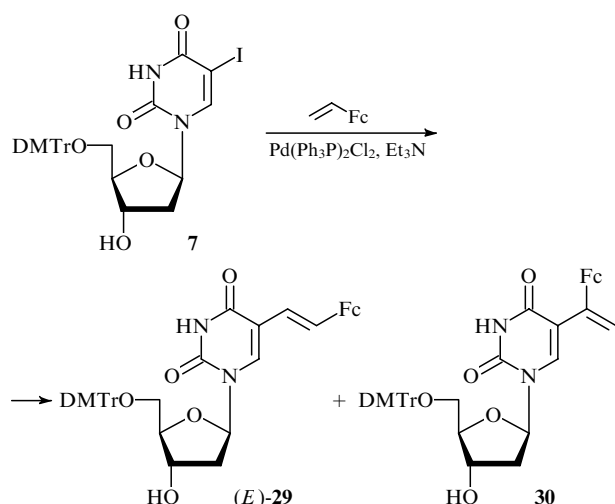
21: R = H (a), OSiMe₃ (b); **23–25**: R = H (a), OH (b).



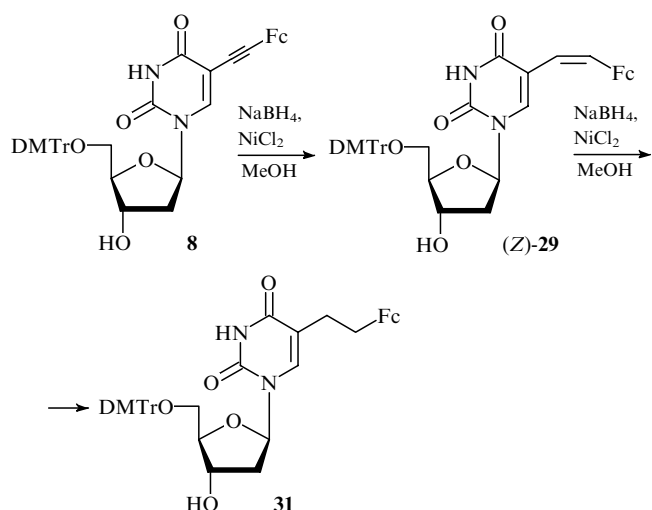
22: R = H (a), OSiMe₃ (b); **26–28**: R = H (a), OH (b).

The cytotoxic activities of deprotected 5-ferrocenylvinyl-2'-deoxyuridine **23a** and 5-ferrocenylvinyluridine **23b** were studied in L1210 cells *in vitro*.³⁵ The lethal dose causing death of 50% of cells (LD₅₀) was by several orders of magnitude lower than that of the traditional antibiotic adriamycin and commensurable with that of ferrocenylmethanol.

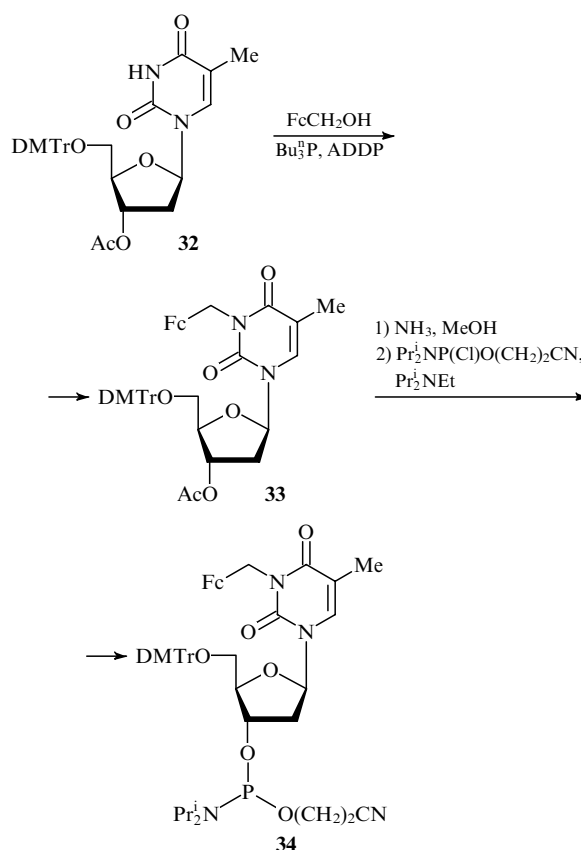
The Heck alkenylation of protected 5-iodo-2'-deoxyuridine **7** with vinylferrocene resulted in the formation of two products, (*E*)-**29** and **30** (3 : 1), in a total yield of 60%.^{39,43} An attempt to separate these compounds by TLC and HPLC failed; however, after deprotection of the 5'-hydroxy group (*E*)-5-ferrocenyl vinyl-2'-deoxyuridine was isolated by recrystallisation.



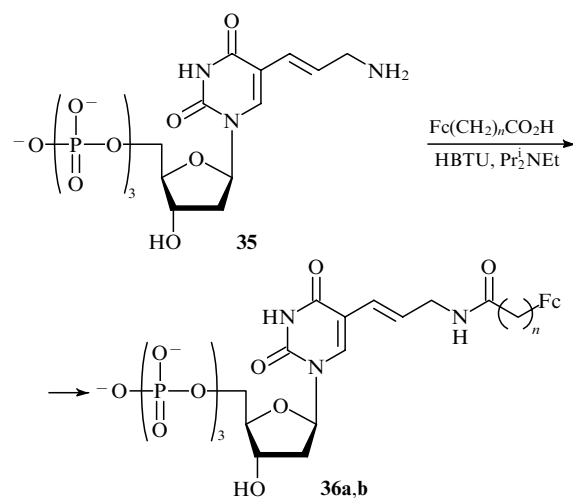
The *Z*-isomer of protected 5-ferrocenylvinyl-2'-deoxyuridine **29** was obtained by Houlton *et al.*^{39,43} by reduction of protected 5-ferrocenylethynyl-2'-deoxyuridine **8** with sodium borohydride in the presence of nickel chloride (yield 30%). Further reduction of compound (*Z*)-**29** under the same conditions afforded 5'-dimethoxytrityl-5-ferrocenylethyl-2'-deoxyuridine **31** in 25% yield.



A method⁴⁸ for the introduction of a ferrocenyl group at the N(3) atom of protected thymidine **32** by Mitsunobu reaction⁴⁹ of ferrocenylmethanol in the presence of tributylphosphine and diethyl azodicarboxylate (DEAD) in THF at room temperature has been proposed. The modified nucleoside **33** was further converted into the phosphoramidite derivative **34** employed for the preparation of ferrocene-containing oligonucleotides. Stacking interactions in such oligonucleotides are strongly violated as can be judged from CD spectroscopic data. As a consequence, duplexes of these oligonucleotides with DNA and RNA are less stable in comparison with natural ones, which makes this modification unacceptable for the design of NA detectors. Incorporation of a phosphoramidite derivative of the modified nucleoside **34** into the oligonucleotides increased the thermal stability of triplexes with double-helical DNA by 1–6 °C; however, their structures differed from the classical one (CD spectroscopic data). An attempt to explain the stabilisation phenomenon failed.⁴⁸

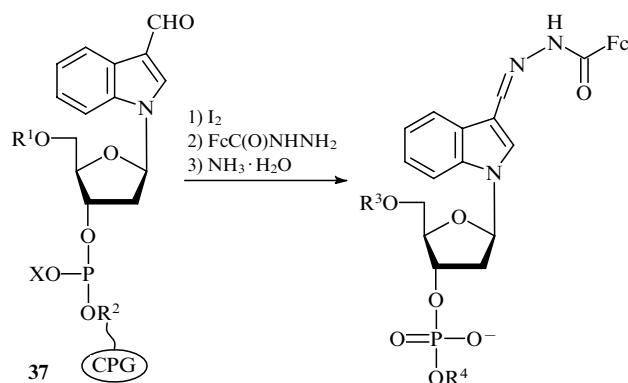


A method for the synthesis of a modified ferrocene-containing nucleoside triphosphate has been proposed.⁵⁰ 5-(3-Aminoprop-1-enyl)-2'-deoxyuridine triphosphate **35** was acylated with ferrocenecarboxylic and ferrocenylacetic acids in the presence of a condensation reagent, *O*-(benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU). The yields of compounds **36a,b** were only 30 and 8%, respectively. Nevertheless, this approach seems to be promising by virtue of its simplicity. Interestingly, the ferrocenecarboxylic acid derivative **36a** is a substrate of DNA polymerase, whereas its structural analogue, the ferrocenylacetic acid derivative **36b**, terminates the enzymatic reaction of elongation of the oligonucleotide chain.



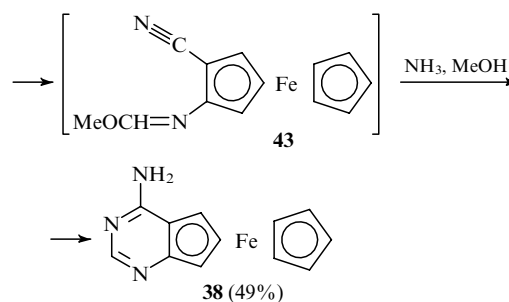
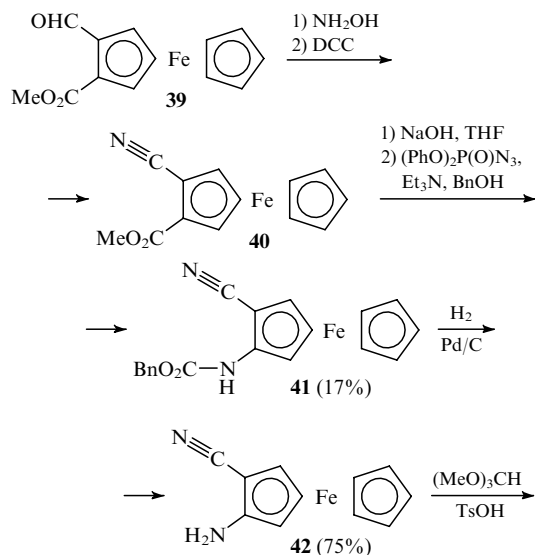
$n = 0$ (**a**), 1 (**b**).

It was recommended⁵¹ to attach ferrocenecarbohydrazide to the aldehyde group of a nonnative heterocyclic base of the oligonucleotide **37** immobilised on a polymeric support. However, the stabilities of the free aldehyde group in compound **37** with respect to oxidation with iodine under conditions of a standard phosphoramidite oligonucleotide synthesis and of the hydrazone formed in the standard postsynthetic treatment with aqueous ammonia are doubtful.



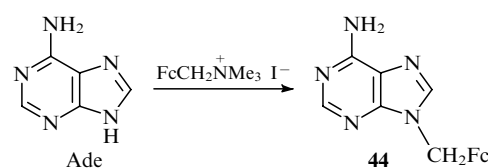
X = NC(CH₂)₂; R¹, R² are fragments of a protected oligonucleotide chain; R³, R⁴ are fragments of an oligonucleotide chain.

A multistep synthesis of an adenine analogue **38** from a ferrocene derivative **39** has been described.⁵² The aldehyde group in the latter was converted into a cyano group in two steps, *viz.*, by reaction with hydroxylamine to give an oxime and dehydration with dicyclohexylcarbodiimide in boiling benzene. The ester group in nitrile **40** was hydrolysed to a carboxy group using NaOH in THF. The reaction of the acid formed with diphenyl phosphoryl azide in the presence of triethylamine and benzyl alcohol was accompanied by Curtius rearrangement and gave compound **41** as the intermediate product; catalytic hydrogenolysis of the latter yielded aminonitrile **42**. Its one-pot reaction with triethyl orthoformate in the presence of *p*-toluenesulfonic acid and treatment of the imidate **43** with methanolic ammonia resulted in compound **38**. The structure of the latter was confirmed by ¹H, ¹³C NMR and IR spectroscopy and mass spectrometry. Further attempts will be aimed at the synthesis of the corresponding adenosine analogue which can be introduced into the oligonucleotide chain and used for the study of electron transfer in DNA duplexes. Most probably, the presence of such a modification within the oligonucleotide chain will strongly impede stacking interactions between 'stacked' heterocyclic bases.

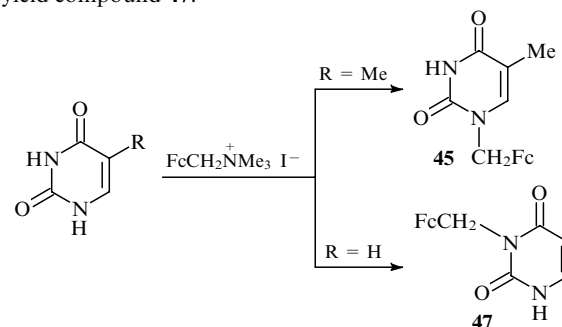


DCC = cyclo-C₆H₁₁–N=C=N–C₆H₁₁–cyclo.

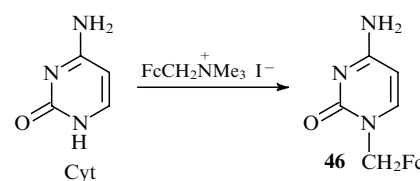
The synthesis of purine and pyrimidine heterocyclic bases containing a ferrocene moiety has been described.^{53, 54} 9-Ferrocenylmethyladenine (**44**) was prepared by alkylation of adenine (Ade) with (ferrocenylmethyl) trimethylammonium iodide.⁵³



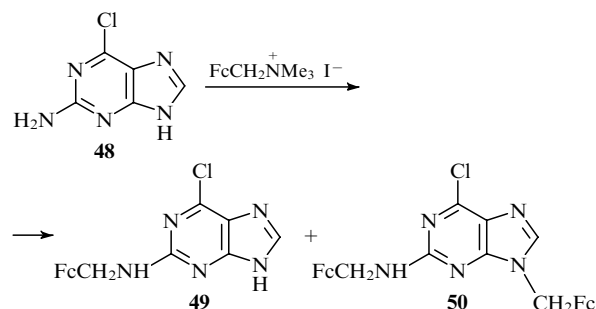
The use of this alkylating reagent enables preparation of N(1) thymine (Thy) and cytosine (Cyt) derivatives **45** and **46** as the main products, whereas uracil (Ura) is preferentially alkylated at N(3) to yield compound **47**.⁵⁴

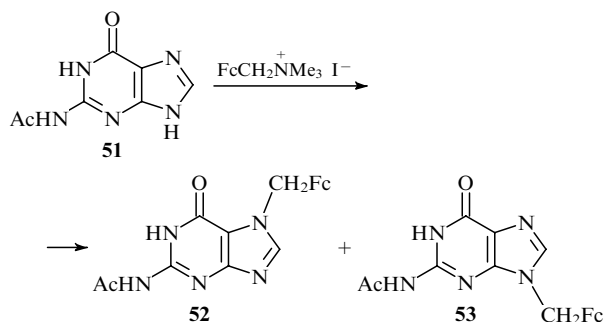


R = H (Ura), Me (Thy).

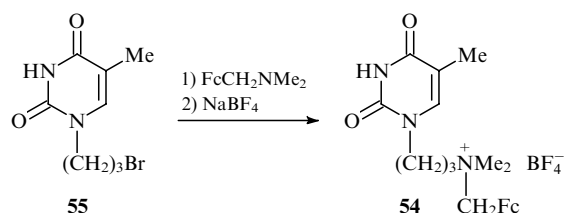


N(2)-mono- and N(2),N(9)-dialkyl derivatives **49** and **50** were isolated from 2-amino-6-chloropurine **48** as the guanine precursor, whereas the alkylation of 2-acetylguanine **51** occurred at N(7) and N(9) and afforded the products **52** and **53**. The structures of the synthesised compounds were established by X-ray diffraction analysis.

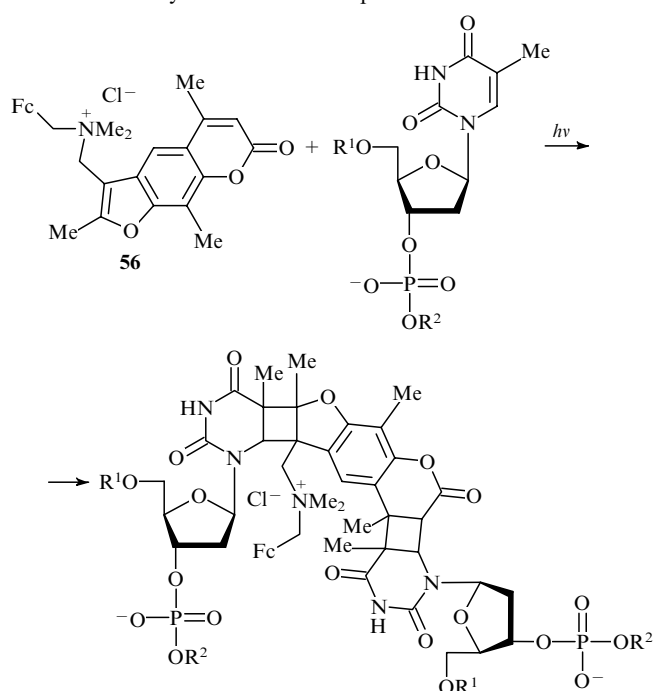




1-[3-(*N,N*-Dimethyl-*N*-ferrocenylmethyl)ammoniopropyl]thymine **54** was prepared by a reaction of 1-(3-bromopropyl)thymine **55** with (ferrocenylmethyl)dimethylamine and isolated in the form of a tetrafluoroborate.⁵³



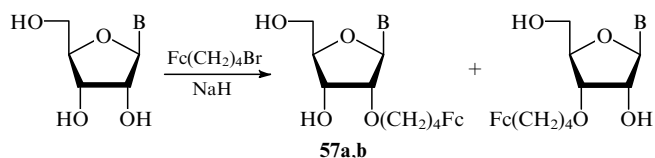
A method for the introduction of ferrocene residues into oligonucleotides based on a photochemical reaction of a ferrocenyl derivative of psoralene with thymine residues within double-stranded DNA has been developed.⁵⁵ To this end, *N,N*-dimethylaminomethylferrocene was alkylated with chloromethyl psoralene and the resulting compound **56** reacted with DNA in a buffer solution upon irradiation with the light of a mercury lamp ($\lambda = 365$ nm) for 10 min. This resulted in an efficient formation of ferrocene-containing conjugates of double-stranded DNA. The presence of a ferrocene residue was confirmed by cyclic voltammetry. This method enables electrochemical identification of double-stranded DNA, since the ferrocenyl–psoralene derivative reacts exclusively with the DNA duplex.



R^1 , R^2 are fragments of an oligonucleotide chain.

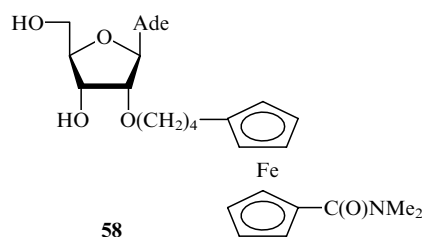
2. Synthesis of nucleosides and oligonucleotides containing ferrocene in the 2'-position of the carbohydrate moiety

There are several methods for the synthesis of 2'-*O*-alkylnucleosides⁵⁶ among which alkylation of free nucleosides with alkyl halides in the presence of sodium hydride is one of the most widespread and efficient procedures. In this case, the selectivity of the reaction involving the 2'-hydroxy group is explained by its higher acidity in comparison with 3'- and, especially, 5'-hydroxy groups. This method was used^{57, 58} for the synthesis of nucleosides containing ferrocenyl units in the 2'-position of the carbohydrate moiety.⁸ The yields of the alkylation products of adenosine **57a** and cytidine **57b** were 40 (isomer ratio 2' : 3' = 2.7 : 1) and 76% (isomer ratio 2' : 3' = 1.8 : 1), respectively.



B = Ade (a), Cyt (b).

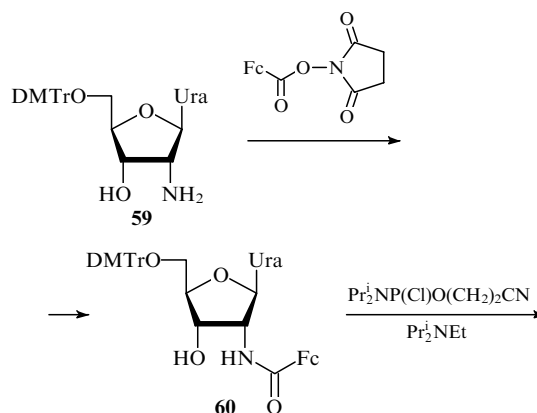
Compound **58** containing a dimethylcarbamoylferrocene residue in the 2'-position was synthesised in a similar way; it possessed a redox potential different from that of ferrocene.



Nucleosides **57a,b** and **58** were converted into phosphoramidite derivatives that were employed in the automatic oligonucleotide synthesis. Incorporation of the modified nucleosides into the oligonucleotide chain did not change the thermal stability of the DNA duplexes, which is typical for 2'-*O*-alkyl nucleosides.⁶⁰

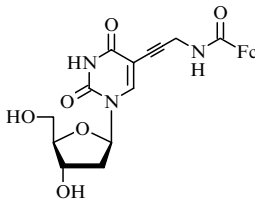
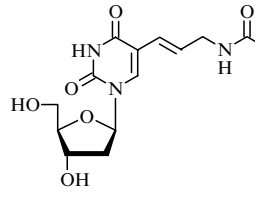
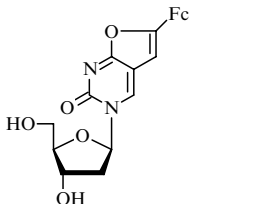
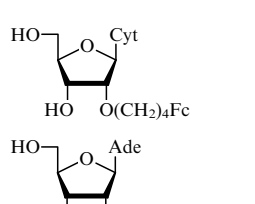
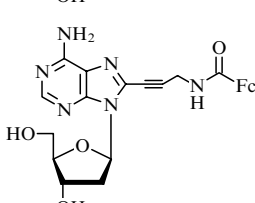
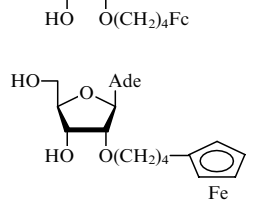
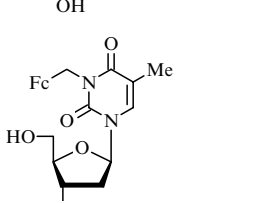
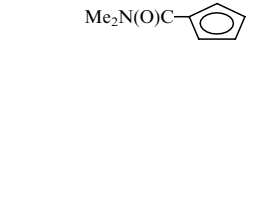
The data on the thermal stabilities of ferrocene-containing DNA duplexes are listed in Table 1.

Acylation of 5'-protected 2'-amino-2'-deoxyuridine **59** with *N*-hydroxysuccinimide ester of ferrocenecarboxylic acid is patented.^{61–63} Subsequent phosphorylation of nucleoside **60** occurred at a low rate and resulted in compound **61** in a low yield (30%), which is due to the presence of a bulky substituent in the 2'-position of the carbohydrate fragment.



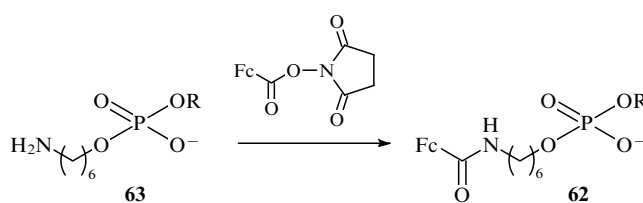
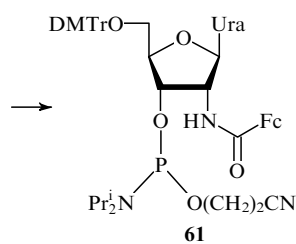
§ The first report on the use of oligonucleotides containing ferrocene in the 2'-position of the carbohydrate fragment was published three years earlier. However, no detailed description of this synthesis was given.⁵⁹

Table 1. Changes in thermal stability (ΔT_m) of DNA duplexes upon incorporation of ferrocene-containing nucleosides into the oligonucleotide chain.

Modified nucleoside	$\Delta T_m / ^\circ\text{C}$ (see ^a)	Conditions ^b	Ref.	Modified nucleoside	$\Delta T_m / ^\circ\text{C}$ (see ^a)	Conditions ^b	Ref.
	–(1.2–2.6)	5 mM NaH ₂ PO ₄ , 50 mM NaCl, pH 7.0	41		–0.8	300 mM KH ₂ PO ₄ , pH 7.0 (see ^c)	
	–(5.5–5.7)	15 mM sodium citrate, 150 mM NaCl, pH 7.0	38		–0.4 to +0.4	15 mM sodium citrate, 150 mM NaCl, pH 7.0	57
	–(7.6–9)	5 mM NaH ₂ PO ₄ , 50 mM NaCl, pH 7.0	41		0.1	the same	57, 58
	–(0.4–7.7) (near the 5'-end) –(4.7–14.1) (inside the chain)	10 mM NaH ₂ PO ₄ , 100 mM NaCl, pH 7.0	48		–0.4	"	58

$$^a \Delta T_m = \frac{T_m(\text{modified DNA duplex}) - T_m(\text{natural DNA duplex})}{\text{number of modifications per DNA duplex}}$$

^b Concentration of the DNA duplex, 2 $\mu\text{mol litre}^{-1}$. ^c Concentration of the DNA duplex, 0.6 $\mu\text{mol litre}^{-1}$.

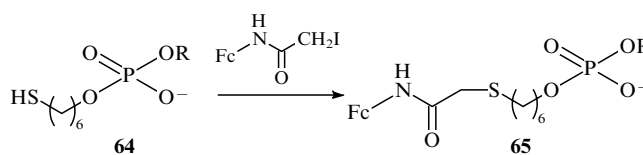


R is an oligonucleotide.

3. Synthesis of oligonucleotides containing ferrocene at the 5'- or 3'-termini

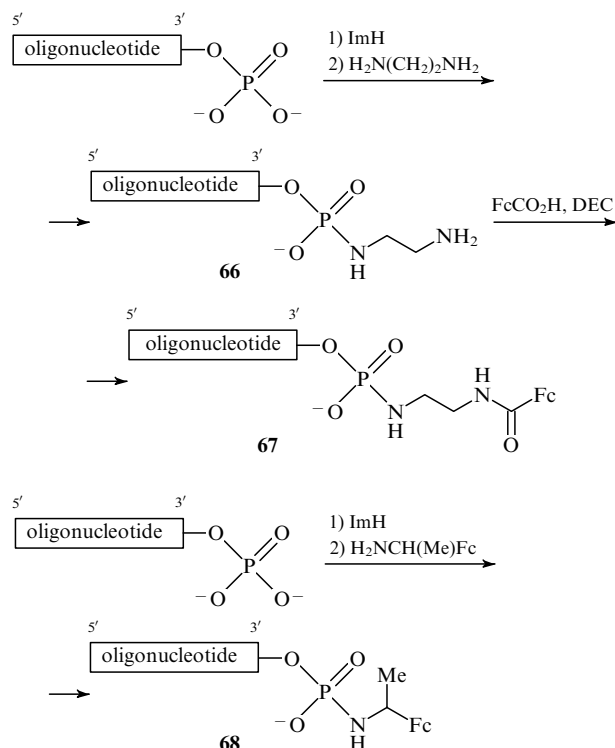
For the first time, the ferrocene-containing oligonucleotide **62** was prepared by acylation of the 5'-terminal amino group of compound **63** by *N*-hydroxysuccinimide ester of ferrocenecarboxylic acid ^{64–66} containing a ⁵⁷Fe isotope. Later, this approach was used many times, ^{67–71} e.g., for the synthesis of an analogous derivative of ferrocenylacetic acid.⁷² Incorporation of the modified compound into the oligonucleotide structure significantly increased the stability of the triplex with double-helical DNA ($\Delta T_m = 2.5–2.6$ $^\circ\text{C}$).

Recently, it has been proposed ⁷³ to use iodoacetamidoferrocene, which interacts selectively with thiols, for modification of biomolecules. The specificity of incorporation of this reagent was demonstrated using the 5'-thiol-containing oligonucleotide **64** as an example.



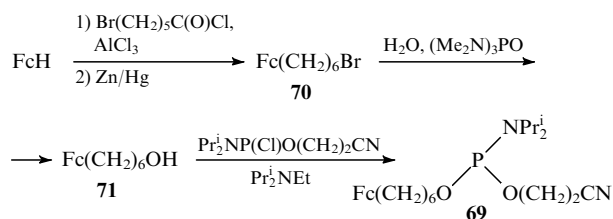
R is an oligonucleotide.

The introduction of a ferrocenyl residue at the 3'-end of the oligonucleotide was carried out using postsynthetic acylation of the 3'-terminal amino group of the oligonucleotide **66** with ferrocenecarboxylic acid in the presence of 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide (DEC)⁷⁴ or the addition of 1-aminoethylferrocene to the activated 3'-phosphate group.⁷⁵

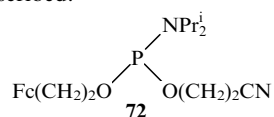


ImH is imidazole.

Letsinger *et al.*⁷⁶ recommended the use of the phosphoramidite derivative **69** for the synthesis of ferrocene-containing oligonucleotides. This approach is widely used for incorporation of such markers as biotin, acridine, fluorescein, *etc.* into oligonucleotides. 6-Bromohexylferrocene **70** was synthesised by the Friedel–Crafts acylation of ferrocene with 6-bromohexanoyl chloride with subsequent reduction of the carbonyl group with zinc amalgam. The bromo derivative **70** was converted into alcohol **71** and then into the phosphoramidite **69**.

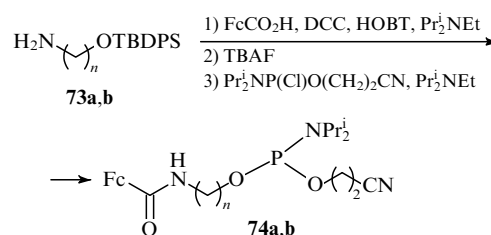


Synthesis of an analogous phosphoramidite **72** and its application for the synthesis of modified oligonucleotides have been described.⁵⁷



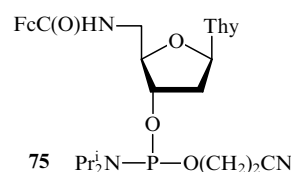
The synthesis of a series of phosphoramidite derivatives including nucleosides entails attachment of a ferrocene residue to the 5'-end of the oligonucleotide.⁷⁷ This is achieved by acylation of amino groups of compounds **73a,b** with ferrocenecarboxylic acid in the presence of a condensation reagent, *viz.*, dicyclohexylcar-

bodiimide. After removal of a *tert*-butyldiisopropylsilyl protective group by treatment with tetrabutylammonium fluoride, the phosphoramidite derivatives **74a,b** were synthesised.

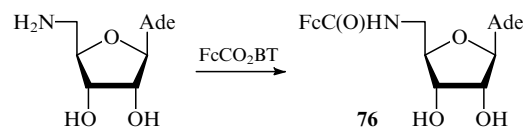


TBDPS = Bu^tPr₂ⁱSi; HOBT = ; TBAF = Bu₄N⁺ F⁻; $n = 2$ (a), 4 (b).

The phosphoramidite derivative of 5'-ferrocenecarboxamido-5'-deoxythymidine **75** was synthesised in a similar way.



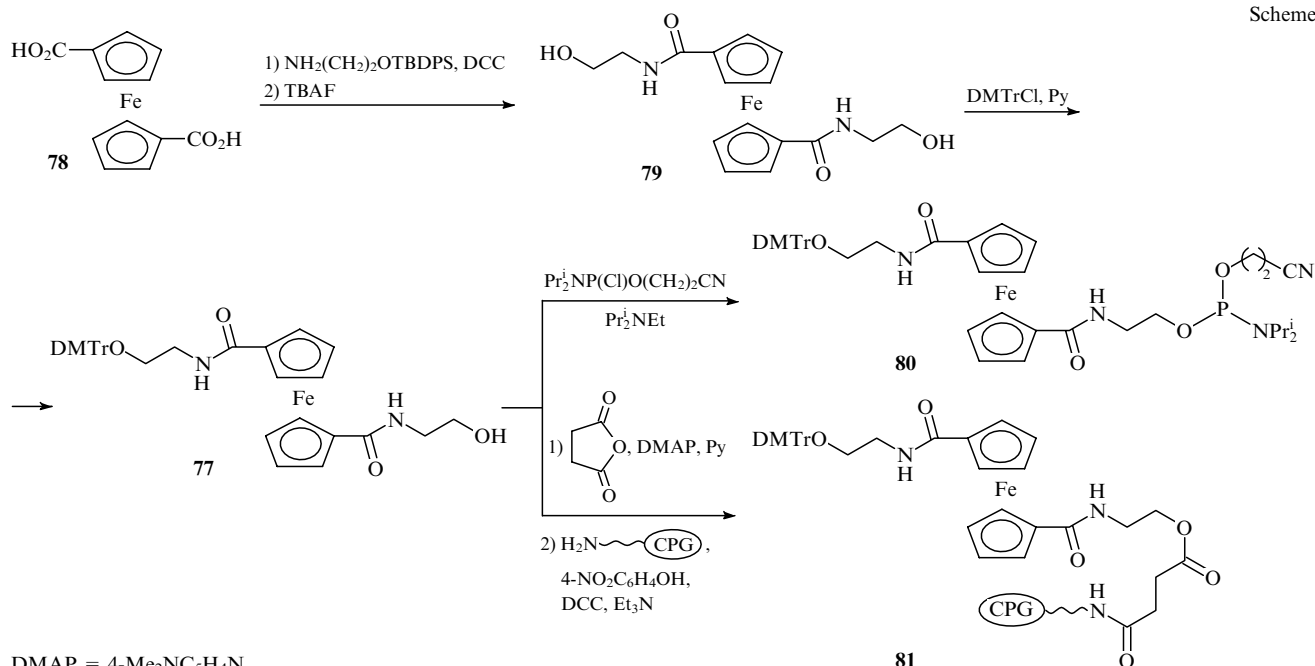
Synthesis of 5'-ferrocenecarboxamido-5'-deoxyadenosine **76** from *N*-hydroxybenzotriazole ester of ferrocenecarboxylic acid has been developed recently by Kraatz and co-workers.⁷⁸



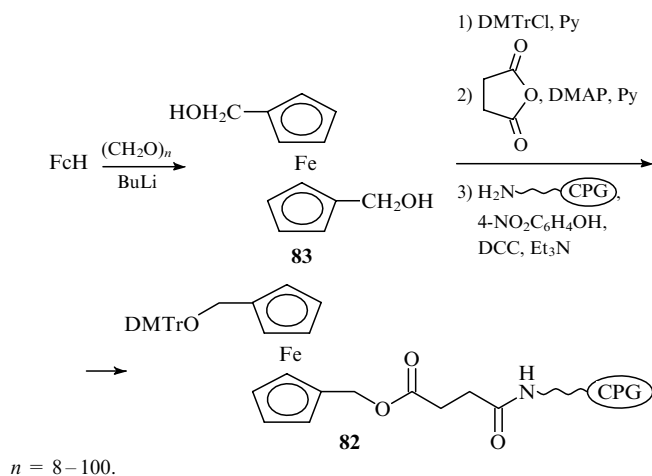
Synthesis of compound **77**, which can be used for incorporation of the ferrocene residue inside or at the end of the oligonucleotide chain, has been described.⁷⁹ Condensation of 1,1'-ferrocenedicarboxylic acid **78** with *O*-protected aminoethanol in the presence of dicyclohexylcarbodiimide and subsequent deprotection of the hydroxy groups afforded compound **79**; treatment of the latter with dimethoxytrityl chloride in pyridine affords the monoprotected derivative **77**. Compound **77** was converted into a standard building block for oligonucleotide synthesis (**80**) by phosphitylation. The reaction of the derivative **77** with succinic anhydride and subsequent immobilisation on a solid phase support containing aminoalkyl groups afford compound **81** (Scheme 2). It is known⁸⁰ that non-nucleoside inserts strongly destabilise DNA duplexes; therefore, compound **80** was attached to the 5'-end of the oligonucleotide in the last step of the synthesis (yield 50%). The ferrocene-containing fragment was attached to the 3'-end using compound **81**. The yield of the target oligonucleotide was 12% (possibly due to degradation of the ferrocene residue in the course of an automatic oligonucleotide synthesis, particularly during oxidation of phosphites into phosphates).

The same work⁷⁹ describes the use of a modified polymeric support **82** for the synthesis of oligonucleotide conjugates containing ferrocene at the 3'-end and of 5'-conjugates for inverted automatic oligonucleotide synthesis. Reaction of ferrocene with paraformaldehyde in the presence of butyllithium gave 1,1'-ferrocenedimethanol **83** in which one hydroxy group was protected by dimethoxytrityl chloride and the other one was acylated with succinic anhydride and immobilised on a solid phase support to obtain compound **82**. A phosphoramidite for incorporation inside the oligonucleotide chain can also be synthesised from the ferrocene derivative **83**.

Scheme 2



Synthesis of ferrocene conjugates with peptide nucleic acids has recently been described.^{81, 82} It is known⁸³ that peptide nucleic acids form stable specific duplexes with DNA. These duplexes when they contain mismatches in base pairs are strongly destabilised.^{81, 82} This property was used in the design of a DNA sensor.^{61, 84}



III. Electrochemical detection of nucleic acids

The need for identification and quantitative determination of NA has stimulated the development of numerous analytical methods. Certain known procedures were adapted to the detection of these biomolecules. Electrochemical methods occupy an important place among other techniques for quantitative and qualitative detection of DNA.

Electrochemical activity of NA was discovered about 40 years ago;⁸⁵ the first evidence for the polymorphism of the double helix of DNA was confirmed some time later using electrochemical methods.⁸⁶

Interaction of NA with a charged electrode surface is usually accompanied by strong absorption and concomitant charge transfer reactions. The electrochemical signals thus generated provide evidence about the type of adsorbed molecules, their concentrations, structural changes and an ability to interact with various compounds. Thus NA fragments immobilised on an electrode surface can be used in the design of NA detectors.⁸⁷ Native DNA

is usually analysed using mercury or carbon (less frequently gold, platinum, copper or silver) electrodes. Solid metal electrodes are more suitable for the study of DNA oxidation; the oxidation of guanine and adenine is also carried out on carbon electrodes, whereas reduction is most conveniently studied on the surface of mercury electrodes. Heterocyclic bases are the main NA fragments involved in the redox reactions on electrodes.

Hydrogen bonds formed by complementary base pairs in electrochemically active DNA molecules influence strongly signals elicited during adenine and cytosine reduction on mercury electrodes and provide information about the presence or absence of complementary interactions on the electrode surface, structural transitions and local conformational changes in DNA molecules.^{88, 89}

Redox reactions of native DNA are irreversible and require the application of high positive or negative potentials, which may cause unwanted destruction of DNA chains. The sensitivity of analytical methods can be increased through incorporation of electroactive reporter groups covalently or noncovalently linked to a single-stranded DNA or a DNA duplex. Such markers are capable of reversible redox conversions at low electric potentials on electrodes. Non-covalent binding of reporter molecules to natural DNA can involve: (1) electrostatic and, as a consequence, nonspecific binding to charged phosphate groups of DNA; (2) minor or major groove binding; and (3) intercalation of aromatic molecules between heterocyclic bases of a DNA duplex. Chelate complexes of transition metals and ferrocene derivatives are often used as markers.^{90, 91}

There are two approaches different in principle to detect DNA. In one of them, complexes of stable isotopes of iron or other metals are used as labels. Incorporation of chemically identical labels carrying different isotopes of the same element into the DNA primers has virtually no effect on their physicochemical properties, *e.g.*, electrophoretic mobilities. This allows sequencing of extended NA fragments with high precision. Labelled DNA fragments are identified using resonance ionisation spectroscopy or mass spectrometry. The efficiency of this method for NA detection in the Sanger sequencing and amplification of DNA in the polymerase chain reaction (PCR) was demonstrated by Jacobson *et al.*^{64, 65} However, despite the significant progress in this field in the early 1990's, this method has not received wide recognition, because many reagents and materials used in molecular biological studies, *e.g.*, nylon membranes, contain iron which decreases drastically its sensitivity.⁹²

An alternative approach consists of the use of amperometric techniques for detecting Fe(II)/Fe(III) redox signals. It should be noted that the use of ferrocene and its derivatives as markers permits directed changes in the halfwave potential ($E_{1/2}$) of the redox pair due to inductive effects of substituents in cyclopentadiene rings. This allows variations of electrochemical properties of reporter groups without any significant changes in their size or reactivity.⁶⁶

1. Redox characteristics of ferrocene-containing nucleic acids

The value of the halfwave redox potential $E_{1/2}$ determined experimentally by amperometric methods is an important characteristic feature of molecules involved in redox processes.

Introduction of electron-donor groups into the cyclopentadiene ring of ferrocene decreases the $E_{1/2}$ value, whereas electron-withdrawing groups increase it as was demonstrated by Morris in 1974.⁹³ There are several groups of nucleoside and oligonucleotide ferrocenyl derivatives with similar redox potentials (Table 2). The simultaneous use of several ferrocenyl derivatives enables parallel detection of different NA fragments, *e.g.*, in a flow.

The change in the redox potential upon absorption of ferrocene-containing derivatives on the electrode surface is due to the increase in the dielectric component of the potential of the adsorbed molecule. A comparison of $E_{1/2}$ values for ferrocene oxidation in oligonucleotides (*e.g.*, at the end of an alkyl linker in the 2'-position of the carbohydrate fragment) and in a water-soluble ferrocenyl ethyl phosphate devoid of nucleotide units has been carried out.⁵⁷ It was found that electrochemical characteristics of ferrocene-containing oligonucleotides in solution differ only slightly from those of other ferrocene derivatives.

Studies by cyclic voltammetry have shown that the electrochemical characteristics of the ferrocene unit have virtually no dependence on either the structures of the complexes of ferrocene-containing oligonucleotides with DNA (a duplex or a triplex) or their nucleotide compositions.⁶⁸ A small (10–30 mV) decrease in the halfwave oxidation potential of the ferrocene unit at the 5'-end of a short oligonucleotide upon its incorporation into a triplex may be attributed to the interaction of the ferrocenyl cation with the phosphate groups as a result of which the former is less exposed to the solution. Thus, it was concluded⁶⁸ that ferrocene

Table 2. Redox potentials (*versus* Ag/AgCl) of conjugates of NA fragments with ferrocene.

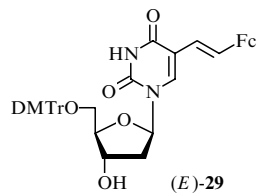
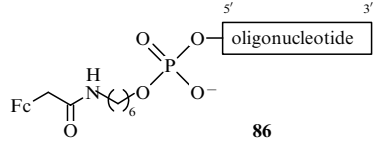
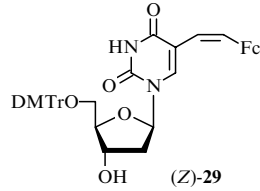
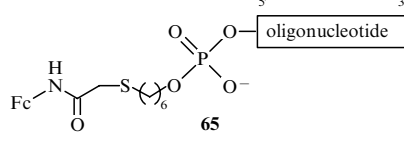
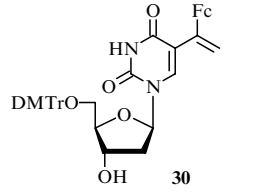
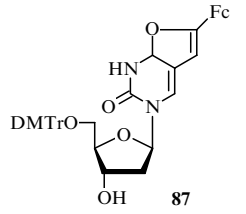
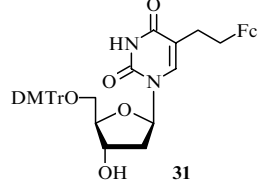
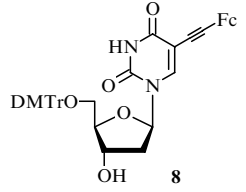
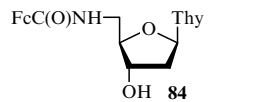
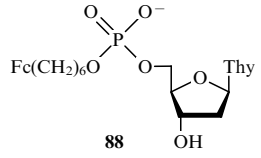
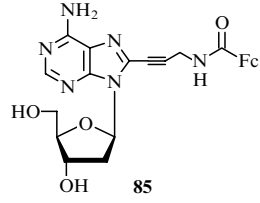
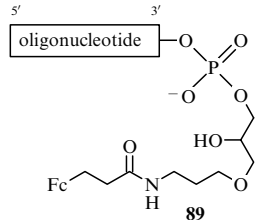
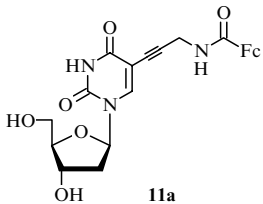
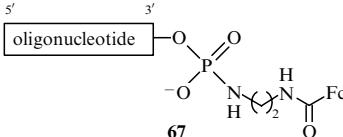
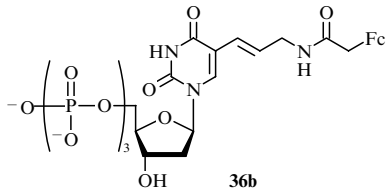
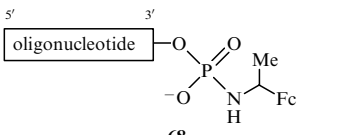
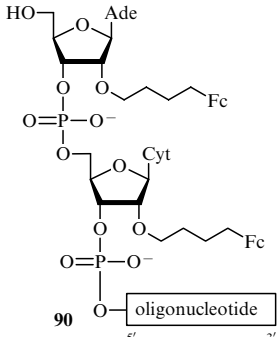
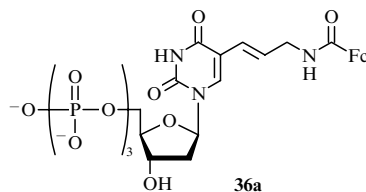
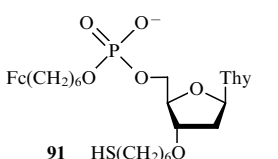
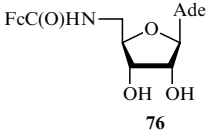
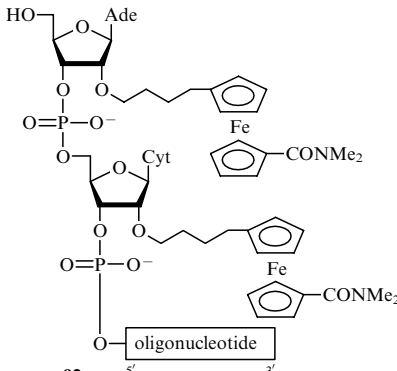
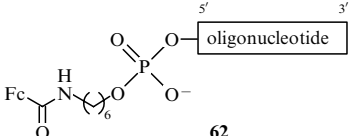
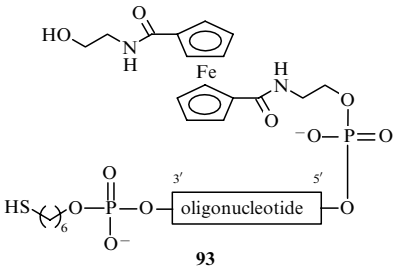
Compound	$E_{1/2}$ /mV	Ref.	Compound	$E_{1/2}$ /mV	Ref.
 (E)-29	27 ^a	39	 86	60	72
 (Z)-29	29 ^a	39	 65	16 ^b	73
 30	21 ^a	39	 87	131 ^a	39
 31	16 ^a	39	 8	140 ^a	39
 84	24	41	 88	110	76
 85	48	41	 89	135 ^c	94

Table 2 (continued).

Compound	$E_{1/2}$ /mV	Ref.	Compound	$E_{1/2}$ /mV	Ref.
 11a	262	40	 67	300	74
 36b	260	50	 68	290	75
 90	181	57	 36a	398	50
 91	220 ^d	76	 76	412	78
 92	324	58	 62	430 645 ^e	68 70
			 93	574 ^d	79

^a Solution in acetonitrile. ^b Versus a standard carbon electrode. ^c Versus a saturated calomel electrode. ^d The nucleotide was immobilised on an electrode.

^e The oligonucleotide was hybridised with a target immobilised on an electrode.

can be used as a versatile electrochemical marker for detection and quantitation of DNA.

2. Electrochemical detection of ferrocene-containing DNA fragments and their complexes using HPLC analysis and capillary electrophoresis

High-performance liquid chromatography with UV detection is a popular conventional procedure for purification and analysis of NA^{95,96} owing to its high efficiency and a relatively low cost. Wlassoff and King⁵⁰ have carried out a comparison of various

UV and electrochemical techniques for detecting ferrocene-containing oligonucleotides to demonstrate that the latter enable quantitative determination of DNA in femtomolar concentrations, while the sensitivity of the optical methods does not exceed picomolar concentrations (Table 3), *i.e.*, it is by about three orders of magnitude lower.

Takenaka *et al.*⁶⁷ have developed a highly sensitive method for detecting polynucleotides in solution by hybridisation with complementary oligonucleotides containing ferrocene residues at the 5'-end followed by HPLC analysis and electrochemical detection.

Table 3. Detection limits of ferrocene-containing oligonucleotides established by different analytical methods.

Method	Detection limit /mol (sample concentration /mol litre ⁻¹)	Ref.
HPLC with electrochemical detection	1×10^{-15} (1×10^{-9})	50
HPLC with electrochemical detection (hybridisation of a ferrocene-containing oligonucleotide with a target)	1×10^{-15}	67
HPLC with electrochemical detection, preliminary PCR	1×10^{-19}	69
Capillary gel electrophoresis with sinusoidal voltammetric detection	3×10^{-14} (3×10^{-9}) 1.8×10^{-15} (9×10^{-10})	72 97
Hybridisation of a ferrocene-containing oligonucleotide with a target bound to an oligonucleotide immobilised on an electrode; differential pulse voltammetry	1×10^{-15}	71
Hybridisation of a ferrocene-containing oligonucleotide with a target immobilised on a chitosan-coated glass electrode; differential pulse voltammetry	2×10^{-11} (2×10^{-9})	75
Hybridisation of a ferrocene-containing oligonucleotide with a target immobilised on a carbon electrode; differential pulse voltammetry	5×10^{-11} (5×10^{-9})	74

The sensitivity of this method is comparable with the detection limit of radioactive labels (10^{-15} mol, see Table 3). It is noteworthy that fluorescent and luminescent methods, which demand preliminary enzymatic amplification of DNA with modified nucleoside triphosphates, appeared to be more sensitive, but were more time-consuming in comparison with electrochemical methods (2–3 days vs. 2–3 hours). HPLC with electrochemical detection was successfully used⁶⁷ for quantitation of a series of natural polynucleotides (transport gene of yeast choline, oncogen *v-myc*, eukaryotic mRNA). The analysis of mRNA is facilitated by the presence of a 3'-terminal poly-A sequence, which enables the use of homothymidine sequence as a signal oligonucleotide.

An improved procedure for the detection of DNA in solution developed in 1997⁶⁹ is based on the combination of HPLC⁶⁷ and PCR, which makes it possible to increase the number of DNA copies using ferrocene-containing oligonucleotides as primers.⁹⁸ The amplification products were analysed by HPLC with electrochemical detection, which significantly lowered the detection limits (see Table 3). Yet another advantage of this method is that the analysis does not require the use of control DNA samples, whereas in routine quantitative analyses using PCR, DNA amplification is performed in the same tube with DNA under analysis. This method was used for quantitation of the oncogen *v-myc* and the human muscular dystrophin gene.

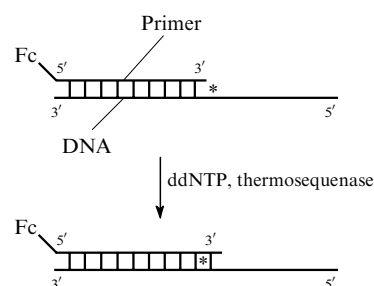
Capillary gel electrophoresis has been extensively used over the past decade for the analysis of DNA. It represents a standard and the most efficient procedure for DNA sequencing.⁹⁹ This method combined with the use of fluorescently labelled NA has received wide acceptance. Detection by mass spectrometry is also becoming very popular.¹⁰⁰ In recently published papers,^{8,101} capillary electrophoresis of PCR products (ferrocenyl derivatives of NA) was carried out with electrochemical detection.^{72,97}

The authors of a device for electrochemical detection of biomolecules in capillary gel electrophoresis by an amperometric method suggested that electrochemical labels were directly incorporated into the molecules to be analysed.⁸ Such an approach

allows simultaneous detection of different molecules and is analogous to fluorescence detection at several wavelengths.

Capillary gel electrophoresis with sinusoidal voltammetric detection¹⁰² was used for selective identification of DNA amplification products.⁹⁷ This method is characterised by high signal/noise ratios and maximum selectivity in detecting electrochemically active molecules based on their unique frequency spectra. Oligonucleotides **62**, **86**, **90** and **92** containing ferrocene residues in their 5'-terminal units were used as PCR primers. The electrochemical originality of each of the four oligonucleotide primers was achieved owing to the presence of substituents in the ferrocenyl fragments able to influence the redox potential of ferrocene. This, in turn, enables detection and analysis of distribution patterns of ferrocene-containing oligonucleotides in electrophoretic fractions. In addition, cyclic voltammetric studies have shown that static voltammograms of ferrocene-containing primers virtually do not differ from those recorded under electric field in the electrophoresis. This allows one to extend the scope of the method, since it does not require the use of additional corrections for an electric field.

It was recommended⁷² to use sinusoidal voltammetry for the analysis of single base extension products of an oligonucleotide chain by capillary gel electrophoresis. This was carried out by hybridisation of a DNA probe with a ferrocene-containing primer followed by addition of 2',3'-dideoxynucleoside triphosphate (ddNTP) complementary to the nucleotide under study and thermostable Ampli Taq polymerase from *Thermus aquaticus* (Fig. 1). The extension reaction stopped in the case of a point mutation in the DNA sample. The unreacted primer was separated from the reaction product by capillary gel electrophoresis.[†] The fractions were analysed by sinusoidal voltammetry. This method allows easy miniaturisation, which makes it a convenient tool for the development of an automatic portable system for detecting mononucleotide polymorphism in the genome.

**Figure 1.** A scheme of a one-unit elongation reaction of an oligonucleotide chain.⁷²

3. Electrochemical detection of ferrocene-containing DNA fragments and their complexes on the electrode surface

A biosensor (or a biodetector) consists of an element that selectively recognises biologically active molecules and is connected to a sensor which converts molecular recognition into a physically measurable quantity.¹⁰³ A standard electrochemical detector for DNA hybridisation represents an electrode with short (as a rule, 15–20-mer) oligonucleotides immobilised on its surface (Fig. 2). When such an electrode is placed into a solution containing DNA to be sequenced, a duplex is formed on the electrode surface. The changes in the surface layer are detected by electrochemical or gravimetric methods. The choice of the elec-

[†] It should be noted that this method allows separation of oligonucleotides differing in one unit and containing up to 250 bases.

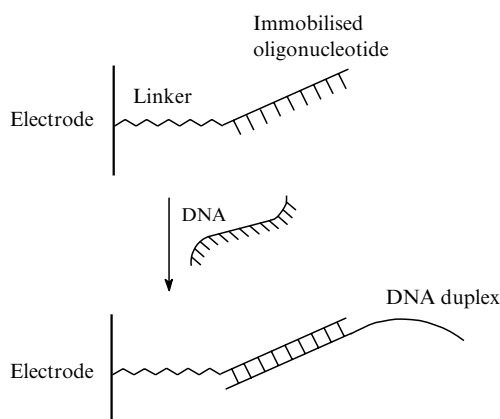


Figure 2. The formation of a duplex on the electrode surface.

trode material and the immobilisation procedure are crucial steps in the design of DNA sensors.

Immobilisation of oligonucleotides is performed by various methods which include covalent and noncovalent binding to the electrode surface. Thus immobilisation on carbon and mercury electrodes is carried out by the electrostatic adsorption method. Adsorption on positively charged electrodes is achieved owing to electrostatic attraction of negatively charged phosphate groups, which leaves heterocyclic bases accessible for the interaction with specific DNA sequences.

Covalent immobilisation of oligonucleotides on the electrode surface, which involves reactive groups of heterocyclic bases, is hardly recommendable because of a decrease in sensitivity of DNA sensors. The attachment of one end of an oligonucleotide molecule to the electrode surface is the most efficient approach. In the general case, covalent immobilisation of oligonucleotides is more convenient for the design of biosensors, since it permits one to avoid nonspecific binding of electrochemically active molecules.⁸⁷

At present, chemisorption of oligonucleotides on an electrode surface makes use of both modified oligonucleotides and electrodes with a modified surface.¹⁰⁴

In 1996, Letsinger *et al.*⁷⁶ developed a procedure for electrochemical characterisation of a monolayer formed by molecules of an immobilised nucleotide **99** on the surface of a gold electrode. This approach entails incorporation, into the nucleotide, of both a 3'-terminal linker with a thiol group essential for immobilisation and a 5'-terminal ferrocene residue. The monolayer formed after chemisorption of such molecules on the electrode surface was studied by cyclic voltammetry. The data obtained suggest that the surface density of nucleotide molecules on gold is 3.0×10^{-10} mol cm⁻². The applicability of such systems for detection of DNA hybridisation has been demonstrated.⁷⁶

An original gene diagnostics procedure has been developed.⁷⁰ In this method, several phosphothioate groups were introduced into the 5'-terminal region of an oligonucleotide complementary to a specific site of the DNA target and the oligonucleotide was immobilised on a gold electrode. After hybridisation with DNA, the electrode was treated with a solution of a ferrocene-containing oligonucleotide **62** complementary to the free region of the DNA molecule (Fig. 3). The detection was performed using differential pulse voltammetry. If a solution contained a DNA target complementary to both fragments, a sandwich-like system was formed on the surface of a gold electrode, which resulted in the appearance of a peak of anodic oxidation of the ferrocene unit of the oligonucleotide **62**. The concentration of the DNA fragment to be assayed was ~ 50 μ mol litre⁻¹. In control experiments with a nucleotide sequence different from that of the DNA target and an oligonucleotide containing only one mismatch within the recognising seven-nucleotide site, the anodic oxidation peak of ferrocene was virtually absent.

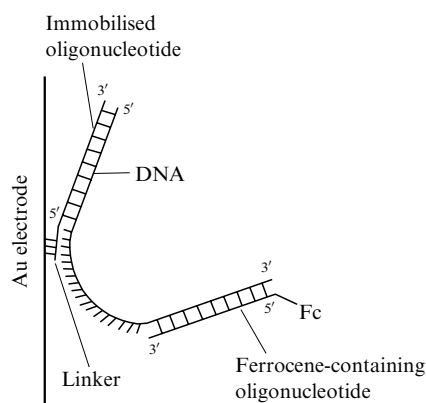


Figure 3. The formation of a three-component sandwich-like system immobilised on a gold electrode.⁷⁰

Later, immobilisation of the phosphothioate-containing oligonucleotide followed by hybridisation with a DNA probe and the signal oligomer **62** were studied in more detail⁷¹ using quartz crystal microgravimetry. The density of the molecules on the electrode surface calculated from the results obtained was equal to 77 pmol cm⁻². Taking into account the magnitude of the square per ferrocene molecule within the complex with DNA (~ 200 – 700 Å²), a conclusion was drawn that the density of the molecules inside the layer was rather high. Since the roughness of the electrode surface was neglected in this study, the theoretically calculated density of the layer package could be significantly overestimated. This, in turn, can be the reason for excessive charge density and a significant (by 215 mV) increase in the redox potential of the ferrocene-containing oligonucleotide **62** in comparison with its oxidation potential in solution (see Table 2). An increase in its potential can be attributed to the destabilisation of the oxidised form of ferrocene in the conjugate, since the DNA chain prevents the approach of counterions to the ferrocenyl cation because of increased density of anionic phosphate groups. This finding is consistent with the results of Letsinger *et al.*⁷⁶ which suggest that the difference in the redox potential values of ferrocene in the immobilised oligonucleotide and in solution amounts to 110 mV. This approach appeared to be extremely sensitive to one-letter substitutions.⁷¹

This method was modified further (Fig. 4).^{58, 59, 61, 62, 105} A gold electrode, following immobilisation of an oligonucleotide, was treated with 16-mercaptohexadecanol in order to protect the

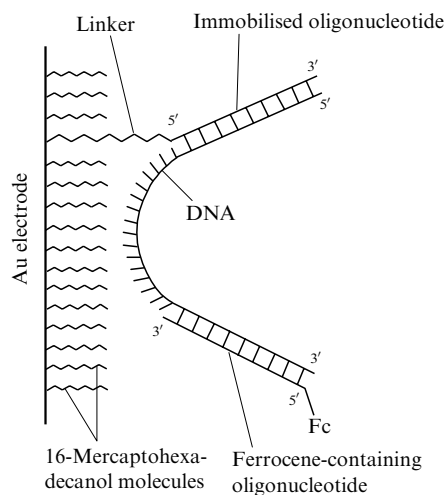
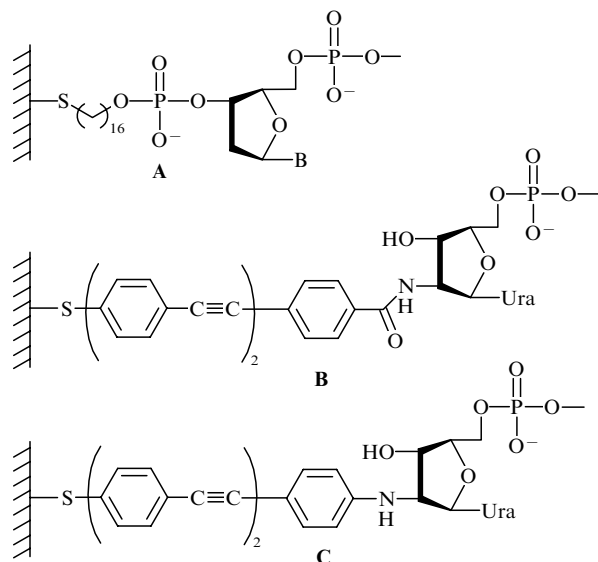


Figure 4. A modified version of an electrochemical analysis of DNA.^{58, 59}

electrode surface from the molecules that can nonspecifically be absorbed and thus violate the results of measurements. This improves the efficiency of measurement.

Immobilisation of oligonucleotides on the surface of a gold electrode was performed using three types of linkers,^{58, 59, 61, 62} viz., a standard linker A and linkers B and C which improve the electron transfer.¹⁰⁶



Immobilisation of sulfur-containing oligonucleotides on the surface of a gold electrode was used in the design of a DNA chip for detecting mutant fragments of DNA in solution at a concentration of $\sim 50 \text{ nmol litre}^{-1}$.⁵⁸ Two ferrocene-containing oligonucleotides differing in their oxidation potentials and complementary to DNA regions of natural and mutant types were used (the probe was taken in a 5–10-fold excess with respect to the DNA under study). Hybridisation of these oligonucleotides with DNA was carried out at an elevated temperature which was optimum for the formation of perfect duplexes. Ferrocene-containing DNA duplexes were detected by alternating current voltammetry. It was found⁵⁸ that such a system enables reliable identification of mononucleotide polymorphism.

The same group of investigators^{105, 107} have developed a new procedure for electrochemical detection of DNA using DNA chips.⁵⁸ This method is based on a comparison of temperature dependences of signal intensities on voltammograms for the formation of perfect and imperfect duplexes with a ferrocene-containing oligonucleotide. With an increase in temperature, imperfect duplexes become unstable, which ensures reliable identification of mononucleotide polymorphism of extended (up to 100 bases) DNA fragments. The advantage of this method includes long-term operation of biosensors without any loss in electrochemical signal intensity.^{105, 107} Such DNA chips were recommended for detection of mononucleotide substitutions in human DNA samples.^{108, 109} The use of DNA chips based on ferrocene-containing oligonucleotides in clinical diagnostic procedures has been surveyed in detail.^{110, 111}

An alternative approach to immobilisation of oligonucleotides has been recently proposed by Houlton and co-workers^{112, 113} who performed direct synthesis of NA on a surface further used as a support.

It is known^{114, 115} that unfolding of hairpin structures of NA can be favoured by interactions with completely complementary oligonucleotides. Detection and analysis of hairpin structures are usually performed with the help of a fluorophore and a fluorescence quencher attached to the opposite ends of the oligonucleotide hairpin (Fig. 5). The formation of a duplex, which competitively interacts with the hairpin, increases the distance between the fluorophore and the fluorescence quencher which results in the enhancement of fluorescence. Such a scheme was

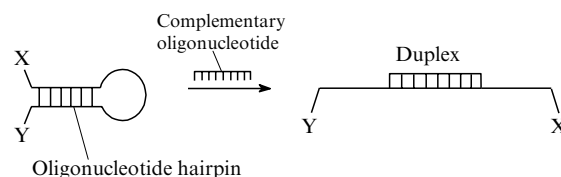


Figure 5. Unfolding of an NA hairpin structure in the presence of a complementary oligonucleotide.^{114, 115} X is fluorophore; Y is fluorescence quencher.

implemented in the case of an oligonucleotide immobilised on gold nanoparticles¹¹⁶ used as fluorescence quenchers.

The same approach was used in the design of a DNA sensor (Fig. 6).^{45, 79} The hairpin immobilised on a gold electrode retains its structure in the presence of mismatching oligonucleotide fragments, while a duplex is formed in the presence of a matching DNA sequence. As a result, the distance between the ferrocene and the electrode increases which reflects on the efficiency of the electron transfer and, as a consequence, on the current.

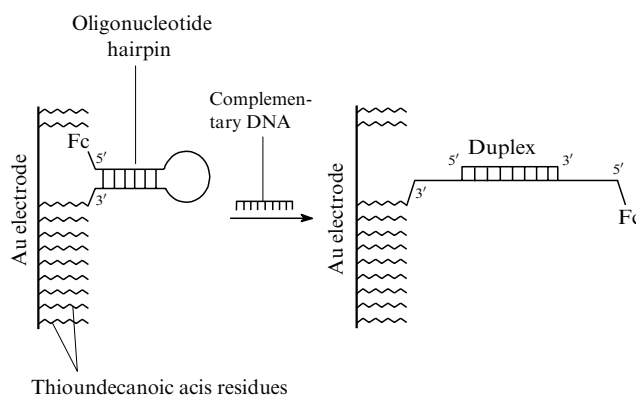


Figure 6. Electrochemical detection of DNA using a hairpin oligonucleotide.^{45, 79}

A method for detecting DNA on the electrode surface⁷⁴ consists of the following. Single-stranded extended DNA fragments that are analysed are immobilised on a carbon electrode by applying an electric potential of +0.5 V as described by Wang *et al.*¹¹⁷ This is followed by hybridisation with electrochemically active DNA fragments containing a residue of ferrocenecarboxylic acid. The resulting conjugates are analysed by differential pulse voltammetry.

Later, this method was optimised.⁷⁵ For the first time, the carbon electrode was replaced by a glass electrode coated with chitosan, a polysaccharide containing amino groups able to electrostatically interact with negatively charged phosphate residues of DNA. This ensures the strongest binding of DNA under study to the electrode surface. A complementary DNA containing a 3'-terminal ferrocenyl residue is used as a probe. After hybridisation, the signal of ferrocene oxidation was recorded by differential pulse voltammetry. In this case, the detection limit could be lowered to $2 \times 10^{-11} \text{ mol}$ (see Table 3) and the selectivity remained high. However, the ability of DNA immobilised on chitosan due to electrostatic interactions to undergo hybridisation with the probe to form a double helix without disturbing these interactions is questionable.

An interesting application of ferrocene-containing oligonucleotides immobilised on a gold electrode as a model in studies of DNA flexibility has been described.⁹⁴ A 20-mer homothymidine oligonucleotide containing a thiol group at the 5'-end and a ferrocene unit at the 3'-end was used as a model DNA. This

oligomer manifests minimum rigidity in comparison with other sequences. After hybridisation of the immobilised oligonucleotide with a complementary template, the mobility of the 3'-terminal fragment containing a ferrocene residue decreased as could be evidenced from cyclic voltammetry data. At high sweep rates, the peak of ferrocene oxidation disappeared from the voltammograms.

A procedure for detecting ferrocene-containing molecules by a flow injection method has been developed.¹¹⁸ Here, quantitative analysis of electroactive molecules is performed in a buffer solution containing potassium hexacyanoferrate(II), the so-called 'sacrificial reagent' which yields hexacyanoferrate(III) upon oxidation. Direct oxidation of the 'sacrificial reagent' on the surface of a gold electrode is excluded due to preliminary immobilisation of an alkanethiol monolayer (Fig. 7). The hydrophobic ferrocene moieties attached to the analyte can be incorporated into the alkanethiol monolayer. If a potential is applied, the ferrocene immobilised on the electrode surface begins to act as a catalytic mediator of hexacyanoferrate(II) oxidation which is recorded by voltammetry. This method has sufficiently low detection limits for ferrocene detection (an amplification factor of about 300 in comparison with direct measurement of ferrocene-containing molecules in solution).

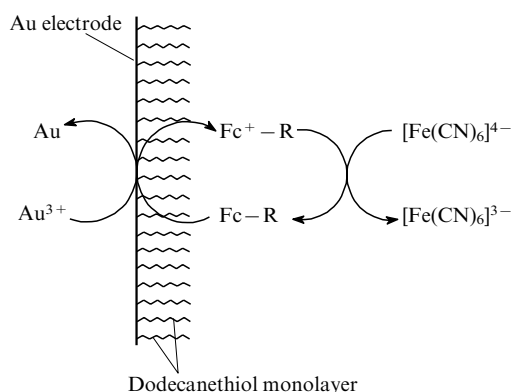


Figure 7. Detection of ferrocene-containing molecules by a flow injection method.¹¹⁸ R is a molecule to be quantified.

In the general case, HPLC and capillary electrophoresis coupled with electrochemical detection (see Table 3) allow attainment of lower limits for DNA detection in solutions than immobilisation of oligonucleotides on electrodes. Nevertheless, the latter approach seems to hold much promise for the detection of one-letter substitutions.

IV. Conclusion

A variety of methods for attachment of the ferrocene residue at the 5'- and 3'-ends and inside the oligonucleotide chain are presently available. Some of them enable incorporation of ferrocenyl derivatives during automatic oligonucleotide synthesis, while others are used for postsynthetic modification. The choice of an optimum procedure is determined by the experimental task; preference is given to postsynthetic attachment of ferrocene. In the first place, this is due to the commercial availability of nucleosides and oligonucleotides containing reactive groups, since ferrocene-containing nucleosides and their phosphoramidite derivatives are commercially unavailable. Moreover, under standard conditions of an oligonucleotide synthesis ferrocene undergoes partial destruction in the oxidation stage of phosphite groups and during postsynthetic workup in alkaline media. The problem of ferrocene degradation in the oxidation step can be solved by replacing iodine by milder commercially available oxidants, such

as *tert*-butyl hydroperoxide or (1*S*)-(+)-(10-camphorsulfonyl)oxaziridine. It is also recommended to use phosphoramidite nucleoside derivatives with labile acetyl or phenoxyacetyl protective groups which can be removed under very mild conditions. This allows one to increase the yields of modified ferrocene-containing oligonucleotides.

Preparation of modified nucleoside triphosphates is yet another trend in the synthesis of ferrocene-containing NA fragments. It has been shown¹¹⁹ that nucleoside triphosphates with substituents at C(5) of pyrimidine or at C(7) of purine bases are ideal modified substrates for DNA polymerase and RNA polymerase. Earlier, it was found¹²⁰ that 2'-deoxyuridine triphosphate derivatives modified at C(5) with propynyl or (*E*)-propenyl groups are substrates for Taq polymerase unlike (*Z*)-propenyl and propyl derivatives. Based on these data, two synthetic strategies can be distinguished: (1) synthesis of a ferrocene conjugate with a modified nucleoside triphosphate residue containing a chemically reactive group and (2) alkynylation or alkenylation of a nucleoside by a ferrocene-containing derivative and its subsequent conversion into a triphosphate. However, account must be taken of the fact that many nucleoside triphosphate (*E*)-propenyl⁵⁰ and propynyl¹²¹ derivatives are not substrates for DNA polymerases and individual testing of each triphosphate of the modified nucleoside may be required.

The possibility of incorporating a ferrocene residue into a predetermined position of an oligonucleotide chain opens up broad opportunities for the development of diverse systems for electrochemical detection of nucleic acid fragments. There are two approaches to the analysis of DNA. One of them consists of enzymatic synthesis of NA by PCR and makes use of triphosphates of ferrocene-containing nucleosides or 5'-ferrocene-containing primers. The product is further analysed by HPLC or capillary electrophoresis with electrochemical detection. This may also include hybridisation of a ferrocene-containing oligonucleotide with an NA target and detection of the duplex formed. This approach enables detection (including quantitation) of very small concentrations (down to attomoles) of polynucleotides.

The second approach includes detection of DNA on the surface of electrodes containing immobilised oligonucleotides bearing covalently linked ferrocene residues. The use of various detection schemes holds great promise for the analysis of SNP in extended DNA fragments. To obvious advantages of this method one can relate its high sensitivity and selectivity; however, in this case larger amounts of NA are required.

Electrochemical detection is far less efficient than the fluorescent method where parallel capillary electrophoresis is used. However, it is a promising tool in the design of DNA chips. DNA chips, eSensorTM (Motorola Clinical Micro Sensors, Pasadena, CA, USA) and an eSensorTM 4800 Reader allowing DNA analysis simultaneously on 48 chips, have been developed based on original publications.^{57–59, 105}

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^a — *Russ. J. Bioorg. Chem. (Engl. Transl.)*

Chemical design of homo- and heteronuclear polyoxomolybdate clusters[†]

S S Talismanov, I L Eremenko

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Abstract. Data on the chemistry of the key types of large homo- and heteronuclear polyoxomolybdate clusters published over the last 10 years are generalised. The bibliography includes 95 references.

I. Introduction

Polyoxometallate compounds formed by d elements of Groups V and VI of the Periodic Table have been attracting the rapt attention of researchers for many years.¹ The interest in these substances is related first of all to the possibility of using them as efficient catalysts, biologically active compounds or new analytical reagents.^{1,2} Polyoxometallate complexes often form unique supramolecular ensembles which possess unusual magnetic or spectral properties. For the preparation and practical application of such systems, reliable and efficient methods for the synthesis of polyoxometallates are needed first of all. It is very important to find approaches to the chemical design of clusters containing open shell metal centres,^{3–7} because these systems are expected to form structures possessing unusual electronic characteristics.⁸ It has been suggested that these polyoxometallates can be regarded as representing a new class of inorganic compounds whose chemical activity can be deliberately controlled. This is due to the exceptionally high reactivity of their molecules with respect to various reagents due to the presence of metal centres of different electronic nature.^{1,9}

Some (giant) polyoxomolybdate clusters can be used to perform the design and deliberate engineering of materials with desired properties.¹⁰ For instance, some polyoxometallates can be employed to model n-type semiconductor oxides.¹ Meanwhile, the capability of binding to one another discovered for giant polyoxomolybdate ring-shaped clusters containing nano-sized cavities opens up prospects for the design of unusual polymeric

materials.¹¹ The possibility of introducing magnetically active centres into polyoxometallates makes these compounds promising for the preparation of molecular magnets — magnetic materials of a new generation. All these facts stimulate studies along these lines; nevertheless, development of target-directed synthesis of polynuclear compounds with a specified structure and elucidation of structure – properties relationships still remain among the most important problems.

II. Key principles of the formation of polyoxometallate clusters

Modern inorganic chemistry often deals with large structured systems. The routes for their formation are usually analysed by means of a fairly versatile strategy that has proved to be efficient. According to this strategy, an object is split (at least, hypothetically) into elementary fragments called building blocks (polygons, polyhedra, aggregates composed of such blocks, *etc.*) and then the rules of interaction and mutual binding of these blocks are studied.¹² Such a strategy is used in this review to consider large polyoxometallate clusters.

The ability of elementary building blocks and their derivatives to be linked to one another in different modes is important in many fields of synthetic chemistry, especially in polyoxometallate chemistry. This permits the synthesis of a variety of compounds including those with nano-size properties. Of interest from this standpoint are anionic species composed of building blocks of the {MO_x} type where M are d elements in high oxidation states.^{1,2,9}

In Nature, complex molecules are often formed stepwise, either under conditions of genetic control or in self-assembly processes under dissipative conditions far from equilibrium. Such complex compounds are normally synthesised using a sequence of several reactions, which often proceed over very long periods of time. During these reactions, functional groups are manipulated to form covalent bonds one after another. Modern knowledge in the field of polyoxometallate chemistry allows the use of self-assembly processes in which fragments formed from simple starting compounds can be linked to each other to form various mesoscopic structures (with linear dimensions of several tens

S S Talismanov, I L Eremenko N S Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation. Fax (7-095) 954 12 79.
E-mail: stal@igic.ras.ru (S S Talismanov)
Tel. (7-095) 952 21 12, (7-095) 955 48 35. E-mail: ilerem@igic.ras.ru (I L Eremenko)

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angstrom or more) and can further form macroscopic substances with network structures.^{13, 14}

The structural principle of the assembly of polyoxovanadates, -molybdates and -tungstates is the same, in particular, in all structures, each metal atom forms a $\{\text{MO}_x\}$ coordination polyhedron mainly due to the $\text{M}-\text{O}$ π -bonding, and these polyhedra, in turn, form the vertices of structural surfaces.¹² Nevertheless, more detailed examination of these unique objects reveals substantial differences depending on the metal atom incorporated in the structure.

The structure of almost any of the very large polyoxotungstate anions, unlike those of vanadates and molybdates, can be represented as being composed of subunits based on defect (lacunary) fragments of the Keggin ion [containing groups of the $\{\text{W}_3^{\text{VI}}\text{O}_{13}\}$ type] or its isomers. This can be explained, in principle, by high stability of such fragments, which is apparently due to the presence of very weak (but not negligible) $\text{W}-\text{W}$ interactions in the $\{\text{W}_3\}$ triangles.¹ A significant feature of polyoxovanadates is the existence of different base types of polyhedra: $\{\text{VO}_4\}$, $\{\text{VO}_5\}$, $\{\text{VO}_6\}$. The pyramidal $\{\text{O}=\text{VO}_4\}$ fragments tend to form cluster shells topologically similar to fullerenes or V_2O_5 layers.^{13, 14}

Most of the very large mixed-valence molybdates can be represented as structures consisting of the same or similar fragments — the $\{\text{Mo}_8\}$ or $\{\text{Mo}_{17}\}$ building blocks, which can be linked in different modes directly to one another or *via* some coordinating centres. Numerous growth processes that conform to these rules have been discovered; they result in the formation of giant ring-shaped, spherical or other systems containing 102, 132, 154, 176 and even 368 molybdenum atoms.¹⁵ The classical $\{\text{Mo}_3\text{O}_{13}\}$ fragment is much less significant and exhibits a much lower tendency for participation in the subsequent assembly of the cluster (at least, in the case of reduced systems) compared to analogous tungstate systems.

Since the chemical behaviours of polyoxometallates derived from different elements are fairly different, the minimum number of metal atoms that allows the cluster to be regarded as large is not the same for vanadates, molybdates and tungstates ($n \geq 19$ for V_n ; $n \geq 24$ for Mo_n ; and $n \geq 20$ for W_n).¹²

This brings about an important question: whether it is possible to assemble even larger molecular structures, for example, clusters of a mesoscopic size. It should be borne in mind that real processes involve binding of a very large number of base fragments. The self-assembly of the tobacco mosaic virus consisting of a large number of pre-organised fragments can serve as an impressive example (see Section VI.1).¹⁶

Undoubtedly, a useful strategy for the formation of giant systems is to create rather large intermediates that could be easily connected in self-assembly processes; in particular, this can involve various cationic metal centres.^{1, 12, 17} Indeed, quasi-pre-organised building blocks present in the solution can be linked to each other either directly or *via* some cations to give giant compounds.¹⁸ At this stage, it is very important to have comprehensive information about the system. The key factor is to preserve high solubility of the intermediates (for example, due to a substantial negative charge), which is necessary to avoid uncontrolled binding and/or too early precipitation. This approach can be illustrated in relation to the replacement of metal centres with a high positive charge by formally less positive centres, in particular, replacement of Mo^{VI} atoms by V^{IV} atoms in the α -Keggin anions $[\text{Mo}_{12}\text{XO}_{40}]^{3-}$ ($\text{X} = \text{P}, \text{As}$). This process gives rise to anionic intermediates with a high negative charge (nucleophiles), which can be either merely stabilised by electrophilic centres or linked by means of these centres to form markedly bigger systems.^{19–21} For instance, during the substitution of vanadium for molybdenum in the $[\text{Mo}_{12}\text{AsO}_{40}]^{3-}$ cluster, the arising intermediates $\{\text{Mo}_8^{\text{VI}}\text{V}_4^{\text{IV}}\text{AsVO}_{40}\}^{11-}$ can be stabilised, for example, by As^{III} centres to give the $[\text{As}_2^{\text{III}}\text{Mo}_8^{\text{VI}}\text{V}_4^{\text{IV}}\text{AsVO}_{40}]^{5-}$ cluster. In the absence of As^{III} and in the presence of NH_2OH as a reducing agent, further condensation takes place.^{19, 21} Finally, the $\{\text{Mo}_{17}\}$ fragments formed as reactive intermediates can be linked in

different ways by cations or cationic groups (VO^{2+} , Fe^{III} , MoO_2^{2+}) to form bigger molecular structures.

According to an empirical rule,¹² if the size of the polyoxometallate anion increases, this anion can participate in further growth processes as a soluble and non-hydrolysable particle only provided that its electron density remains virtually constant (which implies an increase in the overall charge). However, in some cases, the solubility is determined by other factors, for example, the presence of a very large number of coordinated water molecules. The isolation of several giant ring-shaped polyoxomolybdate clusters containing more than 150 molybdenum atoms and anions with low or very low charges can be considered as evidence supporting this statement.²²

To summarise the foregoing, we will list the conditions favourable for the formation of large molecular complex systems from polyoxometallate building blocks in the course of a single reaction (without complicated multistage processes).²³

1. The presence of linkable fragments, *i.e.*, building blocks.
2. The possibility of generating fragments with high values of free enthalpy to initiate polymerisation or growth processes accompanied, for example, by evolution of H_2O molecules.
3. The ready possibility of changing the structure of the building blocks.
4. The possibility of introducing heteroatoms into the fragment blocks.
5. The possibility of forming larger fragment blocks suitable for linking in different ways.
6. Neither too weak nor too strong binding between the fragments.
7. The possibility of controlling structuration processes by templates.
8. The possibility of forming structural defects, for example, lacunary structures, in reaction intermediates.
9. The presence of low-lying unoccupied molecular orbitals in the fragments.
10. The possibility of electron density localisation and delocalisation.
11. The opportunity to control and change the charge, for example, by protonation, electron transfer reactions or by replacement of some fragments.

In principle, by selecting and creating particular conditions, one can synthesise molecular systems comparable in size even with proteins.

III. Formation of cluster anions containing $\{\text{Mo}_{17}\}$ fragments

The fragment containing 17 molybdenum atoms ($\{\text{Mo}_{17}\}$) is one of the most frequently encountered building blocks incorporated in polyoxomolybdate clusters. This fragment can be found in the $[\text{Mo}_{36}\text{O}_{112}(\text{H}_2\text{O})_{16}]^{8-}$ cluster anion (**1a**) (produced upon acidification of an aqueous solution of sodium molybdate with hydrochloric or nitric acid at a 36:64 molar ratio) and the $[\text{Mo}_{36}(\text{NO})_4\text{O}_{108}(\text{H}_2\text{O})_{16}]^{12-}$ cluster anion (**1b**) [formed upon the reduction of aqueous solutions of molybdates(VI) with hydroxylamine].^{21, 24–30}

It is noteworthy that the structures of both cluster anions formally include a large number of diverse coordination polyhedra (Fig. 1, see p. 559), namely, two $\{\text{MoO}_6\}$, four $\{(=\text{O})\text{MoO}_4(\text{H}_2\text{O})\}$, eight $\{(=\text{O})_2\text{MoO}_3(\text{H}_2\text{O})\}$, eight $\{(=\text{O})\text{MoO}_5\}$ and two $\{(=\text{O})_2\text{MoO}_4\}$ octahedra; four $\{\text{Mo}(\text{X})\text{O}_6\}$ pentagonal bipyramids [$\text{X} = \text{O}$ (**1a**), NO (**1b**)] and four $\{\text{Mo}_2\text{O}_8(\mu\text{-O})(\mu\text{-H}_2\text{O})\}$ fragments consisting of two octahedra sharing an edge. Anion **1b** contains two fairly large fragments, $\{\text{Mo}_{15}^{\text{VI}}(\text{MoNO})_2^+ \text{O}_{58} \cdot (\text{H}_2\text{O})_2\}^{20-} \equiv \{\text{Mo}_{17}\}$, connected by two $\{\text{MoO}_2\}^{2+}$ groups in which two terminal oxygen atoms occupy *cis*-positions.

The $\{\text{Mo}_{17}\}$ fragments are composed, in turn, of two $\{\text{Mo}_8\}$ fragments linked through eight oxygen atoms and one molybdenum atom. The centres of these fragments are formed by

{MoXO₆} pentagonal bipyramids, each of them being linked to five {MoO₆} octahedra *via* edges; two of these octahedra are bound additionally to two more peripheral octahedra. The hypothetical replacement of the {MoNO}³⁺ groups by {MoO}⁴⁺ groups results in non-reduced anion **1a**. Similar {Mo₈} fragments can also be found in the structures of molybdenum oxides, Mo₅O₁₄ and Mo₁₇O₄₇ (see Ref. 31).

In anions **1a** and **1b**, the {Mo₁₇} fragments are linked by two {MoO₂}²⁺ centres to *cis*-arranged oxygen atoms. Cluster **1b** is stabilised due to double protonation of two bridging and four terminal oxygen atoms contained in two bridging and four terminal H₂O ligands, respectively. The presence of altogether four bridging H₂O ligands is an interesting structural feature of anion **1b** in which each of the four bridging water molecules belongs to one of four {Mo₂O₈(μ-O)(μ-H₂O)} fragments and participates in the binding of two corresponding octahedra by sharing an edge.

By further reduction of the cluster anion [Mo₃₆(NO)₄·O₁₀₈(H₂O)₁₆]¹²⁻ (**1b**) with excess hydroxylamine, it is possible to isolate a compound containing one-dimensional chains consisting of 38-nuclear cluster anions [(H₂O)Mo_{2.5}{Mo₃₆·(NO)₄O₁₀₈(H₂O)₁₆}O_{2.5}Mo(H₂O)]¹²⁻ (**2a**) (here and below, letter 'a' denotes the cluster anion derived from the corresponding compound).³² Compound **2** can be represented as consisting of initial cluster anions **1b** attached to each other by neutral binuclear fragments, {(H₂O)₂Mo^{VO}Mo^{VO}O₂(H₂O)}, which are shaped like two tetrahedra sharing a vertex. It is considered that not only some molybdenum(VI) ions (arising probably upon the destruction of some cluster anions **1b**) are reduced during the reaction to give binuclear {(H₂O)₂Mo^{VO}Mo^{VO}O₂(H₂O)} fragments but some molybdenum atoms in anions **1b** are also reduced with generation of active sites. These are the active sites that participate in the binding to the {(H₂O)₂Mo^{VO}Mo^{VO}O₂(H₂O)} fragments during further self-assembly and are finally oxidised by air oxygen.³²

The presence of large {Mo₁₇} fragments in type **1b** systems is a very important feature of these clusters. This opens up the possibility of generating larger systems by binding {Mo₁₇} fragments as ligands with a high negative charge by various electrophilic groups. In the case of cluster **1b**, this function is performed by the {MoO₂}²⁺ cations.

When other electrophiles such as Fe^{III} or V^{IV} are used in the preparation of cluster **1b**, this yields giant cluster anions with the {Mo₅₇M₆} metal core. The synthesis can be carried out in two ways by using either compounds of heterometal M in higher oxidation states (Fe^{III}, V^V) in the presence of a reducing agent (NH₂OH·HCl) or a reducing agent alone containing atoms of the heterometal in a lower oxidation state (Fe^{II}, V^{IV}).

The resulting highly symmetrical (*D*_{3h}) cluster anions [{V^{IV}(H₂O)O}₆{Mo^V(μ-H₂O)₂(μ-OH)Mo^V}₃{Mo₁₅^{VI}(MoNO)₂O₅₈·(H₂O)₂}₃]²¹⁻ ≡ {Mo₅₇V₆} (**3a**)²¹ and [{Fe^{III}(H₂O)₂}₆{Mo^V·(μ-H₂O)₂(μ-OH)Mo^V}₃{Mo₁₅^{VI}(MoNO)₂O₅₈(H₂O)₂}₃]¹⁵⁻ ≡ {Mo₅₇Fe₆} (**4a**)¹⁹ each contain 276 non-hydrogen atoms. They tend to form a variety of different coordination polyhedra. Each of these anions (Fig. 2, see p. 559) includes three MoO₆, six (O=)MoO₄(H₂O), twenty four (O=)MoO₅, twelve (O=)₂MoO₄ and six (O=)V(H₂O)O₄ or FeO₄(H₂O)₂ octahedra, six Mo(NO)O₆ pentagonal bipyramids, as well as O₃{Mo^V(μ-H₂O)₂(μ-OH)Mo^V}O₃ fragments, which can be described as two octahedra sharing a face. These structures are formally composed of three above-noted large {Mo₁₅^{VI}(MoNO)₂O₅₈(H₂O)₂}²⁰⁻ ≡ {Mo₁₇} fragments functioning as bridging ligands connecting six cationic centres [(O=)VO₄]²⁺ in anion **3a** and {FeO₄(H₂O)₂} in anion **4a**] and three {Mo^V(μ-H₂O)₂(μ-OH)Mo^V}⁹⁺ binuclear groups. Yet another important feature of structures **1b**, **3a** and **4a** is the presence of bridging H₂O ligands, six in anions **3a** and **4a** and four in anion **1b**. In clusters **3a** and **4a**, these ligands occupy bridging positions between neighbouring Mo^V centres, giving rise to three {Mo^V(μ-H₂O)₂(μ-OH)Mo^V} fragments, which can

be described as two octahedra sharing a face. In anion **1b**, each of four bridging H₂O molecules belongs to one of four {Mo₂O₈(μ-O)(μ-H₂O)} fragments, the corresponding octahedra sharing an edge.

The fairly large cavities inside these cluster anions are formally accessible, for example, to solvent molecules, owing to two 'holes' situated on the S₃ axis. These cavities whose diameter (without taking into account the hydrogen atoms) equals ~0.9 nm in the direction normal to the S₃ axis and ~0.5 nm in the direction parallel to the S₃ axis are formed by the central {O₃₃} polyhedron. Two 'holes' are confined by two nearly planar 12-membered rings with the Mo—O—M—O fragments [M is V (**3a**) or Fe (**4a**)] in which metal atoms alternate.

One more important structural feature of these systems is the presence of three, rather large cavities between the {Mo₁₇} fragments. These cavities are accessible for further coordination of highly electrophilic oxometallate fragments, for example, {MoO}⁴⁺ (see Ref. 8) or {VO}³⁺ (see Ref. 33), which results in discrete growth of such structures to give anions such as {Mo_{57+x}V₆} and {Mo₅₇V_{6+x}} (x = 0–6). Each {MoO}⁴⁺ or {VO}³⁺ group is bound to three oxygen atoms belonging to the {Mo₅₇V₆} core; hence, the metal atoms in these groups exist in a tetrahedral environment. The degree of occupancy of the cavities can be brought in correlation with the degree of reduction of the initial cluster **3a**. The reduction of anion **3a** (Fig. 3, see p. 559) results in an increase in its nucleophilicity, thus initiating the growth, which may involve the insertion of up to six electrophilic centres, {MoO}⁴⁺ or {VO}³⁺, to give [H₃Mo₅₇V₆(NO)₆·O₁₈₉(H₂O)₁₂(MoO)₆]²¹⁻ and [H₃Mo₅₇V₆(NO)₆O₁₈₉(H₂O)₁₂·(VO)₆]¹⁵⁻ clusters, respectively.

Despite the fact that compounds **3** and **4** lose some water of crystallisation when stored in air, this does not influence their stability. According to IR spectroscopy data, they do not decompose up to a temperature of 225 °C. These compounds are also stable in aqueous solutions at pH 2.5–3.5 for several days. At lower or higher pH values, anions **3a** and **4a** decompose instantaneously, apparently, due to the electrophilic character of the NO group.

Note that by addition of various amounts of FeCl₂·4H₂O or FeCl₃·6H₂O to the reaction solution (crystallisation of which gives compound **3**), one can prepare a series of clusters with the same cluster core but with different statistical distribution of oxovanadium(IV), iron(II) and iron(III) centres among octahedral 'heterometallic' positions. Examples of compounds synthesised in this way are compounds with {Mo₅₇V₄Fe₂}, {Mo₅₇V₃Fe₃}, {Mo₅₇V₂Fe₄} and {Mo₅₇VFe₅} cluster anions containing iron(II) and iron(III) and the {Mo₅₇VFe^{III}₅} cluster anion incorporating only iron(III) atoms. It should be noted that both the overall number of inserted iron atoms and the Fe^{II}/Fe^{III} ratio depend on the reaction conditions, in particular, on whether it was carried out in air or under an inert atmosphere.³⁴ This circumstance allows one to change the ratio of the number of vanadium centres to the number of iron centres (*n_V*/*n_{Fe}*) distributed over six positions, which form a trigonal prism inside the cluster, by varying experimental conditions. During the formation of a heterometallic cluster, only a small amount of FeCl₃·6H₂O is required for the insertion of iron into the giant cluster anion. However, when FeCl₂·4H₂O is used as the iron-containing component, a large excess of iron(II) chloride is needed to reach the same *n_V*/*n_{Fe}* ratio. Apparently, this outcome is related, according to the Pearson principle, to the higher reactivity of 'hard' iron(III) centres with respect to 'hard' acids (oxygen atoms), which are present in the coordination environment provided by the shell of the initial homomolybdenum cluster. Upon the addition of excess FeCl₃·6H₂O, compound **4** can be isolated.

Magnetic properties of compounds of this type depend on both the overall content of iron and the Fe^{II}/Fe^{III} ratio. As expected, an increase in the iron content results in an increase in the magnetic susceptibility χ.³⁴ In the case of compounds containing both iron(II) and iron(III), the χ*T*(*T*) curve passes through a

maximum in the field of low temperatures, this maximum being more pronounced for clusters with high contents of iron. Although full analysis of the magnetic parameters for such systems is as yet rather difficult, this type of $\chi T(T)$ dependence is usually observed for ferrimagnetic systems. As the iron content decreases, the χT decreases and the ferrimagnetic properties become less pronounced. In the limiting case, where no iron is involved (e.g., in $\{\text{Mo}_{57}\text{V}_6\}$), as for the intermediate compound (in $\{\text{Mo}_{57}\text{V}_4\text{Fe}_2\}$), the system follows an antiferromagnetic type of behaviour. It is noteworthy that the insertion of iron(II) enhances the ferrimagnetic properties, while the $\chi T(T)$ curve for $\{\text{Mo}_{57}\text{VFe}_5^{\text{III}}\}$, unlike that for $\{\text{Mo}_{57}\text{VFe}_5\}$, does not exhibit a maximum typical of ferrimagnetics. Müller *et al.*³⁴ believe that the pattern of the $\chi T(T)$ curves, especially in the case of ferrimagnetic systems, can be interpreted only by assuming the presence of different paramagnetic centres in the same cluster anion (rather than in different anions with the same average ratio of the numbers of such centres over all anions).

These data may suggest that deliberate variation of the electronic state of heterometallic centres would allow one to control the magnetic properties of the synthesised clusters.

The compound $(\text{NH}_4)_{21}[\text{Mo}_{45}^{\text{VI}}\text{Mo}_6^{\text{V}}(\text{MoNO})_6\text{Cu}_2^{\text{II}}\text{V}_4^{\text{IV}}\text{O}_{178} \cdot (\text{OH})_3(\text{H}_2\text{O})_{16}] \cdot 60\text{H}_2\text{O}$ (**5**), containing three sorts of metal atoms — molybdenum, copper and vanadium,³⁵ is produced in the reaction of the $(\text{NH}_4)_{12}[\text{Mo}_{36}(\text{NO})_4\text{O}_{108}(\text{H}_2\text{O})_{16}] \cdot 33\text{H}_2\text{O}$ cluster (**A**) with excess $\text{Cu}^{\text{I}}\text{Cl}$ on heating in water at 60 °C with subsequent addition of VOSO_4 . The geometry of the corresponding cluster anion **5a** is similar to that observed for structures **3a**, **4a** except that in this anion, about two $\{\text{Cu}(\text{H}_2\text{O})_{1.2}\}^{2+}$ centres (the corrected occupancy of positions is close to unity) and about four $\{\text{V}=\text{O}\}^{2+}$ centres are distributed statistically over six heterometallic positions. Since these centres are disordered, they cannot be distinguished by X-ray diffraction; however, according to elemental analysis, the V/Cu ratio is equal to 4:2. The binuclear linkers in anion **5a** are fully reduced, and their structure can be described as $\{\text{Mo}^{\text{V}}(\mu\text{-H}_2\text{O})_2(\mu\text{-OH})\text{Mo}^{\text{V}}\}^{9+}$.

Thus, the synthetic strategy chosen can be used to prepare giant cluster anions $\{\text{Mo}_{57}\text{M}_x^{\text{I}}\text{M}_{6-x}^{\text{II}}\}$ with metal atoms of different sorts, which is especially important as regards the development of multifunctional catalysts.

As noted above, the $\{\text{Mo}_{57}\text{M}_6\}$ type anions are formally assembled from different blocks and linkers. However, due to the presence of reactive fragments, they can themselves function as building ‘superblocks’ for the formation of supramolecular structures. For instance, the reaction of cluster **A** with excess $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ on heating in water (65 °C) gave the compound $^{36} \{(\text{NH}_4)_{12}[\text{Mo}_{45}^{\text{VI}}\text{Mo}_6^{\text{V}}(\text{MoNO})_6\text{Fe}_6^{\text{III}}\text{Fe}_{1.5}^{\text{II}}(\text{OH})_3(\text{H}_2\text{O})_{30}] \cdot 64\text{H}_2\text{O}\}_n$ (**6**), containing a $\{\text{Mo}_{57}\text{Fe}_{6.5}^{\text{III}}\}^{12-}$ type cluster anion (**6a**), which is similar in structure to other clusters of this family considered above. Three large $\{\text{Mo}_{17}\}$ building blocks are linked to each other by three binuclear $\{\text{Mo}^{\text{V}}(\mu\text{-H}_2\text{O})_2(\mu\text{-OH})\text{Mo}^{\text{V}}\}^{9+}$ fragments and six octahedral $\{\text{Fe}(\text{H}_2\text{O})_2\}^{3+}$ centres. However, the structure of **6** has a significant distinction from the structures of **3–5** (Fig. 4), namely, the crystal contains additional $\{\text{Fe}(\text{H}_2\text{O})_4\}^{2+}$ centres in 12 symmetrically equivalent positions, the degree of occupancy of each of them being 25% (which corresponds to 1.5 Fe^{II} centres per one cluster anion). The ^{57}Fe Mössbauer spectrum of compound **6** recorded at 150 K contains two doublets, $\delta_1 = 0.48/\Delta E_1 = 1.10$ (typical values for $\text{Fe}^{\text{III}}\text{O}_6$) equal to 80%; $\delta_2 = 1.29/\Delta E_2 = 3.13$ (typical values for $\text{Fe}^{\text{II}}\text{O}_6$) equal to 20% (δ_i is the position of the line centre, ΔE is splitting). The $\text{Fe}^{\text{III}}/\text{Fe}^{\text{II}}$ ratio according to Mössbauer spectroscopy is also equal to $6/1.5 = 4$. These additional metal centres play a role of linking fragments between the clusters; they form a planar network structure in which any two neighbouring cluster anions are bound according to the $\text{Mo}-\text{O}-\text{Fe}^{\text{II}}-\text{O}-\text{Mo}$ pattern (see Fig. 4).

Compound **6** is the first example of polymeric anionic networks formed by the $\{\text{Mo}_{57}\text{M}_6\}$ cluster blocks. The principle of formation of this structure can be clearly followed: first, the $\{\text{Mo}_{17}\}$ fragments are connected by $\{\text{Fe}(\text{H}_2\text{O})_2\}^{3+}$ linkers to

form cluster anions of the $\{\text{Mo}_{57}\text{Fe}_6^{\text{III}}\}$ type, while the resulting fragments are connected by the $\{\text{Fe}(\text{H}_2\text{O})_4\}^{2+}$ linkers to form a cross-linked network. Finally, the chemical and physical properties of this compound are determined by a diversity of metal centres in different oxidation states (Mo^{VI} , Mo^{V} , Fe^{III} , Fe^{II}). Its electronic structure may be favourable for the temperature-dependent transfer of electrons in anion **6a**.^{37,38}

IV. Interconversions of some polyoxomolybdates in organic solvents

Whereas studies dealing with the chemistry of water-soluble polyoxomolybdates carried out in recent years revealed a great number of diverse structures containing giant cluster anions including mixed-valence and heterometallic ones (see, for example, Refs 12, 23), the chemistry of polyoxomolybdates in solutions in organic solvents has been much less studied. The studies mainly dealt with modification of the known polyoxometallate systems such as the $[\text{Mo}_6^{\text{VI}}\text{O}_{19}]^{2-}$ anion (Lindqvist's structure)³⁹ by various functional groups, resulting in nitrosyl, diazenide, hydrazide, cyclopentadienyl and diazoalkane derivatives.^{40–47} The conditions and ways of generation, and, what is most important, the interconversions of unsubstituted polyoxomolybdates in organic solvents have been little studied. The relevant data are described systematically in a publication.⁴⁸

The exchange reaction of ammonium heptamolybdate $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \cdot 4\text{H}_2\text{O}$ with tetrabutylammonium halides gives, after recrystallisation of the precipitated white solid from acetonitrile, colourless crystals of $(\text{NBu}_4)_4[\text{Mo}_8\text{O}_{26}] \cdot 4\text{MeCN}$ (**7**). According to X-ray diffraction data (Fig. 5), the octanuclear cluster anion $[\text{Mo}_8(\mu_3\text{-O})_6(\mu_2\text{-O})_6\text{O}_{14}]^{4-} \equiv [\text{Mo}_8\text{O}_{26}]^{4-}$ (**7a**) present in this compound contains six Mo^{VI} atoms in an octahedral environment and two Mo^{V} atoms in a tetrahedral environment. Each molybdenum atom in the octahedral environment is connected to two terminal, two μ_2 -bridging and two μ_3 -bridging oxygen atoms, while each molybdenum atom in the tetrahedral environment is linked to one terminal and three μ_3 -bridging oxygen atoms. In the polyhedral representation, anion **7a** can be regarded as an assembly formed by a ring composed of six MoO_6 octahedra, any of which shares two edges with two neighbouring octahedra. This gives rise to a ring closed on two sides by two MoO_4 tetrahedra, which are rotated through 60 ° relative to each other. The solvation acetonitrile molecules occupy the voids between the tetrabutylammonium cations and the cluster anions.

The reaction of cluster **A** with NBu_4^+X^- ($\text{X} = \text{Cl}, \text{Br}, \text{I}, \text{ClO}_4$) in an aqueous solution in air at room temperature followed by recrystallisation of the resulting beige-coloured precipitate from acetonitrile afforded yellow-coloured compound $(\text{NBu}_4)_2[\text{Mo}_6\text{O}_{19}]$ (**8**). The corresponding hexanuclear cluster anion $[\text{Mo}_6\text{O}_{19}]^{2-}$ (**8a**)³⁹ contains six Mo^{VI} atoms in a distorted octahedral environment.⁴⁸ Note that during this reaction, four $\{\text{Mo}^{\text{II}}(\text{NO})\}^{3+}$ groups of cluster **1b** are oxidised, probably, by air oxygen to yield four $\{\text{Mo}^{\text{VIO}}\}^{4+}$ groups. Correspondingly, each 36-nuclear cluster anion **1b** decomposes to give six anions **8a** with the loss of 16 electrons. In cluster **8a**, each of the six molybdenum atoms (Fig. 6) is connected to one terminal, four μ_2 -bridging and one μ_6 -bridging oxygen atoms. In terms of the polyhedral representation, anion **8a** can be regarded as a structure consisting of six MoO_6 octahedra, each of them sharing four edges with four neighbouring octahedra and all six octahedra having one common vertex.

The composition of the products of decomposition of cluster **1b** on treatment with tetrabutylammonium salts depends appreciably on the reaction conditions.⁴⁸ When an aqueous solution of cluster **A** is refluxed in air for 40 min, its colour changes from red-brown to blue-green, while the addition of tetrabutylammonium halides gives rise to a blue-green precipitate. Recrystallisation of this product from acetonitrile in air affords the crystals of octanuclear cluster **7**.

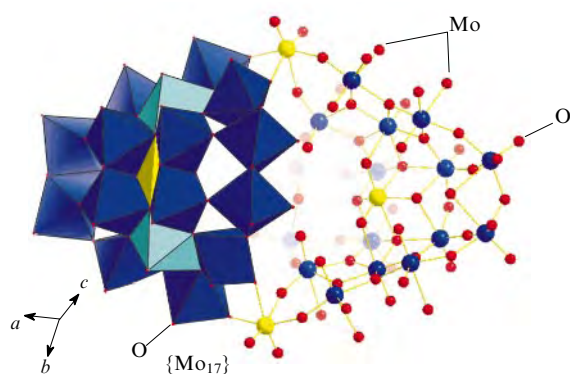


Figure 1. Structure of anions **1a** and **1b**. One $\{\text{Mo}_{17}\}$ fragment is shown in the polyhedral representation and the other is in the atomic representation.

The turquoise-coloured pentagonal bipyramids are the $\{\text{Mo}(\text{X})\text{O}_6\}$ fragments, the yellow octahedron is the $\{\text{MoO}_6\}$ fragment, and blue octahedra are the other fragments; yellow spheres are the molybdenum atoms in the $\{\text{MoO}_6\}$ and $\{(\text{O}=\text{O})_2\text{MoO}_4\}$ fragments and blue spheres are the other molybdenum atoms.

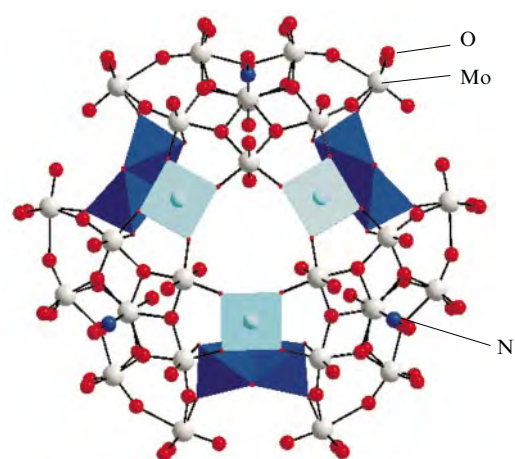


Figure 2. Structure of cluster anions **3a** and **4a**.

In the polyhedral representation, heterometallic centres (turquoise-coloured polyhedra) and binuclear linking groups (blue polyhedra) are shown.

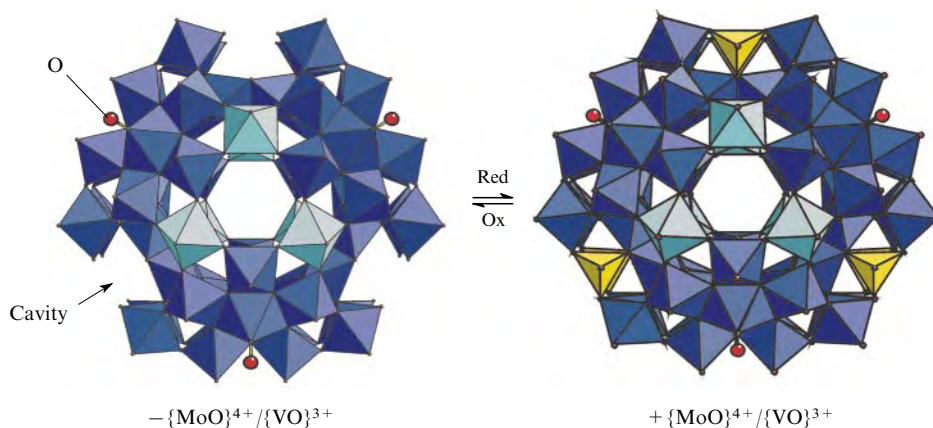


Figure 3. Molecular growth of clusters of the $\{\text{Mo}_{57}\text{M}_6\}$ family with filling of outer cavities.⁸

The turquoise-coloured polyhedra are heterometallic fragments; blue polyhedra are fragments formed by molybdenum atoms; yellow polyhedra are $\{\text{MoO}\}^{4+}/\{\text{VO}\}^{3+}$ fragments.

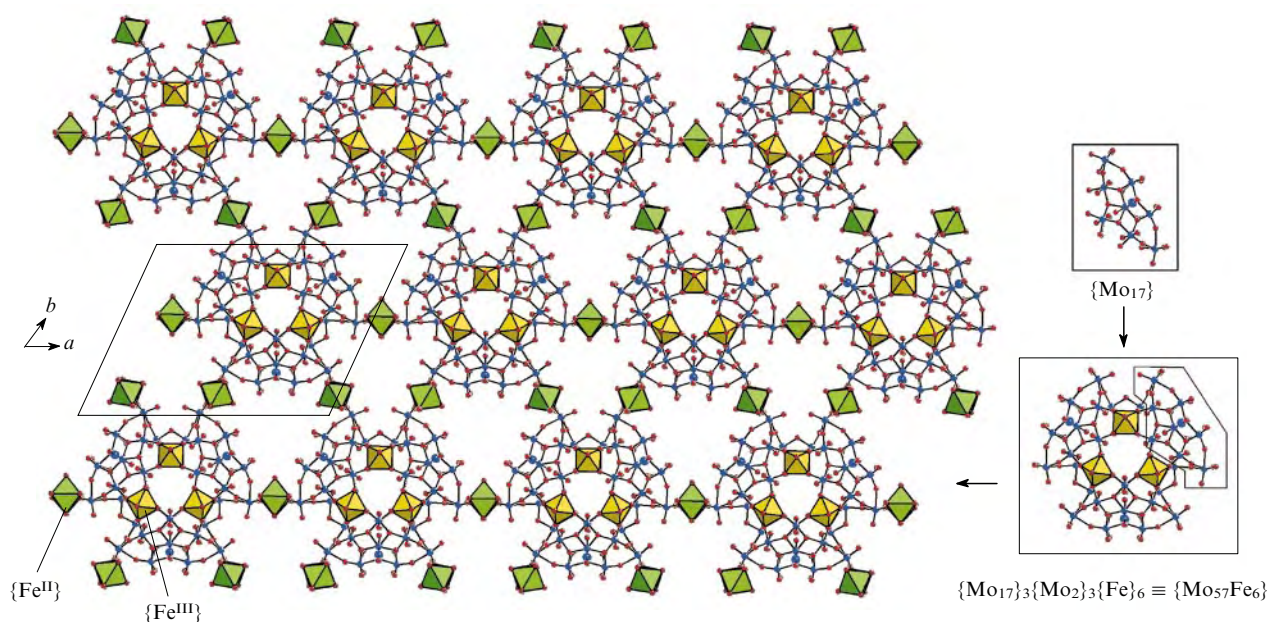


Figure 4. Network structure of cluster **6** and hierarchy of building blocks during its formation.

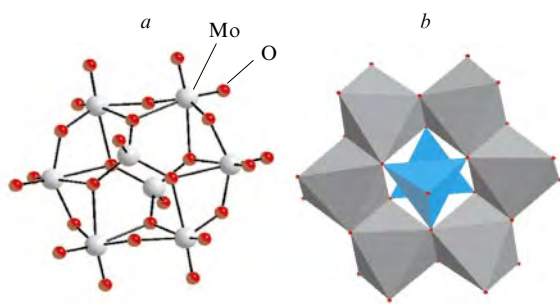


Figure 5. Structure of anion **7a** in the atomic (*a*) and polyhedral (*b*) representations.

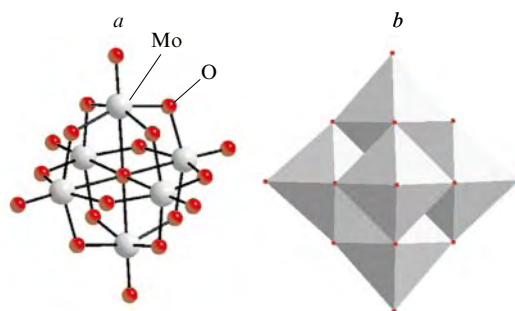


Figure 6. Structure of anion **8a** in the atomic (*a*) and polyhedral (*b*) representations.

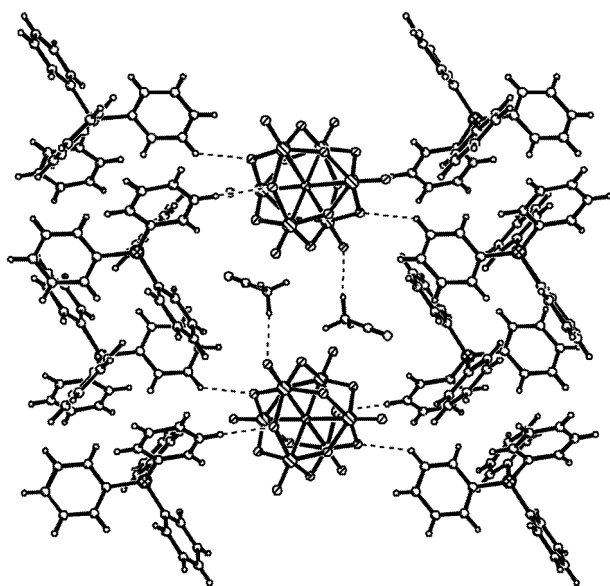


Figure 7. Fragment of the linear supramolecular structure of compound **9**.

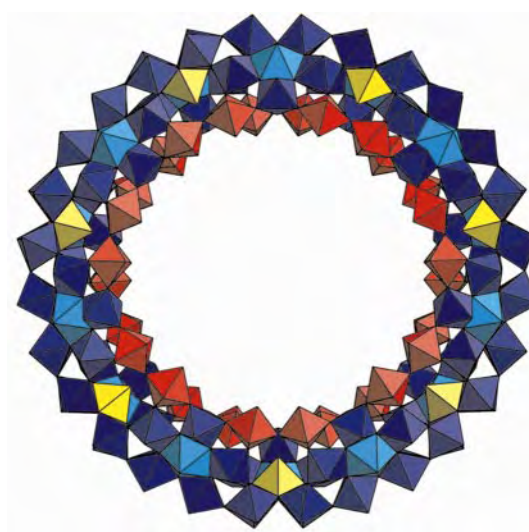


Figure 8. Structure of cluster anion **10a** in the polyhedral representation. Yellow octahedra are $\{\text{Mo}_1\}$ fragments, blue pentagonal bipyramids are the central $\{(\text{O}=\text{O})\text{MoO}_6\}$ parts of the $\{\text{Mo}_8\}$ fragments, red octahedra (in pairs) are $\{\text{Mo}_2\}$ fragments.

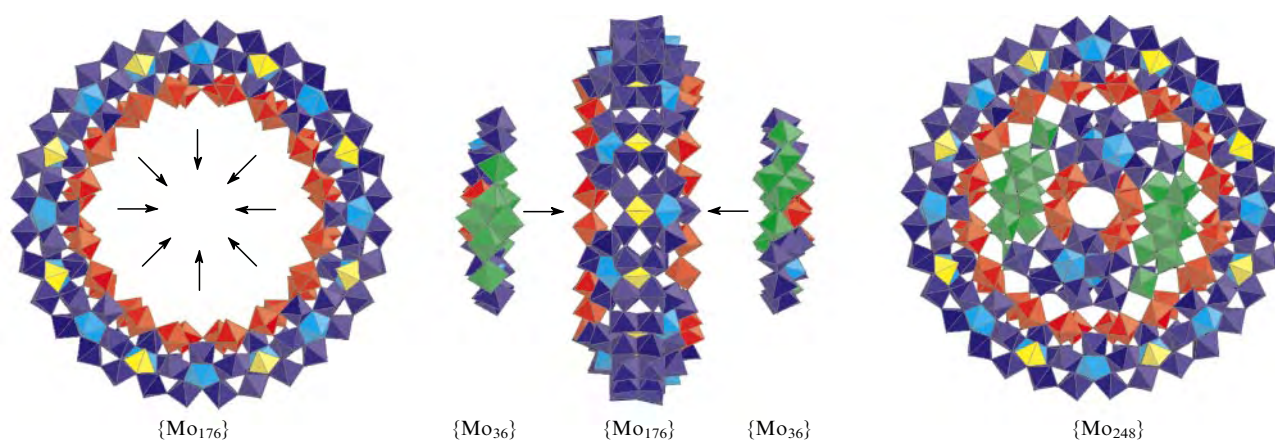


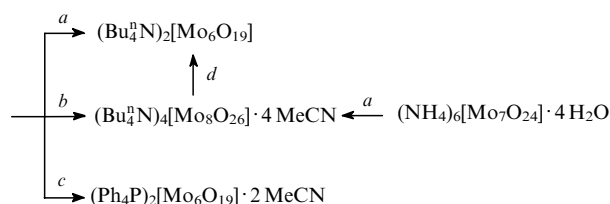
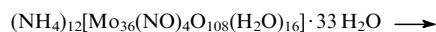
Figure 9. Structure of $\{\text{Mo}_{176}\}$ and $\{\text{Mo}_{248}\}$ cluster anions in the polyhedral representation and scheme of the molecular growth $\{\text{Mo}_{176}\} \rightarrow \{\text{Mo}_{248}\}$.⁵⁸ For designations of the polyhedra, see Fig. 8. The green colour marks fragments that cannot be represented in terms of fragments that constitute ring-shaped anions.

However, refluxing of compound **7** for several hours in a polar solvent such as acetone, acetonitrile or dimethyl sulfoxide induces cleavage of the octamer yielding hexanuclear cluster **8**.

Upon the heterogeneous reaction between cluster **A** in MeCN and Ph_4PCl (refluxing for 3 h), the cluster is completely converted into yellow-coloured compound $(\text{Ph}_4\text{P})_2[\text{Mo}_6\text{O}_{19}] \cdot 2 \text{ MeCN}$ (**9**),⁴⁸ which also contains the hexanuclear cluster anion **8a**. The solva-

tion acetonitrile molecules occupy in the cell the voids between the cluster anions and form shortened contacts between the terminal oxygen atoms of the anions and the hydrogen atoms of the methyl groups. In addition, the presence of shortened contacts between the hydrogen atoms of the benzene rings of the cations and the μ_2 oxygen atoms of the anions is favourable for the formation of a complex supramolecular structure (Fig. 7).

The ways of controlling the structure of the resulting polyoxomolybdate anion by variation of the solvent and the reaction conditions during decomposition of cluster **A** have been summarised in a publication.⁴⁶ This procedure allows deliberate synthesis of octa- or hexanuclear polyoxometallate anions soluble in organic solvents in accordance with the following scheme:



(a) (1) $\text{Bu}_4\text{N}^+\text{X}^-$, H_2O , 20 °C, (2) MeCN; (b) (1) $\text{Bu}_4\text{N}^+\text{X}^-$, H_2O , 100 °C, (2) MeCN; (c) $\text{Ph}_4\text{P}^+\text{Cl}^-$, MeCN, 82 °C; (d) refluxing in polar solvents.

V. Molybdenum blues

Solutions of molybdenum blues are formed almost instantaneously in the reduction of molybdenum(VI) compounds in acid media ($\text{pH} \leq 3$). The suitable reducing agents include metals (Al, Pb, Mo, Cu, Zn, Cd, Hg), B_2H_6 , NaBH_4 , N_2H_4 , NH_2OH , H_2S , SO_2 , SO_3^{2-} , $\text{S}_2\text{O}_3^{2-}$, $\text{S}_2\text{O}_8^{2-}$, SnCl_2 , MoCl_5 , MoOCl_3 , formic acid, ethanol, ascorbic acid, thiourea, hydroquinone, D-glucose, saccharose, hydrogen or CO gas (under pressure). The blues can also be prepared by electroreduction, photochemical reduction or reduction induced by γ -radiation.^{2, 49}

The history of soluble molybdenum blues goes back to 1783 when a study by C W Scheele was published,⁵⁰ although blue waters from the springs of the Valley of Ten Thousand Smokes (Idaho) had been known much earlier. Berzelius was the first to propose the general formula for these compounds, namely, $\text{Mo}_5\text{O}_{14} \cdot n \text{H}_2\text{O}$.⁵¹ Subsequently, researchers have used the formula MoO_x ($2.5 < x < 3$), as they have already believed that several types of molybdenum blues exist. Generations of chemists have attempted without success to crystallise these compounds in order to determine reliably their composition. The problem was in their very high solubility in water, which is now known to be due to the presence of numerous H_2O ligands. In recent years, this problem has been solved by A Müller and co-workers who used high concentrations of electrolytes to destroy the hydration shells. This allowed them to prepare single crystals of a large number of compounds containing giant ring-shaped anions of the $\{\text{Mo}_{154}\}$ (with and without defects) and $\{\text{Mo}_{176}\}$ types.^{10, 11, 18, 52–57} The formulae of some of them are given below:

(1) $(\text{NH}_4)_{28}[\text{Mo}_{154}(\text{NO})_{14}\text{O}_{448}\text{H}_{14}(\text{H}_2\text{O})_{70}] \cdot \text{ca. } 350 \text{ H}_2\text{O}$ (discrete rings);

(2) $\text{Na}_{14}[\text{Mo}_{154}\text{O}_{462}\text{H}_{14}(\text{MeOH})_8(\text{H}_2\text{O})_{62}] \cdot \text{ca. } 400 \text{ H}_2\text{O}$ (discrete rings);

(3) $\text{Na}_{26}[\text{Mo}_{142}\text{O}_{432}\text{H}_{14}(\text{H}_2\text{O})_{58}] \cdot \text{ca. } 300 \text{ H}_2\text{O}$ (discrete rings with defects);

(4) $\{\text{Na}_{24}[\text{Mo}_{144}\text{O}_{437}\text{H}_{14}(\text{H}_2\text{O})_{56}] \cdot \text{ca. } 250 \text{ H}_2\text{O}\}_n$ (chains of rings with defects);

(5) $\{\text{Na}_{16}[\text{Mo}_{152}\text{O}_{457}\text{H}_{14}(\text{H}_2\text{O})_{66.5}] \cdot \text{ca. } 300 \text{ H}_2\text{O}\}_m$ (layers of rings with defects).

It is worth mentioning that the first of these compounds, which contains the $[\text{Mo}_{154}(\text{NO})_{14}\text{O}_{448}\text{H}_{14}(\text{H}_2\text{O})_{70}]^{28-} \equiv \{\text{Mo}_{154}(\text{NO})_{14}\}$ cluster anions (**10a**), can be prepared by acidification and reduction of solutions containing anions **1b**.¹⁸ The

giant ring-shaped anion **10a** (Fig. 8) consists of 140 $\{\text{MoO}_6\}$ octahedra and 14 $\{\text{Mo}(\text{NO})\text{O}_6\}$ pentagonal bipyramids. The diameter of the central cavity in the equator is $\sim 20 \text{ \AA}$. The anion **10a** (approximate D_{7d} symmetry) can be described as an assembly consisting of 14 subunits. Each subunit is an octanuclear fragment with the $\{\text{Mo}_8\}$ core whose centre is the $\{\text{Mo}(\text{NO})\text{O}_6\}$ pentagonal bipyramid connected to seven $\{\text{MoO}_6\}$ octahedra through common vertices and edges. These $\{\text{Mo}_8\}$ fragments are situated above and below the equatorial plane of the cluster. Equivalent $\{\text{Mo}_8\}$ building blocks are also present in anions **1b**, **3a** and **4a** (see Section III). The key difference between two above-mentioned structural types (**1b**, **3a** and **4a**, on the one hand, and **10a** on the other hand) is that the $\{\text{Mo}_8\}$ fragments in clusters **1b**, **3a** and **4a** are arranged exactly one above another being separated by a reflection plane, whereas these fragments in anion **10a** are rotated relative to each other about a C_7 axis through an angle of $360^\circ/14$. Since in anions **3a** and **4a**, the pentagonal bipyramids of each fragment are connected to each other *via* one $\{\text{Mo}_1\}$ fragment located in the equatorial plane, the $\{\text{Mo}_{17}\}$ fragments can formally be regarded as 'pseudo-discrete'. Thus, they can be considered to be isolated transferable ligands linked through the $\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})_2\}^{3+}$ or $\{\text{V}^{\text{IV}}\text{O}(\text{H}_2\text{O})\}^{2+}$ cationic groups or the $\{\text{Mo}^{\text{V}}(\mu\text{-H}_2\text{O})_2(\mu\text{-OH})\text{Mo}^{\text{V}}\}^{9+}$ groups. In contrast to this, the shift of the $\{\text{Mo}_8\}$ fragments with respect to one another in cluster **10a** means that linking of every two of these structural elements requires two equatorial $\{\text{Mo}_1\}$ fragments. Every two neighbouring $\{\text{Mo}_8\}$ fragments situated above and below the equatorial plane are linked additionally through the $\mu_3\text{-O}$ atom. In addition, every two neighbouring $\{\text{Mo}_8\}$ fragments located in one plane are linked by a $\{\text{Mo}^{\text{VI}}\text{O}_2(\text{H}_2\text{O})(\mu\text{-O})\text{Mo}^{\text{VI}}\text{O}_2(\text{H}_2\text{O})\} \equiv \{\text{Mo}_2\}$ group. This gives rise to a ring-shaped structure; in terms of the building block concept, its formula can be written as $[\{\text{Mo}_2^{\text{VI}}\text{O}_5(\text{H}_2\text{O})_2\}\{\text{Mo}_7\text{Mo}(\text{NO})\text{O}_{25}(\text{OH})_2(\text{H}_2\text{O})_3\text{Mo}\}]_{14} \equiv [\{\text{Mo}_2\}\{\text{Mo}_8\}\{\text{Mo}_1\}]_{14}$.

As noted above, a series of similar ring-shaped anions containing no NO groups have been prepared in recent years. Among these, noteworthy is the ring-shaped $\{\text{Mo}_{176}\}$ cluster (**11a**),⁵⁴ which can be represented as consisting of sixteen $[\{\text{Mo}_2\}\{\text{Mo}_8\}\{\text{Mo}_1\}]$ sets instead of fourteen sets (as is observed for anion **10a** and its analogues). In another unusual cluster (which can be prepared by reduction of anion **10a** with ascorbic acid) containing 248 Mo atoms (**12a**),⁵⁸ the $\{\text{Mo}_{176}\}$ ring is capped from two sides by two neutral polyoxomolybdate fragments $\{\text{Mo}_{36}\text{O}_{96}(\text{H}_2\text{O})_{24}\}$ (Fig. 9). Their structure is almost identical to the structure of the crystalline Mo_5O_{14} oxide.⁵⁹ On the one hand, this similarity opens up the way for simulating the crystal growth and especially nucleation processes that take place during the formation of metal oxides and, on the other hand, it allows one to mimic the pattern of organisation of metal centres in biological systems, in particular, for some types of biomineralisation.

Detailed investigation of a large number of diverse structures of molybdenum blues demonstrated that they all contain 14 (or 16 in the case of hexadecamers) $\{\text{Mo}_5\text{O}_6\}$ fragments and each of the fragments has two 4d electrons.⁶⁰

By linking ring-shaped cluster anions including those containing defects (*i.e.*, missing $\{\text{Mo}_2\}$ groups), one can obtain a multitude of solid-state chain or layer structures.⁵⁶ The structures of some of these compounds incorporate nano-sized channels. In addition, it was demonstrated that $\{\text{Mo}_{154}\}$ type ring-shaped anions can form colloid particles with a hydrodynamic radius of $\sim 80 \text{ nm}$ in organic solvents.

The ring-shaped clusters connected in chains can also act as hosts with respect to smaller polyoxometallate clusters, for example, $\{\text{Mo}_{36}\}$ type clusters (**1a,b**). In such supramolecular systems $\{\text{Mo}_{36} \subset \text{Mo}_{148}\}$,²³ the host and the guest (located exactly in the host cavity) are connected *via* 16 hydrogen bonds and four Na^+ cations arranged in the gap between the host and the guest (Fig. 10, see p. 563).

Thus, one can list the following most typical properties and potential applications of the polyoxomolybdate clusters belonging to the ‘molybdenum blue’ class.²²

1. The presence of nano-sized cavities, which opens up broad opportunities for the formation of supramolecular architectures according to the host–guest principle.

2. High hydrophilicity of the surfaces due to the presence of a large number of H₂O ligands, which entails the formation of an unusually extended hydration shell (this accounts for the high solubility of these clusters).

3. The presence of surfaces with large areas, which is the reason for the high affinity of these clusters for adsorbents such as activated carbon or silk.

4. The possibility of formation of discrete structural defects on the outer surface of the cluster rings.

5. Linking of the ring-shaped blocks both during ageing of their solutions and during oriented crystallisation processes.

6. The possibility of introducing molecules onto various sections of the cluster surface by means of replacement of H₂O ligands (this is accompanied by successive changes in the properties of the cluster and especially of its surface) and study of the reactions between molecules placed into the cluster cavities.

7. Structural analogy between the fragments and the catalytically active metal oxides; this allows these clusters to be regarded as molecular models of some heterogeneous catalysts.

VI. Spherical systems (keplerates)

Although molecular systems, even fairly large ones, can, in principle, be obtained by a multistage synthesis, the construction of exceedingly big, giant molecular systems, including those with unusual structures having very high symmetry (similar to the structures of simple spherical viruses) and unusual properties requires different approaches.

For example, in order to construct giant spheres that resemble in size and structure spherical viruses having an icosahedral symmetry (*C*₅, *C*₃, *C*₂), it is necessary to select a reaction system in which pentagonal fragments capable of producing 12 icosahedron vertices upon linking should first be generated.

1. Spherical giant clusters with binuclear Mo^V–Mo^V linkers

In the case of polyoxomolybdates, the {(Mo)Mo₅} pentagonal fragments mentioned above consist of the central MoO₇ bipyramid connected to five MoO₆ octahedra through shared edges. When the solution contains classical binuclear {Mo₂O₄}²⁺ linkers (which are often formed in reduced molybdate solutions in the presence of bidentate ligands)⁶¹ capable of connecting pentagonal fragments, an icosahedral molecular system is formed consisting of 12 pentagons and 30 binuclear linkers mentioned above. If acetate anions function as bridging ligands for the [Mo₂O₄]²⁺ groups, this gives a spherical cluster with the composition [Mo₇₂Mo₆₀O₃₇₂(AcO)₃₀(H₂O)₇₂]^{42–} ≡ {Mo₁₃₂} (13a),⁶² in which the positions of the central Mo atoms in the {(Mo)Mo₅} fragments form 12 vertices, while the [Mo₂O₄]²⁺ groups (with the metal–metal bond and with a Mo–Mo distance of ~2.6 Å) form 30 edges of the icosahedron (Fig. 11). Thus, the formula of anion 13a can be written as follows: [(Mo)Mo₅O₂₁·(H₂O)₆]₁₂·{Mo₂O₄}(AcO)₃₀]^{42–}. The salt (NH₄)₄₂[Mo₇₂Mo₆₀O₃₇₂·(AcO)₃₀(H₂O)₇₂]·300 H₂O·10 AcONH₄ (13) crystallises in the space group *Fm*3 with a close cubic packing of the spherical anions. In the cluster molecule, all the 132 oxygen atoms of the terminal Mo=O groups are directed outside the giant spherical anion 13a, while the *trans*-arranged H₂O ligands of all the 72 Mo^{VI} centres are directed toward the centre of this anion.

This molecular system with sixty MoO₆ subfragments belonging to twelve {(Mo)Mo₅} pentagons is a topological model of spherical viruses, namely, the tobacco mosaic virus. This virus contains 60 identical protein subfragments (coded by only one gene) or, in other words, 12 pentagonal capsomers (morphological fragments). Each capsomer is composed of 5 protomers.⁶³

When the acetate bridging ligands are replaced by formate ones, a guest system represented by a water cluster consisting of ~60 H₂O molecules connected by hydrogen bonds is formed in the cluster anion cavity due to the decrease in the steric restrictions.⁶⁴

The acetate bridging ligands can also be replaced either completely by phosphate or hypophosphite anions or partially by hydrosulfate anions. These groups enter the [(Mo)Mo₅O₂₁·(H₂O)₆]₁₂{Mo₂O₄(H₂PO₂)₃₀]^{42–} (14a) and [(Mo)Mo₅·O₂₁(H₂O)₆]₁₂{Mo₂O₄(HSO₄)₁₈{Mo₂O₄(AcO)}₁₂]^{42–} (15a) cluster anions, formed upon the addition of excess bidentate anions derived from the corresponding acids to freshly prepared solutions of salt 13.⁶⁵

The compound Na₄₆[Mo₆₆Mo₅₀O₃₃₁(AcO)₃₀(H₂O)₅₆]·ca. 300 H₂O (16) (space group *Pmn*2₁) isolated as a salt,⁶⁵ which contains giant basket-like cluster anions (Fig. 12), crystallises from solutions of anions 13a containing Na⁺ cations on keeping in air for a long period. The structure of the [Mo₆₆Mo₅₀O₃₃₁(AcO)₃₀(H₂O)₅₆]^{46–} anion (16a) can formally be obtained from structure 13a by removing the [(Mo)Mo₅](Mo₂O₄)₅ ≡ {Mo₁₆} fragment. The relative content of Mo^V centres in anion 16a is lower than that in anion 13a; therefore, the formation of cluster 16a from 13a can be regarded as partial oxidation.

Salt 16 is much more soluble in water than compound 13, whose anion (13a) contains mainly terminal oxygen atoms as ligands on the surface of a closed sphere. This difference in solubility is due to the easy ingress of solvent (water) molecules inside the cluster anion 16a, whose internal surface is hydrophilic due to the presence of a large number of H₂O ligands. Therefore, salt 16 crystallises only in the case where the equilibrium is appreciably shifted toward the formation of basket-like particles. The solution should always remain dilute in order to avoid crystallisation of compound 13. If the reaction is carried out at high concentrations of sodium acetate (which induces salting-out due to destruction of the hydration shell) or even in the presence of NH₄⁺ ions whose salts are less soluble (than sodium salts), salt 13 crystallises.

The knowledge of the structure of anion 16a is important for understanding the processes of ligand replacement in cluster 13a, resulting in the formation of anions 14a and 15a. In addition, the following facts should be taken into account.

1. Ligand exchange cannot occur through the ‘molecular windows’ present in anion 13a on *C*₃ axes because these windows (formed by {Mo₉O₉} rings) are too small for the anionic ligands.

2. Compounds 14 and 15 can be isolated if a substantial amount of spherical cluster anions remains in the reaction medium.

3. The exclusion of ligand exchange through the ‘windows’ suggests that either the ligands that approach the spherical anion 13a induce its opening or that the closed spherical cluster anions exist in equilibrium with the corresponding basket-like cluster anions.

In terms of the latter assumption, one can explain the easy crystallisation (after the ligand exchange) of compounds 14 and 15 containing spherical cluster anions 14a and 15a. The reason is a lower hydrophilicity of their surfaces compared to that of the surface of cluster 16a. They are much less soluble than the basket-like anions equilibrated with them. Yet another argument supporting the existence of such an equilibrium is the fact that compound 13 can be isolated from solutions of compound 16 and *vice versa*. This does not provide any grounds for suggesting that the {Mo₁₆} fragment is stable in solutions.⁶⁵

2. Spherical giant clusters with mononuclear linking fragments

Binding of pentagonal {(Mo)Mo₅} fragments by fragments other than binuclear {Mo₂O₄L} makes it possible to vary the dimensions and properties of the giant spherical clusters formed. For example, oxidation of the spherical anion 13a with air oxygen at

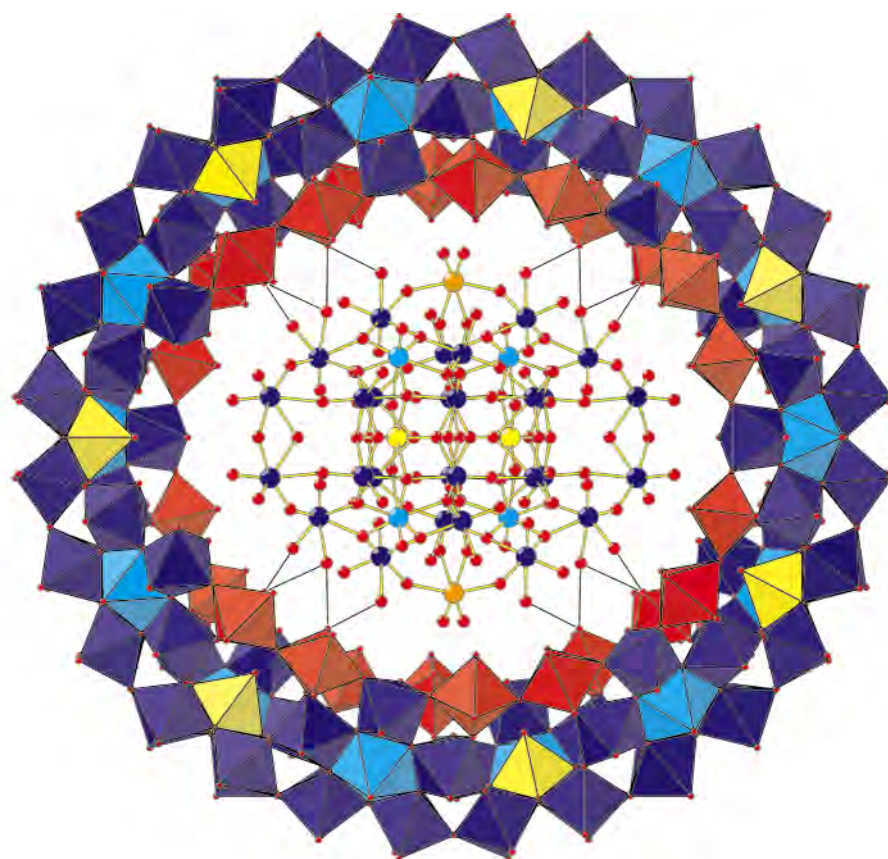


Figure 10. Structure of the $\{\text{Mo}_{36}\}\text{C}\{\text{Mo}_{148}\}$ supramolecular system. The $\{\text{Mo}_{148}\}$ cluster is given in the polyhedral representation and the $\{\text{Mo}_{36}\}$ cluster is in the atomic representation.²³ For designations of the polyhedra, see Fig. 8.

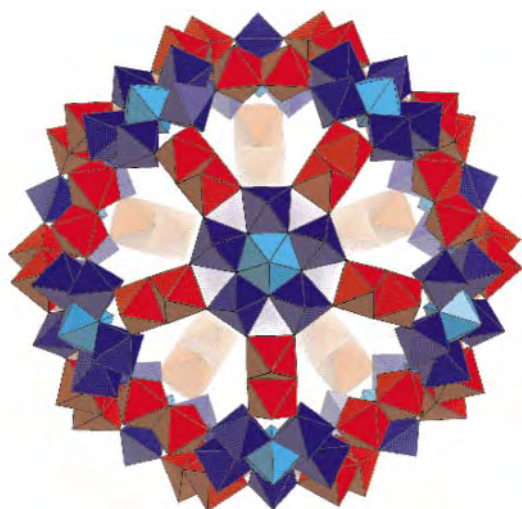


Figure 11. Structure of cluster anion **13a** in the polyhedral representation. Blue pentagonal bipyramids are the central parts MoO_7 of the $\{(\text{Mo})\text{Mo}_5\}$ fragments; red octahedra (in pairs) are the $[\text{Mo}_2^{\text{V}}\text{O}_4]^2+$ fragments.

pH ~ 2.5 and at high NaCl concentrations gives rise to a dark-blue crystalline compound, $[\{(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6\}]_{12} \cdot \{[\text{Mo}^{\text{VO}}(\text{H}_2\text{O})]_{30}\} \cdot \text{ca. } 150 \text{ H}_2\text{O}$ (**17**), containing neutral spherical cluster **17a** (Fig. 13). This product crystallises in the $C2/c$ space group and, unlike cluster anion **13a** (the space group of salt **13** is $Fm3$), it does not form a close cubic packing. Like cluster anion **13a**, neutral cluster **17a** comprises 12 pentagonal fragments,

$\{(\text{Mo})\text{Mo}_5\}$, which are partially reduced (unlike those in anion **13a**). The pentagonal fragments in cluster **17a** are linked to one another by thirty $\text{O}=\text{Mo}^{\text{V}}(\text{H}_2\text{O})$ fragments [the $\text{Mo}=\text{O}$ bond length is $\sim 1.67 \text{ \AA}$; the $\text{Mo}-\text{O}(\text{trans-H}_2\text{O})$ distance is $\sim 2.30 \text{ \AA}$] to form an Archimedean solid, namely, icosidodecahedron. The $\text{Mo}=\text{O}$ groups of the linkers are directed inside the sphere.⁶⁶

In conformity with the Robin–Day classification, cluster **17a** can be defined as a mixed-valence compound of type II,⁶⁷ as indicated by its intensive dark blue colour. Of the 36 4d electrons belonging to molybdenum atoms (which are formally Mo^{V} centres determined by cerium redox titration), 30 electrons are mainly concentrated on the 30 molybdenum atoms that act as linkers, whereas the other six electrons are mainly delocalised among the molybdenum atoms of the pentagonal groups.

It is of interest that the EPR spectra of compound **17** measured at room temperature do not exhibit resonance signals in spite of the presence of a large number of unpaired electrons. Apparently, the absence of signals can be attributed to strong exchange interactions of the antiferromagnetic type.⁶⁶

It should be noted that a structure with $\text{Mo}^{\text{V}}-\text{Mo}^{\text{V}}$ fragments (*i.e.*, with localised $\text{Mo}-\text{Mo}$ bonds) does not exist in cluster **17a**, despite the fairly large number of Mo^{V} centres (formal). Local (partially) single-electron oxidative degradation of the $[\text{Mo}_2^{\text{V}}\text{O}_4]^2+$ linkers under mild conditions corresponds formally to the reaction $\{\text{Mo}_2^{\text{V}}\} \rightarrow \{\text{Mo}^{\text{V}}\} + \text{Mo}^{\text{VI}}$ followed by the formation of soluble polyoxomolybdates(VI). As this takes place, thirty Mo^{V} centers are trapped by a spherical matrix [twelve $\{(\text{Mo})\text{Mo}_5\}$ pentagonal blocks], and their structure does not change. It is significant that this reaction involves the binding functional groups located on the surface of the giant sphere. This inevitably changes the dimensions of the molecule. Further

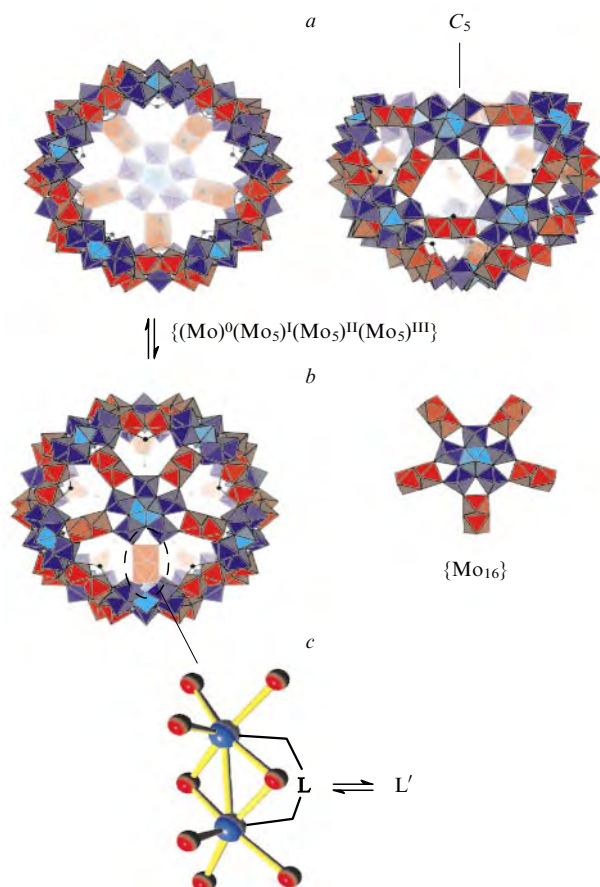


Figure 12. Structure of cluster anion **16a** in two projections in the polyhedral representation (*a*) and its formal difference from anion **13a** (*b*) (the {Mo₁₆} fragment is shown separately). Binuclear fragment {Mo₂O₄L} (*c*) in which the $L \rightleftharpoons L'$ ligand exchange takes place.⁶⁵

oxidation does not take place, as neutral cluster **17** has a low solubility and crystallises immediately after formation.

When a solution of salt **13** reacts with $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (pH ~ 3) in the presence of ammonium acetate, the replacement of the {Mo₂^V} linkers in cluster **13a** by Fe^{III} centres gives rise to a yellow-coloured crystalline compound, $[\{(\text{Mo})\text{Mo}_5\text{O}_{21}\text{L}_6\}_{12}\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})\text{L}\}_{30}] \cdot \text{ca. } 150\text{H}_2\text{O}$ (**18**),⁶⁸ where L is H₂O, AcO[−] or Mo₂^{VI}O_{8/9}[−]. Compound **18** contains 12 acetate ligands and three ‘additional’ Mo₂O_{8/9} fragments (their total charge is -6). The structures of these fragments are given by $\{(\mu\text{-O})_2\text{O}=\text{Mo}^{\text{VI}}(\text{OH})_2(\text{H}_2\text{O})\text{Mo}^{\text{VI}}=\text{O} \cdot (\mu\text{-O})_2\}^{2-}$ and $\{(\mu\text{-O})_2\text{O}=\text{Mo}^{\text{VI}}(\text{H}_2\text{O})\text{Mo}^{\text{VI}}=\text{O}(\mu\text{-O})_2\}^{2-}$ with octahedral and square-bipyramidal coordination environments of the Mo atoms, respectively. These fragments are markedly disordered and function as tetradentate ligands inside the cluster shell. The twelve acetate ligands are also disordered, and their positions cannot be determined exactly, first of all, due to the large number (≥ 120) of possible positions. It is evident that the hypothetical positively charged cluster formed upon substitution of the Fe^{III} centres for all linkers in anion **13a**, namely, $[\{(\text{Mo})\text{Mo}_5\text{O}_{21} \cdot (\text{H}_2\text{O})_6\}_{12}\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})_2\}_{30}]^{18+}$, would be exceptionally unstable under the reaction conditions. Thus, the formula of this compound can be written as $[\text{Mo}_{72}\text{Fe}_{30}\text{O}_{252}(\text{AcO})_{12}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}_2 \cdot \{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}(\text{H}_2\text{O})_{91}] \cdot \text{ca. } 150\text{H}_2\text{O}$.

Compound **18** crystallises in the space group *R*3 and contains discrete neutral spherical clusters **18a**. Each spherical cluster (see Fig. 13) consists of 12 pentagonal fragments of the {Mo}Mo₅ type connected by 30 Fe^{III} centres; thus, the structure of **18a** has an approximate icosahedral symmetry and contains 102 metal atoms, and, in addition, their terminal ligands (O or H₂O) that belong to two concentric spheres. Each octahedron formed by a

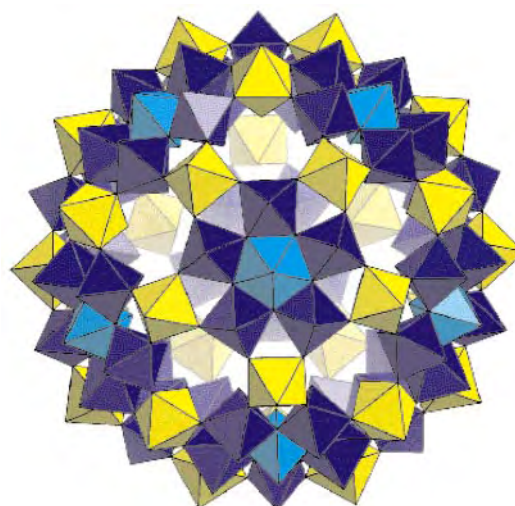


Figure 13. Structure of clusters $[\{(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6\}_{12} \cdot \{\text{MoVO}(\text{H}_2\text{O})\}_{30}]$ (**17a**) and $[\{(\text{Mo})\text{Mo}_5\text{O}_{21}\text{L}_6\}_{12}\{\text{Fe}^{\text{III}}(\text{H}_2\text{O})\text{L}\}_{30}]$ (**18a**) in the polyhedral representation. The yellow octahedra are the {Mo^VO(H₂O)}³⁺ centres (in **17a**) or {Fe^{III}(H₂O)L}³⁺ centres (in **18a**).

Fe^{III} centre is connected to two neighbouring pentagonal fragments. The midpoints of 12 pentagonal fragments, namely the Mo atoms in the MoO₇ pentagonal bipyramids, form an icosahedron, while thirty Fe^{III} centres form an icosidodecahedron.⁶⁹

The Raman spectrum of compound **18** in a concentrated aqueous solution is virtually identical to the spectrum recorded for the solid. It should be noted that these solutions are acidic due to partial deprotonation of the H₂O ligands belonging to the Fe^{III} centres. The slight yellow colouring of the compound corresponds to the presence of polyoxomolybdate(VI) fragments and Fe^{III} centres. Magnetochemical measurements^{70, 71} indicate that cluster **18** contains high-spin Fe^{III} centres (the Fe^{III}–Fe^{III} distance is $\sim 6.4\text{Å}$), which are involved in rather weak antiferromagnetic exchange interactions described by the classical Heisenberg model.^{70, 71} The ⁵⁷Fe Mössbauer spectrum confirms the presence of only Fe^{III} centres in a slightly distorted octahedral oxygen environment.

The reaction of vanadyl sulfate with an acidified solution of sodium molybdate in the presence of high concentrations of an electrolyte (NaCl) gives the compound $\text{Na}_{20} \cdot [\{(\text{Mo}^{\text{VI}}\text{O}_3 \cdot (\text{H}_2\text{O}))_{10}\{\text{V}^{\text{IV}}\text{O}(\text{H}_2\text{O})\}_{20}\{(\text{Mo}^{\text{VI}})\text{Mo}_5^{\text{VI}}\text{O}_{21}(\text{H}_2\text{O})_3\}_{10} \cdot \{(\text{Mo}^{\text{VI}}\text{O}_2 \cdot (\text{H}_2\text{O})_2\}_{5/2}\}_2\{\text{NaSO}_4\}_5\}_2] \cdot 170\text{H}_2\text{O}$ (**19**).⁷² The cluster anion $[\{(\text{Mo}^{\text{VI}}\text{O}_3(\text{H}_2\text{O}))_{10}\{\text{V}^{\text{IV}}\text{O}(\text{H}_2\text{O})\}_{20}\{(\text{Mo}^{\text{VI}})\text{Mo}_5^{\text{VI}}\text{O}_{21} \cdot (\text{H}_2\text{O})_3\}_{10}\{(\text{Mo}^{\text{VI}}\text{O}_2(\text{H}_2\text{O})_2\}_{5/2}\}(\text{NaSO}_4)_5\}_2]^{20-}$ (**19a**) present as a part of this structure is nearly spherical (its greatest and smallest outer diameters are equal to 25 and 23 Å, respectively) and has a *C*₅ symmetry axis (Figs 14, 15). The structure of this anion is best described as a distorted icosidodecahedron containing 20 triangular and 20 pentagonal faces, which are formed by 10 Mo^{VI} centres and 20 V^{IV} centres. Ten triangular faces composed of 20 V^{IV} centres form an unusual equatorial ‘ring-shaped magnetic ribbon.’ The other 10 triangular faces, each being formed by one V^{IV} centre and two Mo^{VI} centres, complete the distorted icosidodecahedron (see Fig. 14).

The cavity of cluster anion **19a** accommodates ten sulfate groups in a previously unknown mode [each group is connected to three neighbouring Mo^{VI} centres of each {Mo^{VI}}Mo₅^{VI} group *via* three oxygen atoms] and ten Na⁺ cations. The Na⁺ cations are located between the neighbouring sulfate groups, which gives rise to two unusual {NaSO₄}₅ rings [the Na–O(SO₃) distance is 2.48–2.60 Å] lying above and below the equatorial ring composed of ten V^{IV} centres. Note that in this case, the Na ions possess a unique pentagonal-bipyramidal coordination environment. Five

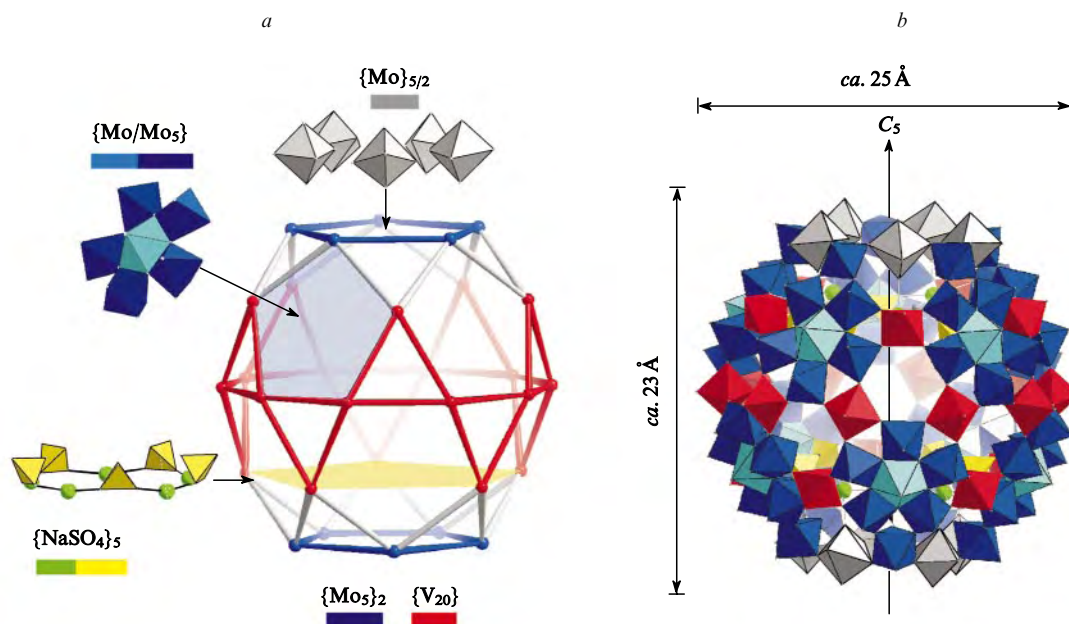


Figure 14. Structure of **19a** in the framework (distorted icosidodecahedron) (a) and polyhedral (b) representations.⁷²

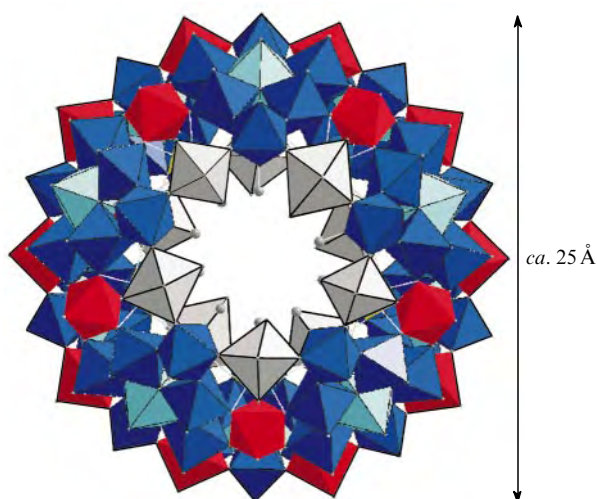


Figure 15. View of the structure **19** parallel to the C_5 axis in the polyhedral representation.⁷²

For designations of the polyhedra, see Fig. 14.

of the seven corresponding oxygen centres belong to the cluster shell.

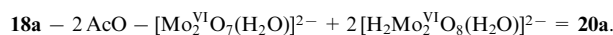
The measurements of the magnetic susceptibility of compound **19** showed a sharp decrease in the χT value in the range from 200 to 100 K ($3.4\text{--}2.3\text{ cm}^3\text{ K mol}^{-1}$), indicating the presence of strong antiferromagnetic exchange interactions despite rather long distances between the V^{IV} atoms ($6.27\text{--}6.46\text{ Å}$).

VII. Spherical giant clusters as building blocks in chemical design

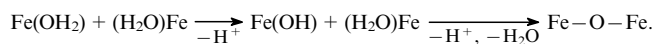
The deliberate design of cross-linked structures having pre-specified properties from reliably characterised building blocks is among the most promising lines of research in modern inorganic chemistry.^{73,74} Thus linking of giant ring-shaped polyoxomolybdate clusters (see Section V) having open nano-sized cavities gives rise to two-dimensional networks.¹¹

By varying the size of cluster anions (and, hence, their inner cavities) and by changing the nature of linkers on passing from

anion **13a** to anion **18a**, one can create unusual chemical structures resulting from absolutely new reactions including insertion of a guest into the host cavity and/or cross-coupling of spherical clusters to form cross-linked polymeric structures. When a freshly prepared solution of salt **18** is acidified by hydrochloric acid to pH 2, the compound $[\text{Mo}_{72}\text{Fe}_{30}\text{O}_{252}(\text{AcO})_{10}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\cdot\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3(\text{H}_2\text{O})_{91}]\cdot 140\text{ H}_2\text{O}$ (**20**) is formed; this product contains neutral spherical clusters $[\text{Mo}_{72}\text{Fe}_{30}\text{O}_{252}(\text{AcO})_{10}\cdot\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3(\text{H}_2\text{O})_{91}]$ (**20a**), very similar to the cluster **18a**. The major difference between compounds **20a** and **18a** is the fact that the former has fewer acetate ligands and more binuclear oxomolybdate ligands. This can be sketched as follows:



However, even such minor changes in the structure of these clusters result in substantial changes in their reactivity: when dried in air at room temperature, compound **20a** undergoes solid-state condensation to give a cross-linked structure, $\{[\text{H}_4\text{Mo}_{72}\text{Fe}_{30}\text{O}_{254}(\text{AcO})_{10}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3\cdot(\text{H}_2\text{O})_{87}]\cdot 80\text{ H}_2\text{O}\}_n$ (**21**) (Fig. 16).⁷⁵ It is noteworthy that this process does not take place during drying of the crystals of **18a** with a different packing of cluster units. The clusters **20a** form the structure $[\text{H}_4\text{Mo}_{72}\text{Fe}_{30}\text{O}_{254}(\text{AcO})_{10}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3(\text{H}_2\text{O})_{87}]$ (**21a**) via closure of Fe–O–Fe bridges between the neighbouring cluster units, which implies deprotonation of the H_2O ligands belonging to the iron atoms with subsequent condensation:



In addition, the intermediate of this process $\{[\text{Mo}_{72}\cdot\text{Fe}_{30}\text{O}_{252}(\text{AcO})_{10}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3(\text{H}_2\text{O})_{91}]\cdot 100\text{ H}_2\text{O}\}_n$ (**22**) was isolated as a single crystal and structurally characterised (so were both compounds described above). In compound **22**, close contacts occur between the $[\text{Mo}_{72}\text{Fe}_{30}\text{O}_{252}\cdot(\text{AcO})_{10}\{\text{Mo}_2\text{O}_7(\text{H}_2\text{O})\}\{\text{H}_2\text{Mo}_2\text{O}_8(\text{H}_2\text{O})\}_3(\text{H}_2\text{O})_{91}]$ cluster units (**22a**); however, chemical bonds between them have not yet been formed.⁷⁵

Since the reaction $\mathbf{20} \rightarrow \mathbf{22} \rightarrow \mathbf{21}$ takes place in the crystal at room temperature and mainly involves the transformation of giant spherical fragments, the crystal unit cells of the three compounds are fairly similar. Compounds **20** and **22** crystallise with a monoclinic space group $P2_1/n$ and have similar unit cell

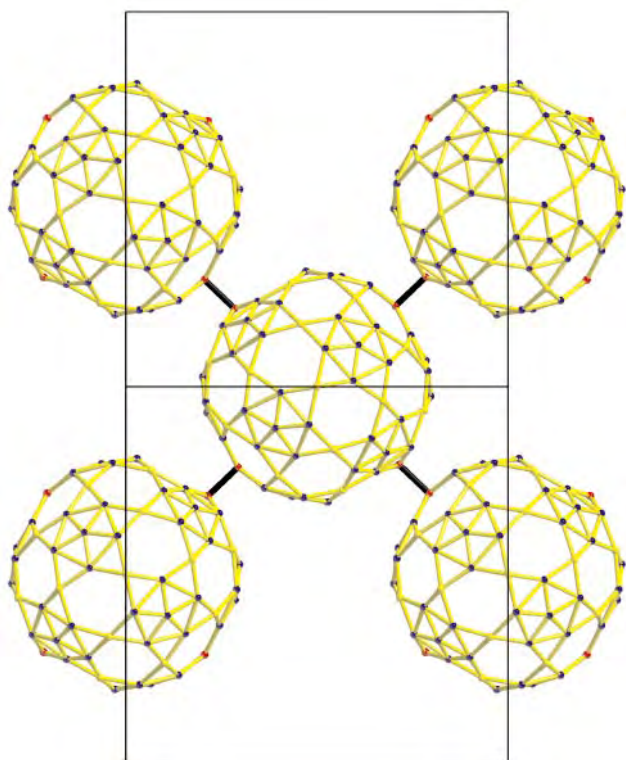


Figure 16. Structure of the metal core of the network structure of cluster **21a**.⁷⁵

Blue spheres are molybdenum atoms; red and yellow spheres are iron atoms involved and not involved in the intersphere binding, respectively.

parameters and similar patterns of packing of the spherical clusters. During the condensation resulting in structure **21**, the clusters are re-oriented; consequently, the structure passes to a more symmetrical orthorhombic system (space group *Cmca*). The cluster re-orientation accompanied by the loss of crystal water mainly involves the translational shift of clusters towards one another with a very slight rotation. The shortest distance between the Fe^{III} centres of neighbouring spheres in structure **20** is 6.74 Å,

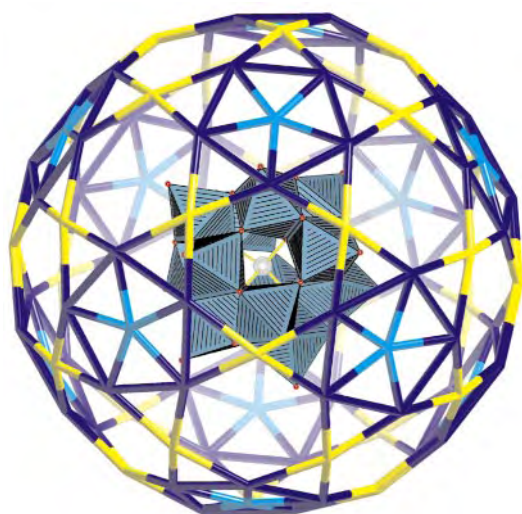


Figure 17. Structure of the cluster composite $[H_2PMo_{12}O_{40} \cdot H_4Mo_{72} \cdot Fe_{30}(AcO)_{12}O_{254}(H_2O)_{98}]$ (**23a**), a fragment of the layered structure **23**.⁷⁷

For designations, see Figs 8, 13. The dashed polyhedra are encapsulated Keggin anions.

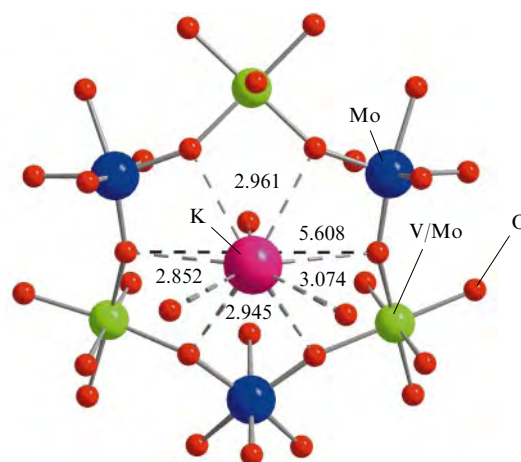


Figure 18. Interatomic distances in the $\{Mo_6O_6\}$ metal rings of the spherical polyoxomolybdate cluster with integrated K^+ cations.⁸⁴

while this distance in cluster **22** amounts to 5.39 Å, and, finally, in structure **21**, the Fe—O—Fe distance is 3.79 Å. Magnetic measurements indicate that cluster **22** contains thirty Fe^{III} atoms, four of which are involved in strong exchange interactions of the antiferromagnetic type.

This process is analogous to classical inorganic condensation reactions, resulting in the formation of polycations;⁷⁶ however, unlike, for example, the hydrolysis of $[Fe(H_2O)_6]^{3+}$, this process is not chaotic.

Even more complex systems based on spherical clusters of the $\{Mo_{72}^{VI}Fe_{30}^{III}\}$ type can be synthesised in one step from simple reactants. Thus the addition of $FeCl_2 \cdot 4H_2O$ in air to an acidic (pH 2) aqueous solution of polyoxomolybdate(VI) containing acetic acid and slight amounts of phosphate induces a complex self-assembling process giving rise to the neutral compound $\{[H_xPMo_{12}O_{40} \cdot H_4Mo_{72}^{VI}Fe_{30}^{III}(AcO)_{12}O_{254}(H_2O)_{98}] \cdot 60H_2O\}_n$ (**23**), which is a novel type layered material (Fig. 17).^{77,78} The building blocks that constitute this system are nano-sized oxometallate composites consisting of paramagnetic icosahedral

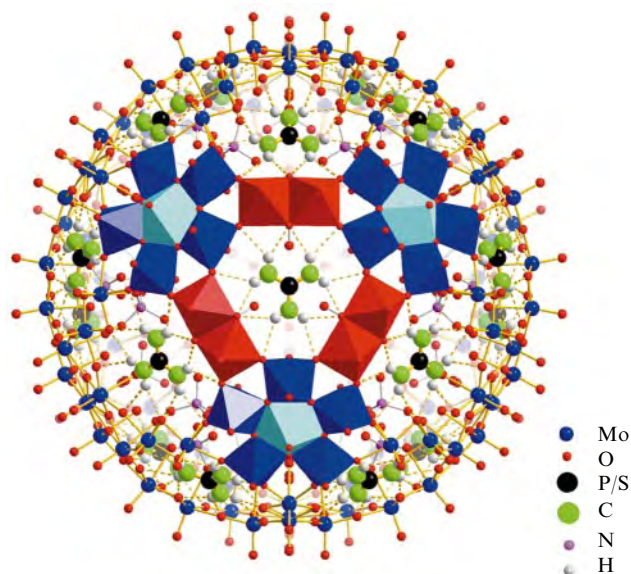


Figure 19. Structural details of cluster anion **24a**.⁸⁴

Three pentagonal $\{(Mo)Mo_5\}$ fragments and three $\{Mo_2\}$ linkers, which form the $\{Mo_9O_9\}$ metal ring encapsulating the $[(NH_2)_3C]^+$ cation are given in the polyhedral representation and the other (similar) parts of the cluster are in the atomic representation.

cluster capsules (the diameter of the inner cavity is ~ 16 Å) of the $\{\text{Mo}_7^{\text{VI}}\text{Fe}_3^{\text{III}}\}$ type as hosts and reduced Keggin ions $[\text{H}_x\text{PMo}_{12}\text{O}_{40}]^{3-x-}$ ($x = 1, 2$; the diameter of the Keggin anion is ~ 14 Å)⁷⁹ as guests. The reduced Keggin ion tightly fits in the cluster cavity, the shortest $\text{O}_{\text{guest}} \cdots \text{O}_{\text{host}}$ distances being ~ 2.6 Å, which is typical of hydrogen bonding. Each of these cluster–cluster composites is linked to four neighbouring ones by Fe–O–Fe fragments, giving rise to a layered structure. The cluster capsule contains twelve pentagonal fragments of the $\{(\text{Mo})\text{Mo}_5\}$ type connected by thirty $\{\text{Fe}(\text{H}_2\text{O})_2\}^{3+}$ linkers. The acetate ligands in them are disordered and are arranged within a sphere, mainly functioning as bidentate bridging ligands between the Mo and Fe atoms.

The binding in cluster–cluster composites is based on the well studied process called inorganic condensation in which the guest molecule acts as the template in the formation of the host (capsule). It is worth noting that composite **23a** can also be prepared by adding a salt of the usual Keggin anion $[\text{PMo}_{12}\text{O}_{40}]^{3-}$ to the reaction mixture described above devoid of phosphate. The method for the synthesis of composite **23a** is a ‘cascade’ procedure, which gives the Keggin ion at an initial stage. However, in the presence of greater amounts of phosphate, the reaction follows a different route and composite **23a** cannot be prepared. One more important point is worth mentioning, namely, only iron(II) chloride $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ is appropriate as the starting reagent, because the use of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ results in an amorphous precipitate of a variable composition and structure.

The physicochemical investigations of the structure of **23** (see Ref. 77) not only proved the presence of separate, not bonded by covalent bonds parts (the capsule and the guest) in each spherical unit of cluster **23a** but also revealed interesting topological, spectroscopic, electronic and magnetic properties. For example, nanocapsules of the $\{\text{Mo}_7^{\text{VI}}\text{Fe}_3^{\text{III}}\}$ type form a system of magnetic dots (each of them is the strongest known molecular paramagnet with the spin $S = 150/2$ at room temperature) and, simultaneously, they encapsulate the reduced Keggin ions (quantum dots) as guests. This system can be considered as a potential electron reservoir. It should be emphasised that the free Keggin ion can be reduced in several stages, its charge remaining constant due to the concomitant protonation.⁸⁰

Evidently, knowledge of the chemistry of nanocapsules with a variable size^{66,68} which can be linked together to form polymeric structures^{76,79} is exceptionally important for the synthesis of new polymeric materials with unique properties. In addition, the possibility of introducing guest molecules (a cluster in a cluster) opens up prospects for target-directed variation of the properties of such materials by varying the properties of guests.

VIII. Polyoxomolybdate clusters as nanoreceptors

As has been noted in Section VI, variation of the nature of linkers allows one to change the overall dimensions of spherical objects constructed as $\{(\text{pentagonal fragment})_{12}(\text{linker})_{30}\}$ and the dimensions of 20 corresponding pores (Mo_nO_n metal rings); the same structural principle is met for spherical viruses.⁸¹ If the linker is represented by the binuclear $\{\text{Mo}_2^{\text{V}}\}$ fragment, the pores on the surface of such spherical system are formed by the $\{\text{Mo}_9\text{O}_9\}$ rings with a diameter of 0.6–0.8 nm.⁶² In the case of mononuclear linkers such as M^{n+} where $\text{M} = \text{Fe}^{3+}$ (see Ref. 68), MoO^{3+} (see Ref. 66) or $\text{VO}^{2+}/\text{MoO}^{3+}$ (see Ref. 72), smaller rings are formed, namely, $\{\text{Mo}_6\text{O}_6\}$, whose size is just appropriate for ‘trapping’ potassium cations.⁸² Note that every one of these 20 pores (rings) has, in principle, the properties of a receptor comparable with those of crown ethers, which are classical objects of supramolecular chemistry.⁸³ It has been shown⁸⁴ that spherical clusters like $\{\text{Mo}_{132}\}$ with different types of ligands stabilising the $\{\text{Mo}_2^{\text{V}}\text{O}_4\}^{2+} \equiv \{\text{Mo}_2^{\text{V}}\}$ groups have pores the sizes (Fig. 18) of which allow encapsulation of rather big complementary substrates present in solution, for example, guanidinium cations. This is especially important, as guanidine, acting as a ligand^{85,86}

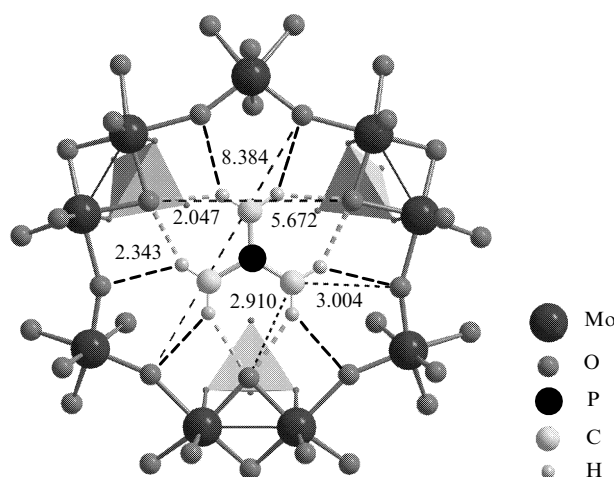


Figure 20. Interatomic distances in the $\{\text{Mo}_9\text{O}_9\}$ metal rings reflecting the interaction between receptors and substrates.⁸⁴

or a receptor of anions⁸⁷ and functioning as a sterically flexible molecule, plays a noticeable role in coordination chemistry, supramolecular chemistry and solid state chemistry and is often used in the chemical design for the formation of cross-linked structures.⁸⁸ For example, the $\{[(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6]_{12}\{\text{Mo}_2^{\text{V}}\text{O}_4 \cdot (\text{H}_2\text{PO}_2)\}_{30}\}^{42-}$ (**14a**) cluster reacts with guanidinium sulfate to give the compound $\{[(\text{NH}_2)_3\text{C}^+]_{20} \subset \{(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6\}_{12} \cdot \{\text{Mo}_2\text{O}_4(\text{SO}_4)\}_{10}\{\text{Mo}_2\text{O}_4(\text{H}_2\text{PO}_2)\}_{20}\}^{32-}$ (**24a**) as a crystalline salt (Fig. 19).

In the structure $\{[(\text{NH}_2)_3\text{C}^+]_{32} \subset \{[(\text{NH}_2)_3\text{C}^+]_{20} \subset \{(\text{Mo})\text{Mo}_5\text{O}_{21}(\text{H}_2\text{O})_6\}_{12}\{\text{Mo}_2\text{O}_4(\text{SO}_4)\}_{10}\{\text{Mo}_2\text{O}_4(\text{H}_2\text{PO}_2)\}_{20}\}^{32-} \cdot 200\text{H}_2\text{O}\}$ (**24**), the guanidinium cations fit exactly into the pores, *i.e.*, the $\{\text{Mo}_9\text{O}_9\}$ rings, owing to their size and symmetry, and are bound by hydrogen bonds formed between the bridging oxygen atoms of the binuclear $\{\text{Mo}_2^{\text{V}}\}$ groups of the metal rings and the NH_2 groups of the cations. The same type of binding of guanidinium cations has been observed for monotopic receptors⁸⁹ (Fig. 20).

It should be emphasised that in this case, highly important is the possibility of ‘plugging’ 20 pores of the giant spherical cluster where the pore sizes are large enough for relatively small substrates to enter the central cavity. This provides the possibility of complete removal of these substrates from a solution — which would be a phenomenon comparable with substrate recognition by nanosponges.⁸⁹ The plugging of pores substantially decreases the negative charge of the cluster, stabilises the cluster and affects the structure of the unique water cluster $\{\text{H}_2\text{O}\}_n$ (see Ref. 90), which is disordered in the case of polyoxometallate clusters with open pores.⁹¹ This process can formally be compared with the process in which a cell converts the extracellular response.⁹² In the absence of encapsulated cations, the structure of the water cluster is determined by interactions with water of crystallisation through open pores.⁸⁴ In the case of anion **24a**, the central cavity contains only highly symmetrical $\{\text{H}_2\text{O}\}_n$ polyhedra — clusters with endohedral hierarchy — an $\{\text{H}_2\text{O}\}_{20}$ dodecahedron is embedded into an $\{\text{H}_2\text{O}\}_{60}$ rhomboicosidodecahedron, which is in turn embedded into another $\{\text{H}_2\text{O}\}_{60}$ rhomboicosidodecahedron.

Thus, various spherical clusters of the keplerate type possess a large number of receptor centres and can act as receptors for both cations and neutral substrates. The variation of linkers (*i.e.*, mono- and binuclear metal centres) makes it possible to change the pore size in metal rings and, hence, such clusters can act as effective and specific nanosponges with respect to complementary substrates. In addition, the reactivity of such nanosponges should differ from the reactivity of monotopic receptors and should change with a change in the electronic properties of the cluster shell.⁹³ This can be compared with the situation where the substrates have been applied onto ‘classical’ surfaces, for example,

onto industrial metal oxide catalysts,⁹⁴ and the reactivity of these substrates can also change upon the variation of the surface properties.⁹⁵

* * *

The data presented in this review demonstrate the scope and prospects of the inorganic synthesis of compounds of a new type — large polyoxometallate clusters of various structures. These objects, the properties of which are being currently studied, are of interest not only from the standpoint of fundamental chemistry but, apparently, can also find application in processes of chemical industry as catalysts and bioactive substances. However, the most important point is that in relation to these compounds, one can follow the development of a new field of chemistry — the chemistry of molecular materials, which are materials of the future.

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Low-temperature reactions in the chemistry of nanosystems

T I Shabatina, G B Sergeev

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Abstract. The results of recent investigations on the reactions proceeding at low and ultra-low temperatures are considered. Trends in development of new avenues of cryochemical research, related to reactions of metal atoms, clusters and nanoparticles and to processes occurring in quantum nanocrystals and superfluid helium nanodroplets are analysed. Specific features of the formation of films and metal-containing nanosystems at low temperatures are discussed. The bibliography includes 265 references.

I. Introduction

Most chemical compounds at low (10–100 K) and ultralow (0.2–10 K) temperatures are in the solid state. Under such conditions, the diffusional mobility is restricted. According to the Arrhenius equation, the rates of chemical processes decrease as temperature decreases, so the reactions become nearly ‘frozen’ at temperatures close to 100 K. These general considerations underlie the development of efficient methods for cryoconservation of various chemical, food and biological products. Nevertheless, the midtwentieth century was marked by the discovery of unusual fast (nearly explosive) reactions proceeding at low and ultralow temperatures. These are reactions of free radicals, halogens and halocarbons with unsaturated compounds, polymerisation of reactive monomers and some other processes.^{1–4}

Advances made in cryochemistry during the last decade include the development of methods for generation and stabilisation of metal atoms and small clusters, metastable complexes and nanoparticles, the number of metal atoms in which varies from several to hundreds and thousands.^{5–8} These high-energy and highly reactive species can participate in various low-temperature chemical reactions resulting in novel hybrid materials possessing unusual optical and electronic properties and in highly active sensor and catalytic systems. Cryocondensates with encapsulated

metal nanoparticles can be considered as novel chemical energy sources and storage systems.

Of particular interest are low-temperature size effects due to dependence of the reactivity of metal clusters and nanoparticles on the number of constituent atoms. Indeed, such systems provide examples of development of a new research avenue, *viz.*, cryonanochemistry. The dependences of diffusion parameters, mechanical stabilities and reactivities of samples of organic and organometallic condensates and co-condensates on the thickness of the growing films can also be considered as the effects specific to cryochemistry. Thus, in cryochemical studies it is possible to draw a line between the microscopic and macroscopic properties of systems comprising atoms, clusters and nanoscale particles.

In this review we analyse experimental data on unusual low-temperature reactions and new phenomena accompanying these processes. We present some examples of chemical reactions in supersonic jets, quantum crystals and liquid helium droplets and on the surfaces of ice crystallites and cosmic dust particles in the interstellar medium. Considerable attention is given to self-assembly of inorganic clusters and nanoparticles in structured polymer matrices and ordered mesogenic systems, resulting in the formation of anisotropic metal–polymer and metal–mesogenic nanosystems. We also illustrate the possibility of targeted preparation of nanostructured materials with prescribed properties.

II. General peculiarities of low-temperature chemical reactions

Radicals, molecules and metal atoms and clusters are usually stabilised using different variants of the low-temperature matrix isolation technique and preparative cryochemistry, which are also employed to study chemical reactions of these species. Usually, low-temperature chemical reactions proceed under conditions of layer-by-layer or co-condensation of reactant vapours or an inert matrix on continuously cooling surfaces of various cryostats *in vacuo*. It should be noted that reactions at the gas–solid, gas–liquid and solid–solid interfaces are also possible. Often, carrying out a chemical reaction between two substances in a co-condensate film requires preliminary formation of labile complexes of the reactants to provide an optimum orientation of the species in the course of mutual diffusion. Evolution of the surface structure and energetics of chemical reactions are studied by structural methods, microscopy, thin-film calorimetry and spectroscopy.

T I Shabatina, G B Sergeev Department of Chemistry, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax (7-095) 939 02 83. Tel. (7-095) 939 54 42.
E-mail: tsh@kinet.chem.msu.ru (T I Shabatina),
gbs@kinet.chem.msu.ru (G B Sergeev)

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1. Sample preparation on cold surfaces: specific features

Sample preparation techniques are critical to cryochemical research. Currently, two methods are most widely used. The first of them, the matrix isolation method, involves co-condensation of the compound under study with a large excess (from a hundred to a thousand times) of inert component (usually, an inert gas or hydrocarbon).^{9, 10}

This technique allowed the discovery and investigation of a new class of compounds, *viz.*, metastable complexes of photochemically generated Rg_n-HX and $H-Rg-X$ ($Rg = He, Xe, Ar$; X is electron-acceptor group, *e.g.*, OH, SH or F, Cl, I) molecules. These species are stabilised in low-temperature matrices of inert gases.^{11, 12} Quantum-chemical calculations of their electronic structures were reported.^{13, 14} Chaban *et al.*¹⁴ studied xenon insertion into some organic molecules (*e.g.*, $HXeC_2H$, $HXeC_6H_5$, $HXeOC_6H_5$) and predicted the existence of stable inclusion compounds and linear oligomers $H(XeC_2)_nXeH$ ($n \geq 1$). The matrix isolation technique has been successfully used for stabilisation and spectroscopic studies of radical and molecular intermediates in pyrolysis and photolysis reactions.¹⁵ It permits identification of labile complexes, various isomers and conformers and investigations of their interconversions.¹⁶ A method for stabilisation and spectroscopic investigation of radicals and short-lived intermediates on an activated silica gel surface has been proposed.^{17, 18}

The second approach is based on co-condensation of reactant vapours on cooled surfaces at rates that exclude collisions between the reactant molecules in the gas phase (molecular beam condensation).¹⁹ Possible modifications of this technique include, *e.g.*, condensation of particles of the same type; layer-by-layer condensation of particles of different types; co-condensation of particles of different types; co-condensation of reactive species with a large excess of inert component; co-condensation of reactive species with a third component (an activator or initiator). In all cases the system can be additionally activated by irradiating samples,^{20, 21} exposing them to high-frequency, ultrasonic and heat fields^{22, 23} and by mechanochemically treating them.^{24, 25} For instance, reactions of photogenerated mobile fluorine atoms with the O_3 , NH_3 , C_2H_4 and HCN molecules in argon matrices at 10–40 K have been studied in detail by EPR, IR and optical spectroscopies.²⁶

A general scheme of physicochemical processes occurring during condensation of atoms and molecules on cooling surfaces is presented in Fig. 1. Condensation-driven growth of a film sample can be accompanied by accommodation effects, surface diffusion, tunnelling interaction, clustering and nucleation. These processes are determined by such parameters as the condensation rate (particle flux through a unit of surface area per unit time) and the surface temperature. Raising the temperature causes diffusion of small particles, which were produced and stabilised in the first stage, in the matrix followed by formation of larger particles and clusters. Clearly, processes occurring (i) in the course of inter-

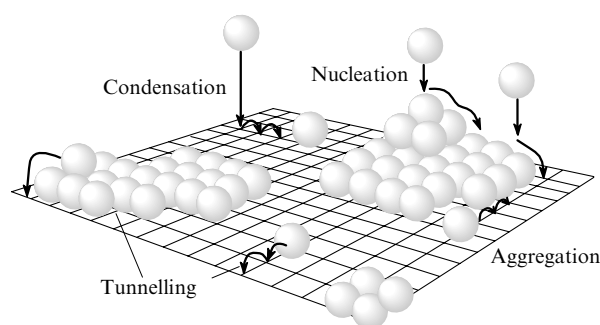


Figure 1. A scheme of physicochemical processes occurring during condensation of atoms and molecules on a cold surface.

action between atom and molecular beams and the surface and (ii) on subsequent heating of the samples are of crucial importance. They determine specific features of low-temperature chemical reactions and control the morphology of newly formed surface nanostructures.

The most stubborn problem is to predict and describe those properties of low-temperature film co-condensates that are due to their inhomogeneity and nonequilibrium nature. There are two important consequences. First, reactive species in low-temperature co-condensates are kinetically and thermodynamically non-equivalent. Second, particles stabilised at low temperatures possess an excess energy (as compared to the mean energy of particles at a given temperature) and, as a rule, high reactivity upon addition of a third reactive component. Therefore, low-temperature co-condensates can be considered as chemical energy storage systems. The excess energy stored in the growing film of a low-temperature co-condensate can be estimated taking into account the following data: the excess energies of metastable crystalline and amorphous phases range from 5 to 20 kJ mol⁻¹, the energies of donor–acceptor interactions and complexation lie between 10 and 40 kJ mol⁻¹, the enthalpies of exothermic chemical reactions are 100 to 200 kJ mol⁻¹, the excess energies of stabilised reactive species (atoms and small clusters) or the recombination energies of radicals vary from 100 to 400 kJ mol⁻¹ and the energy of mechanical stress is nearly 10 kJ mol⁻¹ (see Ref. 7).

2. Size effects

The size effects manifest themselves as dependences of the physical and chemical properties of particles under study on the number of constituent atoms. Usually, they are divided into two main groups. These are internal size effects associated with nonmonotonic change in the bulk-to-surface atom ratio and external size effects due to the interaction of particles of different sizes and shapes with external electric and magnetic fields. The former group of effects is due to changes in the structural and electronic characteristics of particles including their reactivity, binding energy, ionisation potential, melting point, crystal structure parameters, *etc.*^{27–36} External size effects manifest themselves as co-operative electron or lattice excitations, which in the case of, *e.g.*, metal nanoparticles are responsible for the appearance of electron–plasmon resonance bands in the optical spectra.^{37–39}

Two types of size effect can be distinguished in cryochemistry. One of them is the effect of the size of the reacting species (number of structural units, *i.e.*, atoms or molecules) on the mechanism and kinetics of their chemical transformations.⁴⁰ The other effect is the influence of the thickness of the growing low-temperature co-condensate film on its reactivity.^{41, 42} In both cases small variations of the size parameters cause changes in the chemical properties of the system. Studies of interrelations between the reactivity and size of the reacting species (thickness of condensate films) are a topical avenue of cryochemical research.

High reactivity of metal nanoparticles is due to the presence of uncompensated chemical bonds of the surface atoms. According to calculations, almost all of the 10 to 15 atoms constituting a 1-nm particle can be considered as the surface atoms, while 10-nm particles ($\sim 10^4$ – 10^6 atoms) have only 15% of the atoms on the surface. The size effect is illustrated in Fig. 2 in which we present data on the reactivities of niobium clusters of different sizes, prepared using supersonic jet and mass selection techniques, in reactions with alkyl bromides.⁴³

The particle size can be considered as a thermodynamic property determining the state and reactivity of the system at low temperatures. In Fig. 3, the relative reactivities of metal particles are schematically shown as functions of their sizes. According to this scheme, the reactivity reduces as follows: free atoms > oligomeric clusters > nanoparticles > aggregates > bulk metal. Thus, metal atoms and small clusters are the most reactive species. Usually, their properties are investigated using the matrix isolation technique at liquid helium temperatures. An

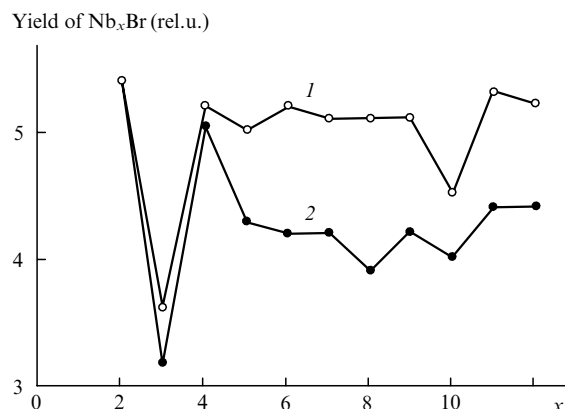


Figure 2. Cluster-size dependences of reactivities of niobium clusters Nb_x in reactions with EtBr (1) and Pr^iBr (2);⁴³ x is the number of atoms in the cluster.

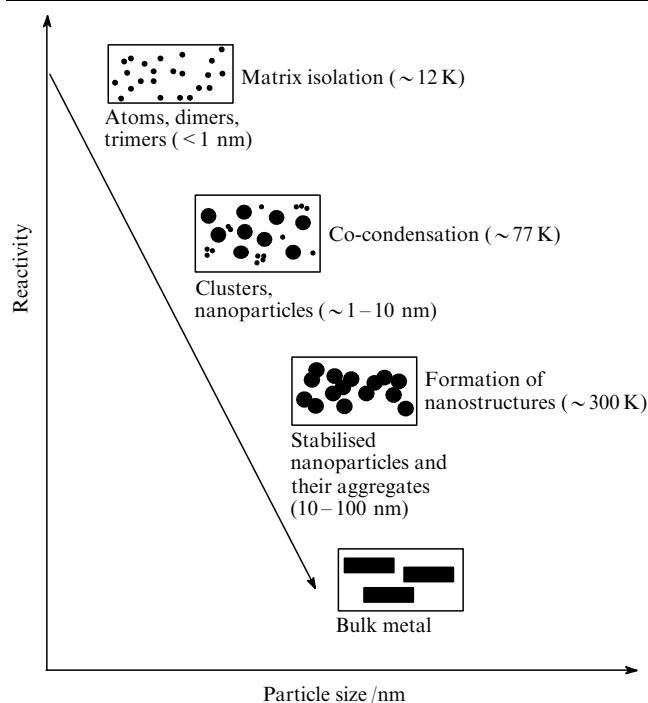


Figure 3. A scheme illustrating changes in the relative reactivities of metal particles as functions of their sizes and temperature of the reaction system.

increase in the particle size reduces the reactivity. It should be noted that this dependence is nonmonotonic because more stable particles, *e.g.*, the so-called magic clusters, are periodically formed. The reactivity is reduced to the greatest extent upon aggregation of small clusters, *i.e.*, as the properties of the aggregates become more and more similar to those of bulk material.

The particle size and reactivity can be preset using some experimentally controllable parameters, *e.g.*, the substrate temperature, metal-to-ligand (inert component) ratio, reactant condensation rate, heat treatment regime of samples and the presence of activators or stabilisers. As the condensation temperature decreases and the proportion of the inert component increases, diffusion-controlled processes in the system become less intense. Using this correlation, it is possible to stabilise high-energy and

highly reactive particles in low-temperature matrices. The ratio of the reactant condensation rates usually has a strong effect on the size of the particles formed at a given temperature. As the metal-to-ligand ratio and temperature increase, the proportion of metal clusters and aggregated particles increases. The reactant condensation rates affect the properties of the growing condensate film in a complex manner. When highly reactive particles (atoms, dimers, trimers) are deposited on a cold surface, their lifetimes are inversely proportional to the condensation rate, being also dependent on the nature of relaxation processes in the system. The collision numbers of the reactant molecules with the surface and with one another are functions of the flux intensity of the particles being deposited. The above-mentioned factors and the chemical nature of the reactants govern the pathways and kinetics of low-temperature chemical reactions.

3. Defects and mechanical stress in the growing surface films

Various defects and mechanical stress produced during the growth of condensate films affect low-temperature chemical processes.^{40,41} Analysis of elastic deformations responsible for initiation of chemical reactions in a film sample⁴⁰ showed that the formation of a co-condensate film begins with growth of islands. The growing islands can merge together, thus forming close-packed columnar aggregates. Interfacial interactions produce mechanical stress. As the growing film thickens, the columnar aggregates increase in size. After reaching a critical film thickness, cracking occurs, being accompanied by structural phase transitions that initiate fast chemical reactions and crystallisation. The initial amorphous system has an excess free energy. An increase in internal mechanical stress during condensation of reactants causes deformation and cracking of the film upon reaching a critical film thickness. Plastic deformations are responsible for enhancement of molecular mobility in the system and subsequent acceleration of chemical processes. Elastic deformations and cracks 'initiate' fast crystallisation of amorphous films.

Development of elastic deformation and occurrence of chemical reactions are interconnected by a feedback. This is a possible reason for autowave chemical transformations in the system during the growth of co-condensate film. The system's behaviour is determined by the particle size, the extent of deviation from the equilibrium state and by the rates of relaxation processes. This approach provides a qualitative explanation for the dependence of the reactivity of the film co-condensate on the growth conditions. Raising the temperature causes enhancement of the molecular mobility, thus favouring the growth of the existing nuclei rather than nucleation. The process is accompanied by relaxation of internal stress due to a decrease in the interface area. This causes weakening of mechanical stress and thickening of the sample.

Mechanical stress and critical thickness of a growing film were measured in a study of condensation of a water film using a low-temperature tensometer and calorimeter.⁴² The results obtained confirmed the existence of an interrelation between spontaneous crystallisation of the film and chemical transformations in the sample. Thus, low-temperature co-condensation is accompanied by generation and storage of the mechanical energy, development of elastic and plastic deformations in the sample, enhancement of the molecular mobility in the system and by cracking. These processes can initiate chemical reactions in the system.

Release of excess energy stored in the mechanically non-equilibrium matrix component of a frozen bulk sample *via* brittle fracture of the sample has been studied.⁴⁴ Initiation of autowave chemical transformations in irradiated, cryochemically stabilised samples subjected to local fracture was observed during chlorination of saturated hydrocarbons, hydrobromination of olefins and polymerisation of 2-methylbuta-1,3-diene. γ -Radiation energy storage in the course of low-temperature radiolysis of solid HCN results in accumulation of stabilised radicals in the matrix.⁴⁵

III. Reactions of metal atoms and small clusters in low-temperature matrices

Metal atoms and small clusters are highly reactive species. Because of this, investigations on their spectral and chemical properties require the use of special equipment and the matrix isolation technique. In particular, the Al_3 , Cu_3 , Ag_3 , Ga_3 and Au_2Ag clusters were studied by EPR spectroscopy⁴⁶ using isolation in matrices of inert gases and hydrocarbons. Dimers and higher clusters of various metals (Na_n , Ag_n , Au_n , Cr_n , Mn_n , Sc_n , Y_n , Ln_n ; $n = 2-9$) were investigated by UV and photoelectron spectroscopies, a fluorescence technique and using quantum-chemical calculations.⁴⁷⁻⁵¹ Currently, matrix isolation of mass-selected clusters is employed to obtain and perform spectroscopic studies of clusters and fragment ions of prescribed size.⁵²⁻⁵⁶ The matrix isolation method allowed one to synthesise, stabilise and spectroscopically investigate a large number of coordinatively saturated and unsaturated metal complexes with N_2 , O_2 , CO , CO_2 , C_2H_4 and C_2H_2 .⁵⁷⁻⁶¹

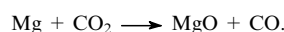
Both UV and electron (ion) beam initiated elementary reactions in low-temperature matrices are accompanied by electronic and structural relaxation of the cryomatrixes containing various 'host' atoms, molecules and ions.^{62,63} Interactions between reactive species including recombination of atoms, radicals and ions are often accompanied by luminescence and exoelectron emission.⁶⁴ Using data on thermally and photo-assisted exoelectron emission and luminescence, one can obtain information on the mobility mechanisms of neutral and charged reactive species and on the electronic relaxation in metastable matrices containing various additives.^{65,66} The mechanisms of diffusion and electron transport in atomic and molecular cryomatrixes (N_2 , CH_4 , CD_4 , Ar and Kr) have been discussed.⁶⁷⁻⁶⁹

As mentioned above, unusual chemical reactions occurring at low temperatures cannot be performed under normal conditions. A general problem of cryochemistry is the impossibility of predicting the chemical behaviour of low-temperature systems containing metal atoms, clusters and nanoparticles based on the properties of bulk samples. Detailed investigations on the conditions for and mechanisms of low-temperature reactions involving metal atoms and clusters have been reported.⁵⁻⁸ When studying reactions of atoms and small clusters, a third reactive component is often introduced in the low-temperature matrix doped with the metal atoms or clusters to provide an additional thermal or photochemical activation of the system. The most impressive examples of such studies are given below.

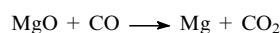
Reactions of the first-row transition metals with CO_2 and its isoelectronic analogues (CS_2 and OCS) in argon matrices were studied by UV and Fourier IR spectroscopies and by density functional quantum-chemical calculations.⁷⁰⁻⁷⁴ These reactions are of interest from the standpoint of activation of the CO_2 molecule to involve it in low-temperature catalytic transformations. The results obtained show that these transition metals (Fe, Co, Ni and Cu) form 1:1 complexes with CO_2 , whereas atoms of the early elements (Sc, Ti, V, Cr) insert into C–O bonds to give oxocarbonyls. Two isomeric Ni– CO_2 complexes differing in stability were found in the carbon dioxide matrix at 10 K.⁷² The yields of the complexes dramatically decrease upon dilution of the system with argon. When using a nitrogen matrix, complexation enhances, resulting in more stable complexes $\text{Ni}(\text{CO}_2)(\text{N}_2)$ and $\text{Ni}(\text{CO}_2)(\text{N}_2)_2$. A co-operative effect of two ligands was pointed out. Namely, coordination of the nitrogen molecule causes hybridisation of the 4s and 3d orbitals of the nickel atom, which increases the degree of Ni → CO_2 charge transfer in the structure of the biligand complex compared to the monoligand complex $\text{Ni}(\text{CO}_2)$. An analogous effect was observed in a study of the reaction of copper vapours with dinitrogen.⁷⁴ Co-condensation of copper with dinitrogen taken in excess results in $\text{Cu}_2(\text{N}_2)$ and $\text{Cu}_2(\text{N}_2)_2$ complexes with ease. Dilution of the system with argon causes a dramatic decrease in the yields of the complexes, while

introduction of CO enhances complexation and favours the formation of mixed biligand complexes.

Reactions of magnesium atoms and clusters with CO_2 and ethylene were studied in argon matrix at 10–80 K (the metal species were stabilised) and in low-temperature co-condensates at 77–100 K by IR and UV spectroscopies and by chromatography.⁷⁵⁻⁷⁷ Both the experimental data and the results of quantum-chemical calculations of the reaction system indicate formation of four- and five-membered cyclic complexes in the first stage.⁷⁸ *Ab initio* MP2/6-31G(d) and QCISD/6-31G(d) calculations⁷⁹ showed that conversion of CO_2 into CO occurs much more easily in the presence of Mg atoms:



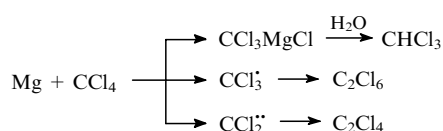
The reaction is spin allowed and the potential barrier to the $\text{CO}_2 \rightarrow \text{CO}$ conversion becomes nearly halved; however, the reaction is still highly endothermic. The reverse reaction



is an exothermic process with a potential barrier of 2.8 kcal mol⁻¹.

Reactions of samarium atoms and clusters with ethylene in the temperature range 12–30 K result in π -complexes $\text{Sm}(\text{C}_2\text{H}_4)$ and $\text{Sm}(\text{C}_2\text{H}_4)_2$.^{80,81} An unexpected effect was observed in studies of reactions of metals (Mg and Sm) with a mixture of C_2H_4 and CO_2 . Under identical conditions samarium reacts only with CO_2 , whereas magnesium forms complexes with both ligands.⁸⁰ The results obtained demonstrate different reactivity of metal atoms and clusters.

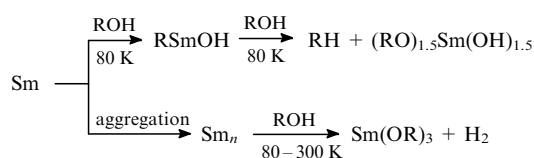
Unusual behaviour of magnesium atoms and clusters in reactions with halocarbons has been reported.⁸²⁻⁸⁵ In particular, carbon tetrachloride does not react with bulk magnesium at ambient temperatures. The situation changes in the case of co-condensation of magnesium vapour and CCl_4 at 77–80 K. Magnesium atoms and clusters efficiently react with CCl_4 to give a variety of intermediates and stable products.⁷⁵



The spectra of $\text{Mg}/\text{CCl}_4/\text{Ar}$ ($\text{Mg}:\text{Ar} = 1:1000$) co-condensates at 12 K first of all exhibited a decrease in the intensity of absorption of small magnesium clusters followed by consumption of magnesium atoms (Fig. 4).⁸³ The results of IR spectroscopic study showed that the major reaction products are C_2Cl_6 and C_2Cl_4 .

Magnesium atoms and clusters possess different reactivities in reactions with alkyl(aryl) halides (RX , $\text{X} = \text{F}$, Cl , Br , I).⁸⁴ Magnesium atoms initiate radical recombination and disproportionation reactions with the formation of various products. Reactions in Mg/RX co-condensates ($\text{Mg}:\text{RX} = 1:1$ to $1:100$) resulted in aggregation of magnesium atoms and preferred formation of CCl_3MgCl (a Grignard reagent). Magnesium and calcium clusters were shown to be more reactive species than the corresponding atoms.⁸⁶ The relative reactivity of metal particles in reactions with alkyl halides reduces as follows: $\text{Ca}_2 > \text{Mg}_4 > \text{Mg}_3 > \text{Mg}_2 > \text{Ca} > \text{Mg}$. The reactivity of methyl halides reduces in the order $\text{CH}_3\text{I} > \text{CH}_3\text{F} > \text{CH}_3\text{Br} > \text{CH}_3\text{Cl}$.

Co-condensation of sodium, magnesium and samarium vapours with alcohols causes a competition between two processes, e.g.,⁷⁵



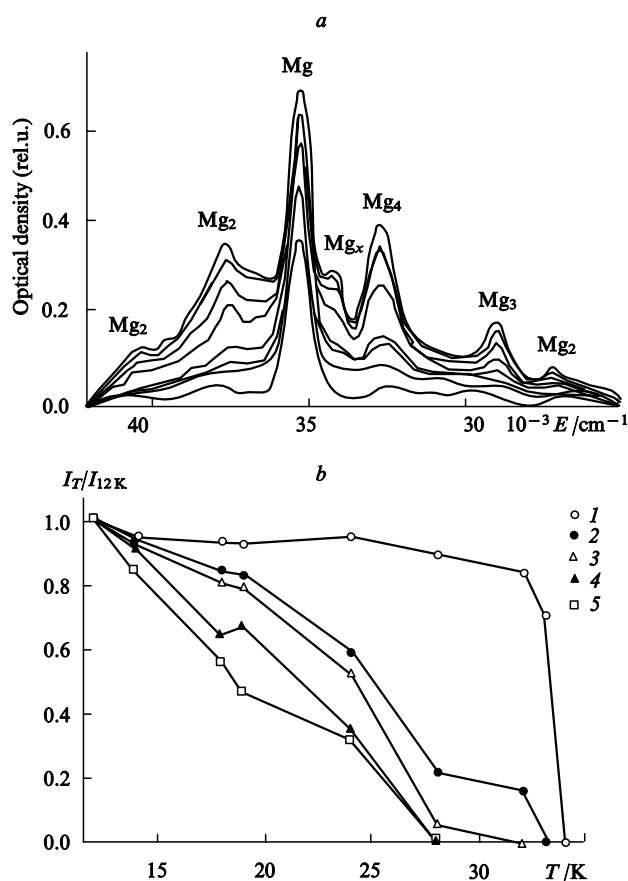


Figure 4. Absorption spectra of 1:100:1000 Mg/CCl₄/Ar co-condensate (temperature increases from the top down in the range 12 to 34 K) (a) and temperature dependence of the normalised integrated intensity of absorption of magnesium atoms and clusters in this co-condensate (b).⁸³ Mg (1), Mg₄ (2), Mg₃ (3), Mg₃ (4) and Mg₂ (5).

At 77 K, metal atoms stabilised at low metal concentrations (metal:ligand $\approx$ 1:500) reduce alcohols to hydrocarbons. Metal clusters formed in co-condensates at metal-to-ligand ratios of about 1:5 form alcoholates.⁸⁷

The dependence of the reactivity of metal particles on the co-condensation conditions was confirmed by the results of studies on the synthesis and catalytic properties of samarium–hydrocarbon co-condensates⁸⁸ with hexane, cyclohexane, hex-1-ene and cyclohexene chosen as the model compounds. Comparison of the catalytic systems obtained by low-temperature co-condensation of (i) samarium and hexane and (ii) samarium and cyclohexene revealed higher activity of the former system in the hydrogenation of hex-1-ene. Similar results were obtained in studies of cyclohexene hydrogenation using a catalytic system prepared by low-temperature co-condensation of samarium and cyclohexane. Thus, there is a ‘matrix memory’ effect, *i.e.*, the system prepared by low-temperature co-condensation governs the reactivity and selectivity of subsequent catalytic transformations. It is possible to draw an analogy to enzymatic reactions, where the enzyme–substrate interactions are accompanied by rearrangement of the active site to match the substrate structure.

A systematic study of co-condensates of some transition metals with CH₄/Ar mixtures at 10 K was carried out by Klambunde *et al.*⁸⁹ Oxidative insertion of electronically excited metal atoms into C–H bonds has been reported.⁹⁰ The reactions of laser ablated iron atoms with methane and ethylene were studied by Mössbauer and IR spectroscopies in doped argon matrices at 17 K; quantum-chemical calculations of newly formed species and stable products were also performed.^{89,90} The excited iron atoms are inserted into the C–H bond of methane to give

CH₃FeH.⁹¹ The first reaction stage involves decomposition of methane molecule to give a methyl radical CH₃ and a hydrogen atom. The reaction in a methane matrix results in products of the interaction between primary radicals CH₃ and H atoms with one another (C₂H₆, C₂H₄, C₂H₂) and with iron atoms, *viz.*, compounds CH₃FeH and Fe₂H₂(CH₃)₄ with Fe–H–Fe bridging bonds. Reactions of iron atoms with dilute ethylene in argon matrix give a Fe(C₂H₄) complex. As the concentration of ethylene increases, complex Fe(C₂H₄)₂ becomes the major product. A study by Mössbauer spectroscopy revealed the formation of monomeric and dimeric halides FeF₃ and Fe₂F₆ and FeI₂ and Fe₂I₄ in the reactions of iron with halogen donors SF₆ and CH₃I.^{92,93}

Co-condensation of transition metal atoms with aromatic hydrocarbons at 77–80 K often results in bisarene complexes of (formally) zero-valent metals.⁹⁴ For instance, co-condensation of lanthanide atoms and 1,3,5-tris-*tert*-butylbenzene produces thermally stable ‘sandwich’ complexes of Nd, Tb, Dy, Ho, Er and Lu, as well as thermally unstable complexes of La, Pr, Sm, Eu, Tm and Yb.⁹⁴ Metal complexes with phosphorus and nitrogen derivatives of aromatic hydrocarbons have been synthesised.⁹⁴ Reactions of titanium and vanadium vapours with 1,4-di-*tert*-butylbuta-1,3-diene resulted in novel compounds of general formula [M(η^2 -Bu₂C₄H₂)₂] (M = Ti, V).⁹⁵ The complexes obtained can be modified by introducing various ligands, *e.g.*, phosphines, diazadienes and isonitriles, which replace the diene ligand, thus forming novel ‘half-sandwich’ complexes.

Low-temperature co-condensates of lanthanides (Sm, Eu) with mesogenic ligands 4-pentyl-4'-cyanobiphenyl (5CB) and 4-octyl-4'-cyanobiphenyl (8CB) were studied by IR and UV spectroscopies in the temperature range 90–300 K. Formation of two labile complexes with 1:2 and 1:1 metal-to-ligand ratios was established.^{96,97} Complex Sm(CB)₂ undergoes a solid-phase transformation into Sm₂(CB)₂ (CB is 4-alkyl-4'-cyanobiphenyl) in the temperature range 170–210 K. The process exhibits a polychronous kinetics,⁹⁷ which can be due to the presence of some solid-phase reactivity distribution of the complexes.⁹⁸ The IR spectra of Sm/5CB co-condensates with various metal-to-ligand ratios were studied at 95–273 K and at 95 K. Two new (compared to the IR spectrum of a neat 5CB film) bands with maxima at 2135 and 2085 cm⁻¹ were observed in the region of stretching vibrations of the CN group. Based on a nearly 100 cm⁻¹ shift towards the low-frequency region, these bands were assigned to the absorption bands of π -complexes. At 90–95 K, the spectrum of co-condensate exhibits a single absorption band at 2135 cm⁻¹. The absorption at 2085 cm⁻¹ increases, while the absorption at 2135 cm⁻¹ decreases on heating of the sample from 95 to 213 K. Thus, here we deal with conversion of one complex into the other. In addition, changes in the band intensity ratio upon variation of the metal-to-ligand ratio suggest the presence of two complexes of different compositions.⁹⁷ The UV and visible spectra of Sm/5CB film co-condensates revealed two new overlapped absorption bands with maxima at 390 and 420 nm.⁹⁷ Absorption in this spectral region is characteristic of charge-transfer complexes of transition metals with molecules of unsaturated organic compounds. The band intensities are also temperature dependent. This trend serves as an additional argument in favour of the existence of two complexes.

Labile 1:1 complexes of difluorostannylene (a hetero-element carbene analogue) with some aromatic molecules (benzene, chlorobenzene and toluene) were obtained and characterised by matrix IR spectroscopy.⁹⁹ Co-condensation of vanadium and chromium vapours with tetraphenylsilane ligands results in stable ‘sandwich’ complexes. Low-temperature co-condensation of vapours was employed to prepare novel di- and trinuclear clusters of molybdenum, rhenium and palladium.¹⁰⁰ Iron complexes containing η^6 -arenes and trichlorosilyl ligands (Fig. 5) were also synthesised by co-condensation of vapours of the corresponding reactants.¹⁰¹

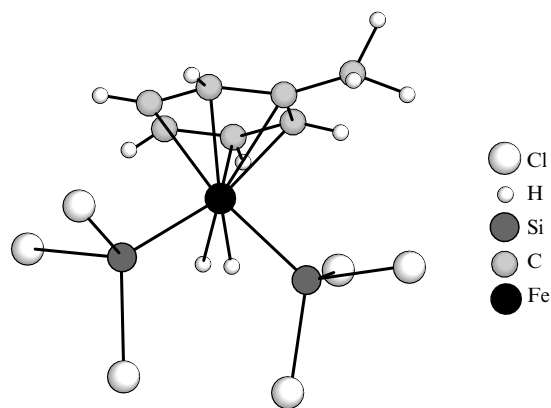


Figure 5. Structure of iron complexes containing η^6 -arenes and trichlorosilyl ligands.¹⁰¹

Reaction products of iron atoms with polycyclic aromatic hydrocarbons (PAH) pyrene and coronene were studied by UV and Fourier IR spectroscopies in argon and nitrogen matrices.¹⁰² The spectra of the co-condensates revealed the presence of mononuclear π -complexes of iron atom with pyrene, $\text{Fe}(\text{C}_{16}\text{H}_{10})_n$ ($n = 1, 2$), which are stable at temperatures of up to 24 K. In the structure of the π -complex, the iron atom is above the centre of one of the two outer aromatic rings. Formation of unstable Fe–H complexes with one or two hydrogen atoms of one aromatic ring of the ligand molecule or with two hydrogen atoms of different rings was also detected. The coronene molecule, which contains a large number of fused aromatic rings, preferentially reacts with iron dimer to give π -complexes $\text{Fe}_2(\text{C}_{24}\text{H}_{12})_n$ ($n = 1, 2$). These species are thermally stable up to the sublimation temperature of the argon matrix (40 K) and exhibit stability to 200–700 nm radiation. Two iron atoms can be arranged above two adjacent aromatic rings of the same ligand molecule or perpendicular to the ring plane, thus bonding two ligand molecules. The latter type of bonding can result in ‘multi-sandwich’ complexes. Relatively stable iron–PAH compounds comprising several iron atoms, small (nanoscale) iron aggregates formed under the action of external factors and thin films on carbon surfaces can be responsible for characteristic 3.3, 7.8, 8.6 and 11.3 μm IR radiation, which is often observed in space.^{103–105}

IV. Reactions in quantum crystals and superfluid helium nanodroplets at ultralow temperatures

The use of quantum crystals (solid ^3He , ^4He , ortho- and para-hydrogen, HD)^{106–109} and nanodroplets of quantum liquids (superfluid liquid helium) as matrices is of particular interest for investigations of chemical reactions at ultralow temperatures.^{110–113}

Here, one deals with weak intermolecular interactions (absence of matrix effects), absence of ‘cage effects’ for photo-induced processes and quantisation of rotational motion of guest molecules. As a consequence, IR spectra exhibit narrow spectral lines with fully resolved rotational structure.^{114–116} The effects observed are of great importance for astrophysics and astrochemistry^{117,118} because the most abundant substances in space are hydrogen, helium and products of their ionisation by cosmic rays (H_2^+ , H_3^+ and He^+).

The use of superfluid helium nanodroplets (He_N , $N \approx 10^2$ – 10^5) as matrices opens up new prospects for investigations of atoms, clusters, metastable molecules and complexes.¹¹⁹ Nanodroplets are prepared by supersonic expansion of helium gas jets under high pressure at low temperatures. Surface evaporation causes cooling of a nanodroplet, so a temperature of 0.2 to 0.4 K is maintained inside it. Atoms and molecules can be included into helium nanodroplets by trapping the dopant in the gas phase

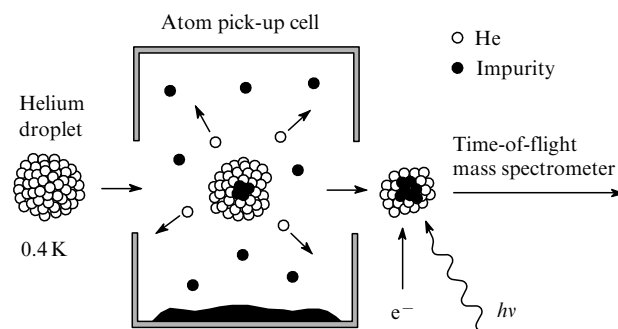


Figure 6. A scheme of formation of helium nanodroplets containing encapsulated impurity atoms (molecules).¹²⁰

(Fig. 6).^{120–123} Molecules, clusters and loosely bound complexes can be synthesised immediately during trapping of dopant atoms (molecules) into helium nanodroplets. Currently, this method is employed to obtain and perform spectral characterisation of alkali metal,^{124,125} magnesium¹²⁰ and silver^{126,127} clusters and rubidium–helium exciplexes.¹²⁸ Alkali metal atoms form loosely bound surface states due to Coulombic repulsion between the helium electrons and the valence electrons of the metal. The van der Waals metal clusters formed on the surface of nanodroplets are in the high-spin state. This phenomenon was studied by femtosecond multiphonon ionisation spectroscopy.¹²¹ The mass distribution of spin-polarised clusters is shown in Fig. 7. Thus, even large clusters ($N > 10$) are completely spin-polarised. The observed alternation of the intensities of the peaks corresponding to clusters of different sizes is due to specific features of the mechanism of laser-induced spin relaxation.

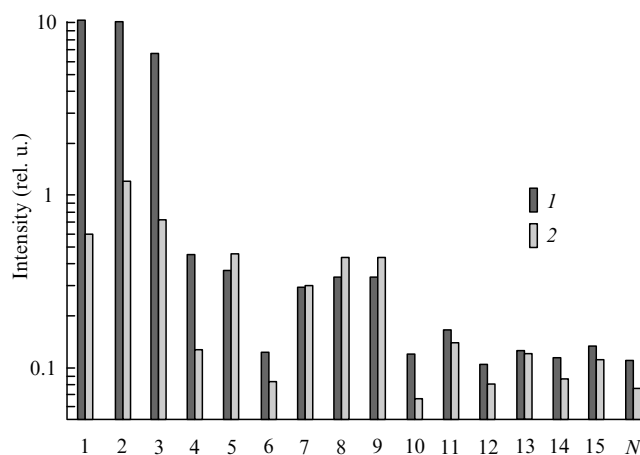


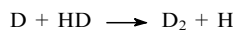
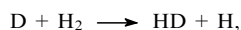
Figure 7. Mass distribution of Na_N clusters (N is the number of atoms in clusters). Laser excitation at 850 (1) and 425 nm (2).¹²¹

The vibronic spectra of mixed clusters M^4He_N and M^3He_N comprising aromatic molecules (M) and helium atoms have been studied at 0.4 K.¹²⁹ Taking these systems as examples, the intramolecular fine vibronic structure of $S_0 \rightarrow S_1$ electronic transitions in the spectra of various molecules was experimentally studied. Peculiar features of formation of atomic and molecular clusters during free gas expansion in vacuum have been considered.¹³⁰

The structures of impurity systems prepared by trapping D_2 , Ne, N_2 and Kr into the bulk of superfluid ^4He were studied by X-ray diffraction and ultrasonically.¹³¹ The van de Waals interactions between the components result in the formation of a nanoscale system similar to aerogel, which comprises clusters of impurity molecules and atoms of size 50 ± 20 Å and density of up

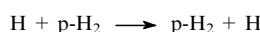
to 10^{20} atom cm^{-3} . The possibility of stabilisation of high concentrations of atoms in such systems makes them promising energy sources. Water nanoclusters surrounded by layers of solid and liquid helium have been reported. They form a specific 'watergel', which acts as a matrix stabiliser and a dispersion medium.^{131, 132}

Unusual tunnelling chemical reactions of light impurity atoms and molecules

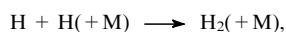


were investigated in solid helium at ~ 1.35 K.^{133, 134} Deuterium atoms efficiently replace hydrogen atoms in the H_2 and HD molecules, thus favouring accumulation of rather high steady-state concentrations of hydrogen atoms (up to 10^{18} cm^{-3}).

An EPR study of tunnelling reactions of hydrogen atoms produced by γ -radiolysis of a mixture of ortho- and parahydrogen at 4.2 K^{135, 136} showed that diffusion of atoms in solid hydrogen occurs by repeating tunnelling reactions



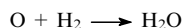
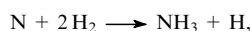
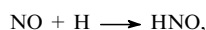
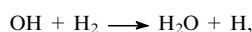
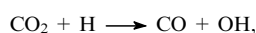
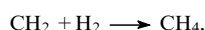
and is completed with a highly exothermic reaction



where M is a third particle acting as an energy drain.

Radiolysis of solid parahydrogen containing small amounts of deuterium impurity at 4.2 K causes formation of electron 'bubbles' that dissociate *via* tunnelling recombination with cations stabilised in the system.¹³⁷ In both cases the efficiency of tunnelling reactions is determined by weak interactions with orthohydrogen impurity and by energy dissipation in the matrix.¹³⁵ The contributions of two main mechanisms (sequential two-body process involving quasi-bound resonant states and tunnelling and a direct three-body recombination involving matrix atoms or molecules) to atom–atom recombination in matrices of inert gases have been analysed.^{138, 139}

Studies on photoinduced reactions of dopant molecules (CH_4 , CO_2 , NO) in solid parahydrogen matrices have been reported.^{140, 141} The absence of cage effects for the primary radicals and efficient reactions of 'hot' photofragments



are due to weak intermolecular interactions with the matrix molecules.

The possibility of using tunnelling reactions of hydrogen atoms for hydrogenation of various organic and inorganic compounds under conditions of cryochemical synthesis has been considered.^{142, 143} Experiments carried out at 10 K showed that cyclic olefins (cyclopentene and cyclohexene) nearly instantaneously (in a few seconds) react with hydrogen atoms to give the corresponding cyclic alkanes.^{142, 143} The reaction of hydrogen atoms with solid CO results in quantitative yields of formaldehyde and methanol.¹⁴⁴ The last-mentioned compound is efficiently formed upon additional UV irradiation of the system. These laboratory studies have first demonstrated the possibility of synthesis of these compounds in interstellar ice as a result of tunnelling reactions of hydrogen atoms with CO molecules. It was also shown that matrix-stabilised C, O and N atoms can be involved in reactions occurring on spraying H atoms over solid samples at 10 K. The reactions result in CH_4 , H_2O and NH_3 . The authors of this study¹⁴⁴ considered the possibility of tunnelling

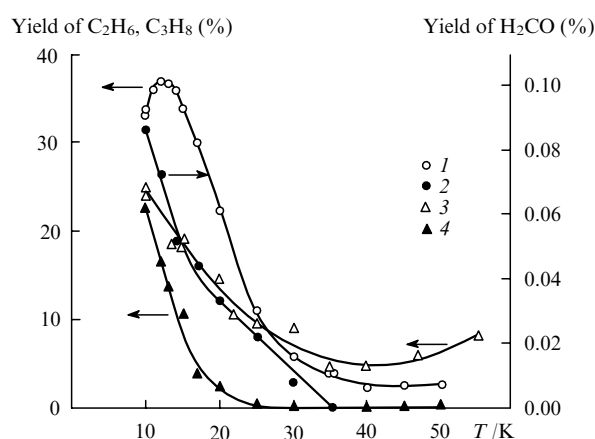


Figure 8. Yields of products of tunnelling reactions of H atoms with C_2H_4 (1), CO (2), C_3H_6 (3) and C_2H_2 (4) as functions of temperature in the range 10–60 K.¹⁴⁴

interaction of H atoms with acetylene, ethylene, propylene and carbon monoxide in the temperature range 10–60 K. In all the cases the reaction rates increase as the temperature decreases from 50 down to 10 K and reach maximum values at 10 K (Fig. 8). Negative temperature dependence of the rate constant for tunnelling reaction of hydrogen atoms with acetylene in highly dilute samples in xenon or carbon dioxide matrices was unambiguously proved. The effect observed was explained by the possibility of increasing the steady-state concentration of hydrogen atoms in the solid film and by an increase in the rate constant for tunnelling reaction on lowering the temperature. Negative temperature dependences of the rate constants for tunnelling reactions were theoretically predicted by Hiraoka and Sato.¹⁴⁴ The influence of various factors (mutual arrangement of atoms, structural rearrangement of reactants and medium, orientational intermolecular vibrations) on the rates of tunnelling reactions and on the temperature dependence of the rate constants for tunnelling reactions involving hydrogen atoms has also been analysed.^{139, 145–149}

V. Reactions in low-temperature film co-condensates

Vacuum co-condensation of reactant vapours on cooled surfaces of spectral and preparative cryostats provides conditions that exclude collisions between the reactant molecules in the gas phase. As a rule, in this case the reaction occurs within a thin surface layer. On heating, chemical reactions proceed in the bulk of the sample due to enhancement of the molecular mobilities of the reactants. In Fig. 9 we present a general scheme of successive and concerted reactions occurring in the course of low-temperature co-condensation of vaporous metals (M) and various organic or inorganic ligands (L). At low temperatures and high dilutions, reactions of metal atoms mainly occur. In more concentrated systems, aggregation is possible, resulting in the formation of clusters, nanoparticles, organometallic compounds and ligand-stabilised mono- and polynuclear complexes of metals and nanoparticles.

Fast spontaneous reactions occurring in the absence of external factors are of greatest interest for cryochemistry of film co-condensates. Such reactions involve consumption of internal energy stored in the film co-condensate; some of them are considered in this review. They proceed by different mechanisms but exhibit an identical kinetics pattern, namely, these are fast (almost explosive) solid-phase low-temperature reactions.

Examples can be found in such reactions as olefin halogenation and hydrohalogenation involving formation of unstable donor–acceptor complexes that prescribe a certain organisation of the reactant molecules, which is necessary to perform the solid-

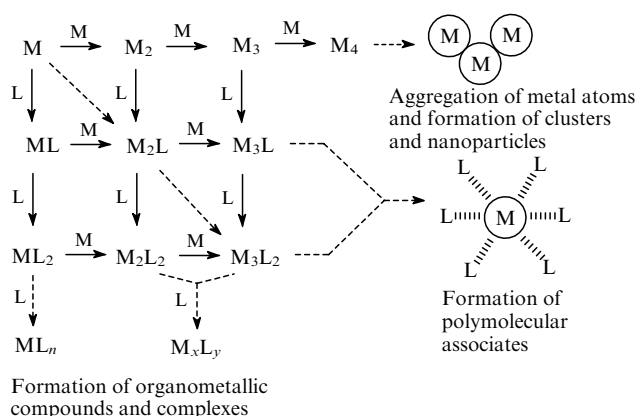
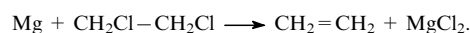


Figure 9. Scheme of successive and concerted reactions proceeding in the course of low-temperature co-condensation of metal (M) and ligand (L) vapours.

phase chemical transformations.^{150, 151} No reactions occur in the absence of complexation. This is confirmed by the results of hydrohalogenation of 2-methylbut-2-ene. The reaction rate depends on the extent of complexation in the system 2-methylbut-2-ene–HCl (HCl : olefin = 6 : 1) at 80 K as follows:

Degree of complexation (%)	100	50	0
Conversion (%)			
on co-condensation	39	22	0
on annealing	25	13	0

An explosive reaction was observed in the growing films of magnesium – 1,2-dichloroethane co-condensate⁴¹



The reaction products were obtained in nearly 100% yields as the film thickness reaches a critical value (L_c). There is a clear-cut distinction between the reacted and unreacted film regions. Explosive reaction can be accompanied by mechanical fracture of the film. The critical thickness depends on the reactant ratio and on the temperature of the sample. The L_c value is minimum at 1 : 1 Mg : CH₂Cl–CH₂Cl ratio. As the temperature of the sample increases, the region of the explosive reaction becomes more narrow. The reaction is accompanied by fast heat release and crystallisation of the initially amorphous co-condensate film. The process acquires a wave character and the internal energy stored in the co-condensate film initiates explosive reaction. A decrease in the reactant condensation rates and an increase in the temperature of the co-condensate improve the efficiency of relaxation processes in the film, thus making explosive processes less probable. Similar effects were also observed in a study on the reactions of acetyl chloride with diethylamine and cyclopentadiene with titanium tetrachloride.¹⁵² Growth of co-condensate film is accompanied by generation and accumulation of internal strain (excess internal energy) in the sample, which initiates a vigorous reaction and fast crystallisation of the co-condensate after reaching a critical value. Explosive polymerisation reactions initiated by magnesium vapours were observed.¹⁵³

The HCN molecule was found in various space objects, namely, giant clouds of interstellar dust, comets and other galactic objects.^{154, 155} It is commonly accepted that the formation of this molecule is a result of one of the main stages of pre-biological chemical evolution, because processes involving HCN can result in amino acids, purines, pyrimidines and other bioactive compounds.¹⁵⁴ Chemical reactions of HCN and its derivatives, *viz.*, cryopolymerisation of HCN and its copolymerisation with acetaldehyde and ethylene oxide as well as polymerisation of cyanogen bromide under conditions similar to those in the interstellar medium (low temperature and initiation by γ -radiation and local brittle fracture) have been studied in detail.^{156–158}

VI. Cryochemical synthesis and reactions involving metal nanoparticles

Metal nanoparticles of size 1 to 10 nm are of crucial interest for cryochemical research, because in this case small variations of the particle size cause significant changes in their physical and chemical properties. Such objects can be considered as surface structures, because most of the constituent atoms are surface or near-surface ones. An increase in the concentration of uncompensated valence bonds enhances the particles' reactivities.

Main methods for preparation of metal clusters and nanoparticles have been well documented.^{159–162} Going to low and ultralow temperatures opens up new prospects for production of small metal particles.

Interesting results were obtained using metal evaporation under static pressure of inert gas in the reaction vessel or the inert gas stream technique. A metal can be evaporated by resistive heating and by exposing it to electron or laser beams. Metal clusters and nanoparticles are deposited on internal walls of a reactor or on various substrates.¹⁶⁰ In particular, copper, silver and gold particles of size nearly 10 nm were produced by gas-phase evaporation followed by trapping the freshly obtained particles in frozen liquids (ethanol, methanol and some alkanes).^{6, 163} Magnesium particles of size 2 nm were obtained by condensation in liquid helium nanodroplets; larger magnesium particles of size ~100 nm were prepared by condensation in solid argon.¹⁹ Laser evaporation has been employed in studies of almost all metals. For instance, low-energy neutral clusters of iron, cobalt, nickel and nanostructured films of thickness up to 100 nm were produced by deposition on various cooled substrates.¹⁹ Laser and electron beam evaporation of metals are convenient for preparation of bimetallic nanoparticles. A mass spectrometric study of particles formed by co-vapourisation of zinc, cadmium, mercury and sodium revealed the possibility of formation of bimetallic particles comprising one heavy atom surrounded by several (up to 18) sodium atoms.¹⁹ Experiments with sources of ionised cluster beams allowed control of the kinetic energy of the clusters deposited by applying an accelerating potential difference.^{164, 165} Gas-phase cluster beams can be size selected and deposited on appropriate substrates. For instance, Pt_n and Pd_n ($n = 1–15$) particles were produced on the (100) surface of Ag single crystals.¹⁶⁶

Novel organometallic clusters and solvated metal nanoparticles are also obtained by condensation of metal vapours.^{5, 19} Usually, vapours of metals and organic components are co-deposited on the surfaces of reaction vessels cooled down to 77–100 K and lower temperatures. At such temperatures, metal atoms and clusters insert into solid organic matrices. During warm-up of the samples the atoms and small clusters aggregate into large metal clusters and particles of size 10–30 nm, which form stable colloidal solutions at room temperature. Further growth of the particles is restricted by solvation and electrostatic effects.

Co-condensation of silver and methyl acrylate vapours on the surface cooled to 77 K followed by heating of the system to room temperature causes partial polymerisation of methyl acrylate and formation of organic colloids comprising silver nanoparticles stabilised by the polymer layer. At room temperature, the optical absorption spectrum of molten co-condensate exhibits a maximum at 400 nm, which is characteristic of spherical silver particles of diameter less than 20 nm.¹⁶⁷ Transmission electron microscopy data indicate formation of silver particles of size less than 15 nm. Co-condensation of silver, lead and methyl acrylate vapours results in colloids of polymer-stabilised bimetallic nanoparticles.¹⁶⁸ The size of lead particles and bimetallic Pb/Ag particles thus obtained is at most 5 nm, which is much smaller than the size of individual silver particles formed under analogous conditions.

Formation of metal nanoparticles during low-temperature co-condensation of silver and 2-(dimethylamino)ethyl methacrylate vapours was studied by optical spectroscopy and dynamic light

scattering.¹⁶⁹ Experimental data as well as the results of electron microscopy investigation of the co-condensates heated up to room temperature indicate initial formation of silver nanoparticles 5 to 12 nm in diameter stabilised in the polymer layer. Low-temperature synthesis of colloidal silver nanoparticles in water, acetone and toluene has also been reported.¹⁷⁰

Co-condensation of two metals allows preparation of bimetallic core-shell particles. For instance, analysis of Fe/Li co-condensates revealed the presence of particles comprising an iron metal core coated with a $\text{Li}_2\text{O}/\text{Li}_2\text{CO}_3/\text{Fe}_2\text{O}_3$ protective layer.¹⁷¹ The same approach was employed for the synthesis of bimetallic core-shell nanoparticles in Fe/Mg co-condensates (Fig. 10).¹⁷² These results have first demonstrated the possibility of using cryochemistry for preparation of bimetallic metastable clusters of metals that are immiscible under normal conditions.

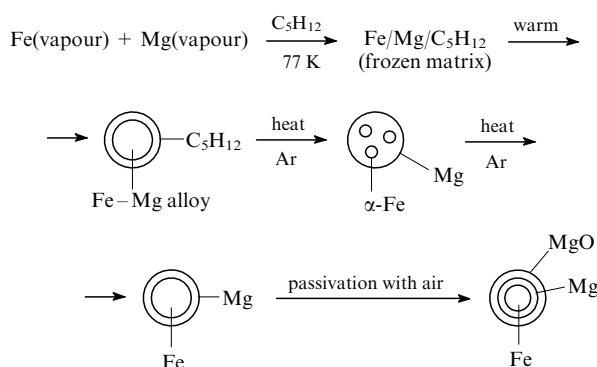


Figure 10. Scheme for preparation of bimetallic core-shell nanoparticles in Fe/Mg co-condensates.¹⁷²

Surface-immobilised metal particles of size 3–8 nm were obtained by impregnating oxide (Al_2O_3 , SiO_2 , MgO) matrices with molten organometallic co-condensate.¹⁷³ Bimetallic particles stabilised on an oxide surface were also prepared by co-condensation of reactant vapours.¹⁷⁴ Colloidal solutions of metal nanoparticles provide an efficient tool for fabrication of nanostructured metallic coatings by solvent evaporation. Such films possess unique properties, *viz.*, a higher resistance compared to metal films produced by other methods and the ability to redissolve in appropriate solvents.

Redox reactions on the surface of gold nanoelectrodes, resulting in deposition of the second metal (Pb, Cd, Tl), have been studied.¹⁷⁵ The reactions are initiated by electron transfer from radiolytically generated organic free radicals to the gold nanoparticles rather than application of an external electric field. Because of the large surface area of nanoparticles the reaction can be monitored with a spectrophotometer. Deposition of the second metal causes changes in the size, chemical nature and redox properties of the gold nanoparticles. The physicochemical behaviour of the bimetallic particles thus produced depends on the electronic properties of the adatom layer and on electron exchange at the interface between two metals with different electron work function.

Bukhtiyarov and Slin'ko reported a comprehensive review on the properties of metal nanoparticles stabilised on solid surfaces.¹⁷⁶ They analysed the reactivities and selectivities of metal particles in relation to particle size and to the atomic and electronic structure of bulk metals. This allowed consideration of the properties of metal clusters and nanoparticles and of the active sites of heterogeneous catalysts in the framework of a unified approach.

Studies on the reactivity of metal nanoparticles over a wide temperature range revealed novel unusual chemical reactions. Namely, silver nanoparticles encapsulated into poly(*p*-xylylene) films possess catalytic activity in the reaction of methanol oxida-

tion into formaldehyde, silver nanoparticles stabilised on an alumina surface catalyse epoxidation of ethylene⁷ while the reaction of zinc nanoparticles with CCl_4 in water causes an increase in the rate of dechlorination and results in methane.¹⁷⁷

VII. Assembly of hybrid nanostructures at low temperatures

Novel technologies widely use nanoscale hybrid materials (organic compound-metal; metal-semiconductor; metal-dielectric) that are stable at room temperature.¹⁷⁸ These materials are characterised by large interface areas and extended boundaries between different structural elements. Interactions of such nanoscale structures with photons and electrons cause manifestation of unusual optical, magnetic and electrophysical properties.^{179, 180} The properties of individual nanoparticles and nanostructured films, methods for their preparation, self-organisation of nanoparticles, growth of oriented nanoscale films and template synthesis of nanoparticles have been reviewed.^{27–33} In the text below we present some examples of preparation of these materials using cryochemical techniques.

1. Low-temperature condensation and surface reactions

Various hybrid nanostructures were fabricated by condensation of atom-molecular beams on cooled dielectric, semiconductor and metal surfaces. For instance, multilayer dinitrogen films adsorbed on a graphite surface were studied at 12–20 K.¹⁸¹ This allowed determination of the tilt angles of the molecular axes with respect to the graphite surface and establishment of two main types of molecular packing within the layer with an increase in the surface coverage from submonolayer to formation of a bilayer structure. Detailed neutron diffraction studies on the growth mode of methyl chloride (CH_3Cl), dichloromethane (CH_2Cl_2) and chloroform (CHCl_3) condensate films on a graphite surface have been reported.^{182, 183}

Monolayers of long-chain saturated hydrocarbons were adsorbed on the Cu(111) surface cooled down to 80–160 K.¹⁸⁴ At low temperatures, octane forms a commensurate crystal lattice and undergoes a first-order phase transition on heating. Nonane forms a domain surface structure with parallel arrangement of molecules and experiences an unusual, strongly broadened phase transition on heating. This is consistent with the known odd-even effect observed in the structures of solid alkanes. Whereas alkanes $\text{C}_n\text{H}_{2n+2}$ with even n values have structures with monoclinic or triclinic unit cells, odd-numbered alkanes have an orthorhombic unit cell. These organic layers adsorbed on metal surfaces can be used in molecular electronics and optoelectronics.^{185–187} Electron transfer in structured layers of hexafluorobenzene and phenylthiol on the Cu(111) surface has been studied.¹⁸⁸ The interaction between organic molecules and the surface layer of the metal crystal affects charge transfer across the interface.

Ultrathin gold films were prepared by low-temperature condensation on a silicon surface at 173–300 K.¹⁸⁹ It was found that the surface of the silicon crystal and the pure metal layer are separated by a layer of amorphous gold silicide 13–28 Å thick.¹⁹⁰ A study of 0.3 nm silver films deposited on the Si(111), Si(100) and Ge(001) surfaces at 100–300 K revealed formation of ordered 2D structures,¹⁹¹ which are assigned to the most promising objects for creation of a novel class of 2D superconductors with $T_c = 2–8$ K.¹⁹¹ As the thickness of the silver layer increases, island 3D structures are mainly formed. Cold-deposited silver thin films exhibited second harmonic generation.¹⁹² Analysis of the results obtained confirmed a homogeneous structure of the deposited 3D silver films of thickness 15–20 nm. Lead films prepared by depositing Pb on the Si(111) surface provide the most convenient system for analysing various effects in the absence of interdiffusion and chemical reactions.¹⁹³ The Schottky barrier to a Pb/Si diode depends on the structure of the near-surface layer at the interface. Using surface X-ray diffraction, it was shown that growth of initially amorphous film is followed by

its crystallisation to well-ordered Pb(111) structures after reaching a critical thickness of 5 atomic Pb layers. Layer-by-layer deposition at 100 K allows suppression of the growth of 3D island structures.

Interfacial bimetallic systems formed by deposition of adatoms of the second metal on the crystal surface of the major metal component are of considerable interest.^{194–196} Catalytic activity of such systems has long been known; however, reliable investigation techniques were developed only in the last decade. Condensation of adatoms on metal surfaces at 100–200 K eliminates all types of mobility, except for surface diffusion during the film growth. Specific features of nucleation and the kinetics of formation of layer-by-layer deposited surface monolayers and island films as well as the growth of bulk 3D phases are first of all determined by close values of the lattice parameters of the two metals, by the ability to form bimetallic compounds and alloys, by strain in the growing film and by the relaxation mechanism of excess elastic energy. The lifetime of the adatom in the excited state and the electron states of the metal surface at low temperatures can be studied by time-resolved two-photon photoemission spectroscopy.¹⁹⁷ It was established that ternary hybrid metal nanostructures Cu/Co/Cu(001), Pd/Co/Pd(001) and Fe/Cu/Fe(001) possess unusual magnetic properties including magnetic anisotropy and tunnelling magnetoresistance. Substances exhibiting these properties can be used as magnetic sensors and magnetic recording systems.¹⁹⁸ Deposition of metal atoms and clusters on an oxide surface is of particular interest because this technique allows preparation of size-selected metal particles and modelling of the efficiency and selectivity of catalysts.^{199,200}

The vapour deposition technique allows controlled condensation of atoms and clusters on various surfaces by thermal or photochemical decomposition of precursor vapours.²⁰¹ Controlled adsorption and decomposition of iron pentacarbonyl, chromium hexacarbonyl and cyclopentadienylrhodium dicarbonyl on the single-crystal surfaces of Ag, Pt, Au and Cu at 80–300 K were studied by reflection absorption IR spectroscopy.^{202,203} Photodissociation of neutral molecules on cold surfaces of various metals was studied; some examples are provided by the CH₃I/Cu(110),²⁰⁴ Bu^tNO₂/Ag(111)²⁰⁵ and NH₃/Pt(111), Ge(100), Si(100) pairs.^{206,207}

Yet another promising method of cryochemical research, which allows preparation of hybrid nanostructures, involves the action of aggressive gases on the surface of metal crystals at low temperatures. Chlorination of different crystallographic planes of silver and copper single crystals has been studied.²⁰⁸ A 2-nm thick metal chloride layer is formed upon exposure of the Ag(111) surface to chlorine gas at 150–250 K. Thin layers of silver and copper chlorides can be used for fabrication of nanocrystalline materials (metal clusters dispersed in the bulk of the chloride phase: Ag_x/AgCl and Cu_x/CuCl). Local oxidation of titanium, aluminium and copper surfaces was performed by exposing them to an oxygen stream accompanied by scanning the corresponding local area with the probe tip of a scanning tunnelling microscope. By applying an appropriate potential difference between the surface and the probe tip and moving the probe tip across the specified surface area it is possible to 'draw' metal oxide lines 10–20 nm thick (Fig. 11).²⁰⁹ A local nanoscale etching technique was also used for modification of the surface of a silicon crystal.²¹⁰ Nanoscale silicon rods on the surface treated were prepared by nitration and subsequent oxidation of the surface monolayer. Efficient etching of the Si(111) surface by thermalised hydrogen atoms was performed at 105 K.^{207,211} The products obtained, silanes and disilanes, were removed from the surface by heating the samples to 480 K.

Silver, copper and platinum crystals are good catalysts of oxidation processes. However, organic molecules are poorly adsorbed on their surfaces at temperatures above 150 K. The situation changes in the presence of adsorbed oxygen.²¹² Efficient low-temperature oxidation of cyanogen (CN)₂, carbon monoxide, ethyl iodide, methanol, nitrobenzene and styrene molecules on the

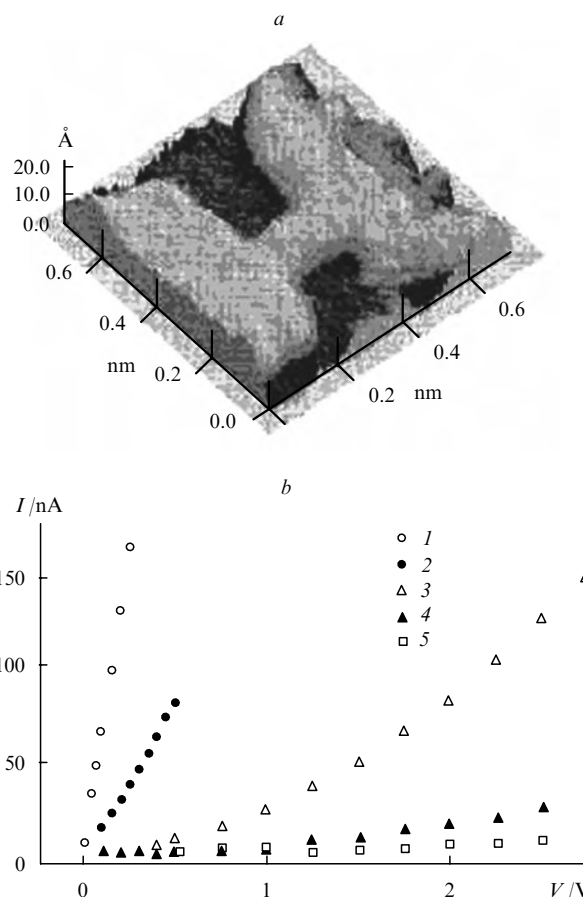
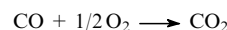


Figure 11. AFM image of crystalline titanium surface after nanoscale local oxidation by simultaneous action of oxygen and the probe tip of a tunnelling atomic force microscope (a) and the current-vs.-voltage curves for the system at different temperatures (b).²⁰⁹ T/K: 250 (1), 190 (2), 130 (3), 90 (4) and 77 (5).

Ag(110), Pt(113) and Cu(110) surfaces was carried out in the presence of adsorbed oxygen.^{213–215}

The most important oxidation processes in the environment and in living organisms involve dioxygen. They can also retain selectivity at low temperatures as, e.g., industrial catalytic processes involving C₁-molecules on gold-containing catalysts. A complete catalytic cycle for the transformation



on gold cluster anions Au_N[−] is illustrated by Fig. 12. The reaction exhibits nonmonotonic cluster-size dependences of the amount of adsorbed carbon oxide and of the conversion efficiency (Fig. 13). This reflects improved stabilities of nanoclusters with closed outer electron shells (N = 8, 14, 18 and 20).^{216–218}

Dissociative adsorption of methane on the surface of Ni single crystals was considered as a model for reforming on small nickel crystallites dispersed in a highly porous Al₂O₃/MgO matrix.²¹⁹ Reactions of hydrogen atoms with acetone on graphite monolayers coated on the Pt(111) surface were studied by high-resolution electron energy loss spectroscopy and thermal desorption spectroscopy at 90 K.²¹⁹

2. Polymer films containing metal nanoparticles

Low-temperature vacuum codeposition of metal (Ag, Mg, Cd, Zn, Pb, Sm, Sn, Mn) vapours with *p*-xylylene, which polymerises at low temperatures (100–120 K), was employed to prepare metal nanoparticles (d = 5–10 nm) encapsulated into polymer films.^{220–227} Polymerisation at cryogenic temperatures and formation of the polymer network preclude subsequent aggregation

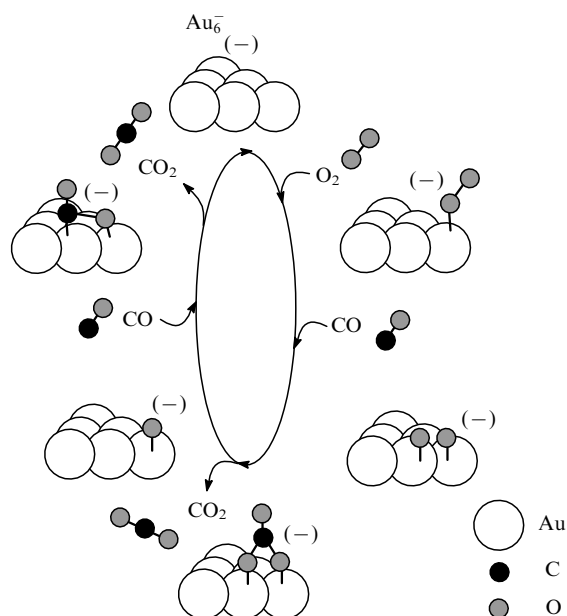


Figure 12. Scheme of complete catalytic cycle for conversion $\text{CO} + 1/2 \text{O}_2 \rightarrow \text{CO}_2$ on gold clusters Au_N^- (see Ref. 216). N is the number of atoms in the cluster.

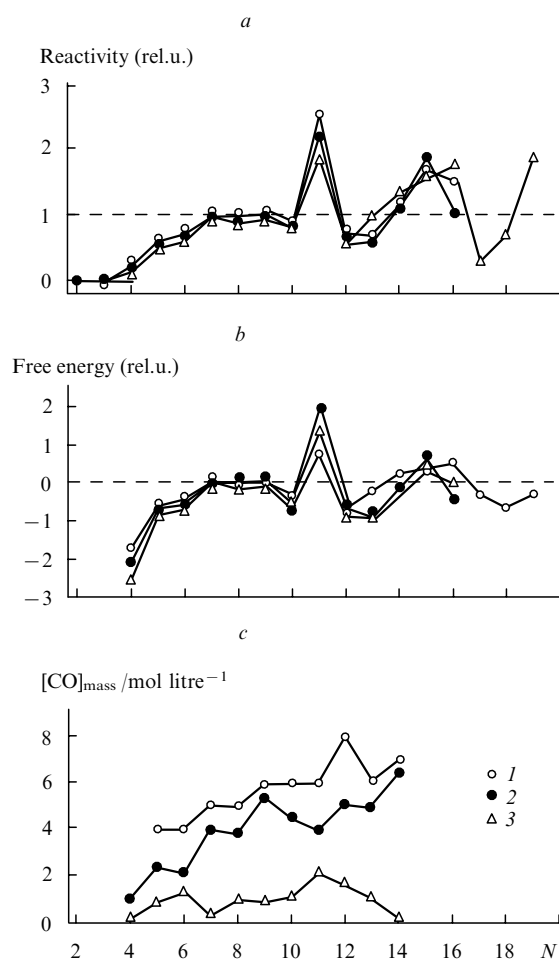
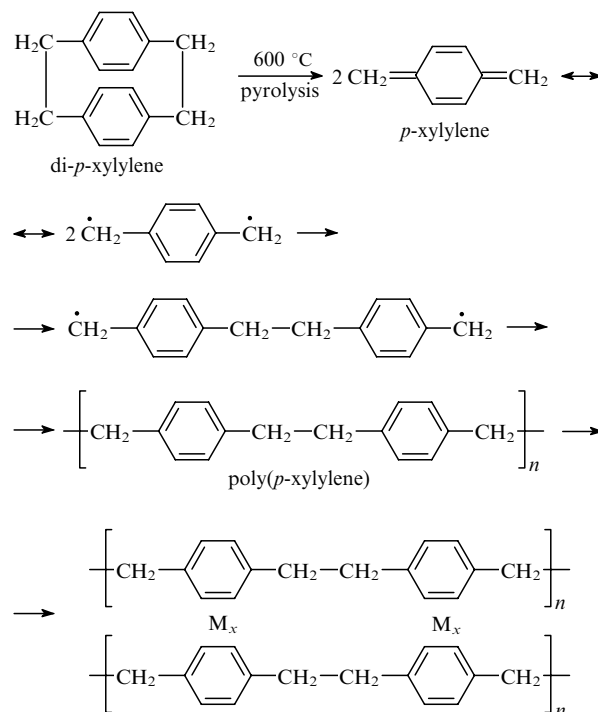


Figure 13. Dependences of the reactivity (a), free energy (b) and amount of adsorbed carbon oxide (c) on the size of Au_N^- clusters at different exposure times in CO (1–3).²¹⁶

of the metal particles. Poly-*p*-xylylene films containing encapsulated metal nanoparticles can be separated at room temperature and investigated by various spectral and physicochemical methods. The following scheme of cryochemical synthesis of poly(*p*-xylylene) films containing nanoscale metal particles (M) was proposed:



The films obtained were studied by transmission electron microscopy and X-ray diffraction. The content of metal in the samples was determined by X-ray fluorescence analysis. It was found that globular lead particles are homogeneously dispersed in the film (Fig. 14). The average particle size was 5.5 nm, being independent of the metal content in the film from 0.1 to 6.5 mass %. The particles were treated as crystals.²²⁴ The lattice parameters of the zinc and cadmium particles encapsulated into poly(*p*-xylylene) films were in good agreement with the lattice parameters of bulk metals. Exposure of the films to oxygen over a period of several days led to formation of new metal-oxide crystalline phases ZnO and CdO.²²⁴

Poly(*p*-xylylene) is a typical insulator. Encapsulation of lead nanoparticles into the film (up to 10% by mass) has no effect on the material's characteristics, the resistivity of the films is $10^{16} \Omega \text{ cm}^{-2}$ (see Ref. 225). Changes in the conductivities of the

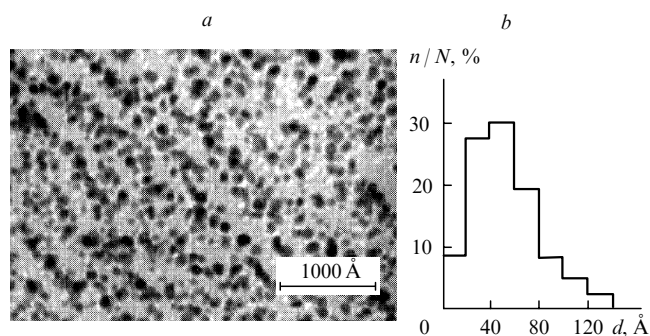


Figure 14. Electron micrograph (a) and size distributions (b) of lead particles stabilised in poly(*p*-xylylene) films ([Pb] = 6.5 mass %);²²⁴ n is the number of nanoparticles of a given size and N is the total number of nanoparticles.

samples were studied during low-temperature co-condensation of vaporous components and on heating of the samples in the temperature range 80–300 K.²²⁵ Polymer films containing nanoscale lead particles exhibit activity as gas and vapour sensors towards various organic and inorganic substances.^{226–230} The conductivity of the film samples varies by four to six orders of magnitude.

3. Hybrid metal–mesogen nanosystems

Ordered nanoscale structures are of considerable interest because of unusual physical and chemical properties. The use of liquid crystals as self-organising organic matrices opens up new prospects for the synthesis of anisotropic metal nanoparticles and their compounds and for fabrication of organised ensembles of nanorods and nanowires based on them.

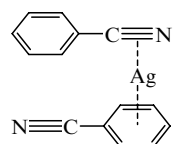
Silver-containing cyanobiphenyl films were prepared by vacuum co-condensation of vaporous components on cooled CaF_2 , quartz and copper surfaces.^{231–233} Silver/4-alkyl-4'-cyanobiphenyl co-condensate samples were studied by EPR, IR and UV-visible spectroscopies in the temperature range 80–350 K and by transmission electron microscopy at room temperature. The spectral features observed were analysed using the results of model quantum-chemical calculations of the equilibrium structures and vibrational analysis.²³⁴

Spectroscopic studies of binary Ag/CB co-condensate films with the component ratio varied from 1:1 to 1:100, as well as investigation of ternary Ag/CB/decane co-condensate films at 90 K revealed the presence of metastable complexes formed as a result of interaction between silver atoms and cyanobiphenyl molecules. In particular, the IR spectra of the Ag/5CB co-condensates exhibited two new bands at 2080 and 2030 cm^{-1} in the region of CN stretching vibrations (see Ref. 231). These bands are shifted by -150 and -200 cm^{-1} , respectively, with respect to the corresponding band of 5CB (2230 cm^{-1}). The observed decrease in the stretching vibration frequencies indicates the formation of a silver–cyanobiphenyl π -complex. Indeed, partial donation of electron density from the bonding orbital of silver to the ligand antibonding orbital should cause elongation of the multiple bond in the complex and, hence, a decrease in its vibrational frequency. The frequency shifts by 100–200 cm^{-1} towards the low-frequency region were observed in a study on π -complexation of some transition metals with unsaturated compounds.²³⁵ The spectra of the Ag/5CB and Ag/5CB/ $\text{C}_{10}\text{H}_{22}$ co-condensates also exhibited a new band in the region 650–660 cm^{-1} , which was assigned to the vibrations of the metal–ligand bond in the π -complex Ag(5CB). Similar results were obtained for co-condensates of silver with 8CB and 4-octyloxy-4'-cyanobiphenyl (8OCB). In both cases the intensities of the IR bands of π -complexes changed with the co-condensate temperature following an identical pattern. Because of this, the bands were assigned to the same complex. Complexes Ag(CB) are stable at low temperatures and decompose on heating of the co-condensates to 200–300 K into starting CB and silver clusters. At room temperature, the IR spectrum of Ag/CB co-condensate is similar to that of the CB condensate film. The results obtained are consistent with the low thermal stabilities of the complexes of zero-valence metals with unsaturated compounds.

The formation of π -complexes in the system under study was confirmed by the results of quantum-chemical calculations of 5CB and of the central cyanophenyl fragment of the complex.²³⁴ The calculations were carried out by the multiconfiguration self-consistent field method and by the restricted Hartree–Fock method for open-shell systems. The Stevens–Basch–Krauss effective core pseudopotential was employed for all heavy atoms. Both geometry optimization and of vibrational analysis for the $(\text{PhCN})\text{Ag}$, $(\text{PhCN})\text{Ag}^+$ and $(\text{PhCN})\text{Ag}_2$ particles have demonstrated that global energy minima for these systems correspond to σ -complexes with linear arrangement of the $\text{C}–\text{N}\cdots\text{Ag}$ fragment. The shifts of the $\text{C}–\text{N}$ stretching vibration frequencies in the complexes relative to the corresponding value for the ligand

molecule were $+9$, -7 and $+20 \text{ cm}^{-1}$ for the equilibrium $\text{N}\cdots\text{Ag}$ distances of 2.81, 2.24, and 2.46 Å, respectively. Therefore, the calculated configurations do not correspond to real structures in the Ag/5CB films since the experimentally observed shifts of the CN stretching vibration frequency are -150 and -200 cm^{-1} .

At the same time liquid-crystalline cyanobiphenyls are known to form dimeric structures in the solid and liquid-crystalline phases. Structural studies^{236,237} showed that cyanobiphenyl molecules in the solid phases are arranged in the ‘head-to-tail’ manner. Based on this, the following structure of the silver–cyanobiphenyl complex was proposed (shown is the central part of the complex):



The cyano groups in this structure are nonequivalent and give two bands in the IR spectrum of the complex.

Multiconfiguration self-consistent field calculations revealed the possibility of two ground-state electronic configurations of the complex, $(\text{PhCN})_2\text{Ag}$ and $(\text{PhCN})_2\text{Ag}^+$.²³⁴ At long interligand distances R ($R \geq 4.7 \text{ Å}$), neutral silver atoms fill the interligand cavities. At $R < 4.7 \text{ Å}$, the charge-transfer configuration $(\text{PhCN})_2\text{Ag}^+$ dominates. If $R = 4.4 \text{ Å}$ (a charge-transfer complex), the calculated shifts of the $\text{C}–\text{N}$ vibrational frequencies in the $(\text{PhCN})_2\text{Ag}$ complex relative to the corresponding value for the PhCN molecule (2501 cm^{-1}) were found to be -150 and -175 cm^{-1} , which is in agreement with the experimentally observed shifts for the Ag/5CB films at 90 K.

Thermal behaviour of the metal-containing atom–molecular systems based on co-condensates of silver and mesogenic cyanobiphenyl 5CB was investigated in the temperature range 80–300 K.²³³ At 80 K, the EPR spectra of the co-condensates exhibited well-resolved signals of hyperfine coupling (HFC) with the metal atoms. This indicates formation of complexes between silver atoms and mesogenic ligands under conditions of low-temperature co-condensation. The parameters of the doublets, obtained by simulating the spectra of the Ag/5CB and Ag/5Py co-condensates are characteristic of π -complexes of the ^{107}Ag ($J = 1/2$) and ^{109}Ag ($J = 1/2$) atoms. By comparing the HFC constants of the complexes with those of free atoms [$A(^{107}\text{Ag}) = 611$ and $A(^{109}\text{Ag}) = 705.4 \text{ G}$]⁴⁶ it is possible to estimate the unpaired s-electron density on the metal atom: $\rho_s = 0.89$ (Ag/5CB). The central signal in the region characteristic of the g-factor of a free electron is due to absorption of the silver clusters stabilised in the 5CB matrix. Similar signals were observed for concentrated samples of co-condensates of silver with inert gases and hydrocarbons. They were treated as the spin resonance signals of conduction electrons in the metal nanoclusters. The average size of silver clusters in the Ag/5CB co-condensate (Ag:5CB = 1:10) estimated from the experimental spectrum recorded at 90 K is 1–2 nm (several tens of atoms). Raising the temperature from 80 to 150 K causes a decrease in the relative intensities of the doublets in the spectrum and an increase in the relative intensity of the central component, which indicates thermal degradation of the complex and the growth of silver nanoclusters. The possibility of formation of silver nanoclusters by UV irradiation of samples at 80–90 K was demonstrated.²³⁸ Heating of such samples above 200 K also causes a rapid decrease in the intensity of the central line in the EPR spectra and the appearance of a broad background absorption, which can be explained by the formation of larger silver nanoparticles and their aggregates.

At 90 K, the optical absorption spectra of Ag/5CB co-condensates exhibited²³³ a structured band at 360 nm. Quantum-chemical calculations of excited states of the complex revealed a number of intense transitions corresponding to

metal–ligand and ligand–ligand charge transfer in this region.²³⁹ It should be noted that small clusters of silver can also absorb in the region 390–420 nm.³⁷ The structured band at 360 nm disappears on heating of the co-condensate film to 200–300 K.²³⁴ Thus, heating of the sample to room temperature causes thermal degradation of the complex and aggregation of the silver atoms thus released. The broad band with a maximum at 440 nm which appeared in this case is due to absorption of surface plasmons of nanoscale silver particles²⁴⁰ that are formed as a result of aggregation of silver atoms upon decomposition of the complex. Fast heating of the co-condensate to 300 K causes a transition of the sample to the nematic mesophase. This is followed by an increase in the absorption of the plasmon resonance in the long-wavelength region of the UV spectrum, which can be due to both the growth of silver particles due to further aggregation and the formation of non-spherical anisotropic metal particles in the orientationally ordered matrix.

Thus, the sample prepared by low-temperature co-condensation of the metal (silver) and mesogenic component vapours and heated to room temperature is a material containing silver nanoparticles stabilised in the cyanobiphenyl matrix.²⁴⁰ The material retains nematic properties. The samples obtained and the pure 5CB are characterised by an identical thermogram pattern and by textures typical of the nematic phase.

Low-temperature layer-by-layer co-condensation of silver, 5CB and *p*-xylylene vapours followed by heating of the film sample results in encapsulation of the metal–mesogen system into the polymer film.²⁴⁰ An electron microscopy study of the films prepared by encapsulating silver-containing 4-pentyl-4'-cyanobiphenyl into poly(*p*-xylylene) under conditions of vacuum co-condensation of reactants revealed the presence of two types of

metal particles stabilised in the mesogenic matrix at room temperature.²⁴⁰ These are globular silver particles of diameters 15 to 30 nm and anisotropic rod-like particles more than 200 nm long (Fig. 15). The UV spectrum of the Ag/5CB films in poly(*p*-xylylene) exhibits a broad absorption band at 440–600 nm at room temperature. An increase in the metal-to-ligand ratio in the sample causes a preferred growth of rod-like silver particles.

Thus, silver-containing mesogenic cyanobiphenyl films prepared by low-temperature co-condensation of component vapours (molecular beam regime) incorporate metastable π -complexes of the metal with dimeric cyanobiphenyl molecules. The formation of metastable π -complexes in the temperature range 90–200 K was confirmed by EPR, IR and UV spectroscopies and by the results of quantum-chemical calculations of a model silver–cyanophenyl system. Raising the temperature causes degradation of thermally unstable complexes and aggregation of silver atoms in the anisotropic liquid-crystalline matrix, resulting in silver nanoclusters and nanoparticles. Thermal and photo-induced decomposition of the complexes in the temperature range 90–200 K is accompanied by the formation of nanoscale silver clusters and further aggregation of these species in the anisotropic matrix. The formation of globular metal particles (15–30 nm) and anisotropic metal–mesogen nanostructures including rod-like aggregates more than 200 nm long stabilised in the cyanobiphenyl matrix was established.

4. Nanoparticle ensembles and superlattices

Recently, intensive research on preparation and self-assembly of nanoparticles on various surfaces has been carried out.^{241,242} These investigations are aimed at finding possible applications of surface nanostructures and nanostructured films in various nanoelectronic data recording and processing devices, optical and magnetic filters, displays, switches, etc.

Silver and gold nanoparticles are convenient for studying self-assembly effects. Periodic structures are formed immediately in colloidal solutions of gold and silver nanoparticles stabilised by a variety of thiol- and nitrogen-containing ligands^{125,243} and on various surfaces modified with amines and thiols.²⁴⁴ Formation of alternating positively and negatively charged gold and silver nanoparticles and their organisation into ordered structures on glass surfaces in the presence of 4-aminothiophene and 4-carboxythiophene was observed.²⁴⁵ Detailed analysis of the stabilisation of the metal nanoparticles by ligands and of their organisation into periodic 1D, 2D and 3D structures has been reported.²⁴⁶

Self-assembly of spherical gold nanoparticles 2–5 nm in diameter into rod-like aggregates has been studied.²⁴⁷ It was shown that the size, shape and morphology of aggregates can be controlled by varying the substrate temperature. For instance, the species prepared were spherical aggregates of particles of diameter 97 ± 17 nm (23 °C), spherical particles of size 0.5–1 μ m (–23 °C) and nearly 50-nm long chain-like 1D aggregates comprised of spherical units (intermediate temperature, 10 °C). It was assumed that the formation of large globular aggregates from small spherical particles involves an intermediate stage in which linear aggregates are formed and that this stage is controlled by the enthalpy-to-entropy contribution ratio. Orientationally ordered gold nanorods were prepared.²⁴⁷ Using femto- and nano-second lasers, nanorods were reversibly transformed into spherical nanoparticles.

Self-assembly of Sb₄ clusters on the surface of highly ordered pyrolytic graphite or molybdenum disulfide was studied.²⁴⁸ The evolution of the structure and morphology pattern of the particles with an increase in the surface coverage was studied by electron microscopy and electron diffraction (Fig. 16). It was found that amorphous spherical nanoparticles are formed at low surface coverages. After reaching a critical size of 120 nm (at room temperature), finger-like island and planar 2D structures were formed. Well-shaped, orientationally ordered 3D nanocrystals

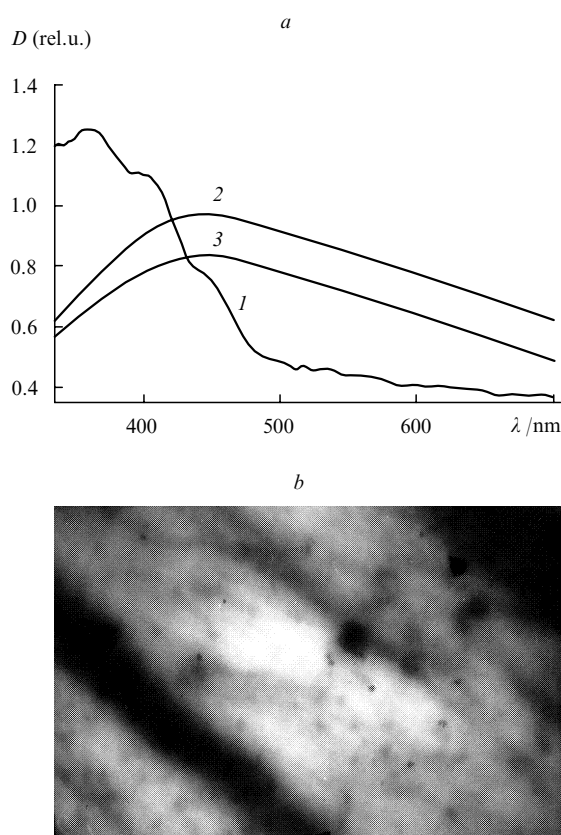


Figure 15. Optical absorption spectra of a Ag/5CB (Ag : 5CB = 1 : 10) co-condensate film at 90 (1), 200 (2) and 300 K (3) (a) and an electron micrograph of the film at 300 K (b) (1 cm = 100 nm).²⁴⁰

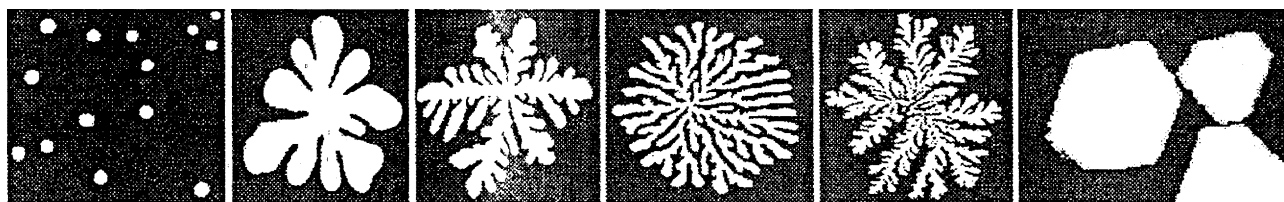


Figure 16. Evolution of the morphology pattern of antimony nanoclusters Sb_4 on the surface of highly ordered pyrolytic graphite with an increase in the surface coverage (from left to right) according to electron microscopy data.²⁴⁸

with narrow size distribution grew with increasing surface coverage. Thus, the authors of this study observed a size-dependent structural phase transition from the amorphous to the crystalline state. An analogous transition was earlier observed in the formation of gold nanocrystals by deposition on a graphite surface²⁴⁹ and ice crystals from amorphous supercooled water vapour.²⁵⁰ The phase transition observed depends on the condensation rate, surface coverage and the temperature of the sample.

The influence of the nature and surface morphology of the substrate (pyrolytic graphite or molybdenum disulfide) on the formation of ordered 2D and 3D superlattices was observed taking dodecanethiol-stabilised silver nanoparticles of diameter 5.8 nm as examples.²⁵¹ Control of substrate morphology is of great importance for pharmaceutical and food-industry applications.²⁵² For instance, self-assembled organothiol monolayers on the Au(111) surface were used as templates for the growth of glycine crystals.²⁵² Highly ordered styrene structures on the Si(100) surface were produced by scanning the corresponding local areas with the probe tip of a scanning tunnelling microscope. By modifying the silicon surface it is possible to change the orientation and length of molecular arrays on the surface, control their direction and vary the angle of chain propagation.

Self-ordering of alkanethiol monolayers on the surface of gold nanoparticles has been reported.²⁵³ Introduction of fluorocarbon substituents improves the stability of the ordered layers. Their thermal stability increases with an increase in the number, n , of methylene groups in the organic stabiliser molecule. At $n = 33$, the ordered films do not experience thermal degradation at 150 °C for 1 h in air. Gold nanoparticles stabilised by fluoroalkyl ligands can form hexagonal close-packed and cell structures.²⁵⁴ The type of ordering is primarily determined by the nanoparticle size ratio and by steric hindrance produced by the stabilising ligands. Stable nanosystems comprising gold particles ($d = 4$ nm) incorporated into polyethyleneimine and poly(L-lysine) films and additionally stabilised by carboxylic acids were obtained.²⁵⁵

Monolayers of ordered 2D structures comprised of ligand-stabilised nanoparticles can be used as selective chemoresistive sensors for volatile organic compounds. In particular, ordered 2D structures formed in monolayers of gold nanoparticles stabilised by alkanethiol ligands (Fig. 17) are highly sensitive to toluene, tetrachloroethylene, propan-1-ol and water vapour.²⁵⁶ Ordered thin-film surface structures built of functionalised organic molecules specifically bound to the surfaces of metallic and polymeric substrates also exhibit the properties of selective sensors. As an example, Fig. 18 presents a scheme of organisation of resorcin-[4]-arene monolayers that are covalently bound to the Au(111) surface and can selectively bind various organic molecules ($\text{CCl}_2 = \text{CCl}_2$, $\text{CCl}_2 = \text{CHCl}$, CCl_4 and toluene).²⁵⁷

Highly ordered organic monolayers adsorbed on the surface of inorganic nanoparticles can be used for selective binding of various functional blocks to organise hybrid nanostructures. This can be done using, *e.g.*, biomacromolecules. In particular, the ability of peptides and DNA molecules to show molecular 'recognition' can be modelled using relevant synthetic analogues.

Recent advances in molecular biology allowed one to obtain natural and synthetic biomolecules, which can selectively bind metal and metal oxide particles. There are two approaches to exploiting biomolecules as the 'glue' for different inorganic blocks.²⁵⁷ The first involves mutual organisation due to 'programmed' interaction between biomolecules with the known 'recognition' mechanism. In this case, the hybrid material is generated from two different inorganic blocks modified with molecules of peptides, antibodies, oligonucleotides or other bioligands complementary to one another. The second strategy involves specific interactions between inorganic blocks bearing particular functional groups and the bifunctional biomolecule. Recently, this approach was implemented practically.²⁵⁸

Nanostructured surfaces prepared by deposition of size-selected metal clusters and nanoparticles can be used for selective binding and immobilisation of particular biomolecules. Such systems are promising for fabrication of sensitive biochips. For instance, by depositing size-selected gold clusters onto graphite surfaces it is possible to create stable organised structures for selective binding of such practically important biomolecules as peroxidase and DNA.^{259–260} This method also permits optical detection of individual biomolecules bound to the nanoparticle surface.²⁶¹

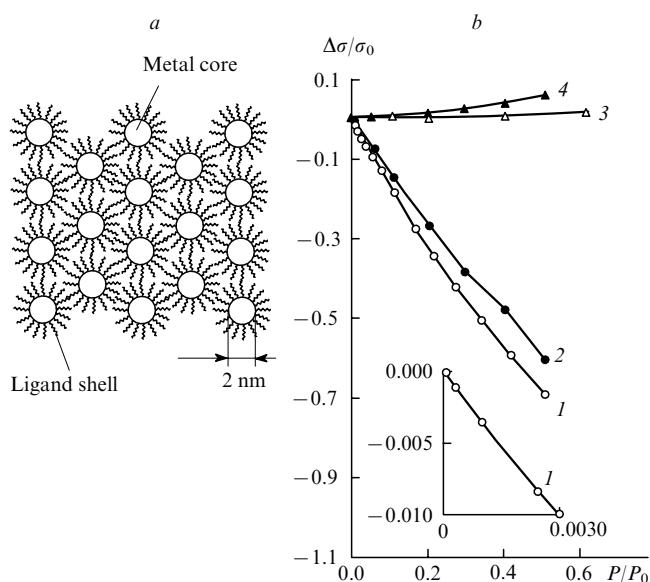


Figure 17. Ordered 2D structures formed in monolayers of gold nanoparticles stabilised by alkanethiol ligands (a) and their sensitivity to toluene (1), tetrachloroethylene (2), water (3) and propan-1-ol (4) vapours (b).²⁵⁶

$\Delta\sigma/\sigma_0$ is the relative change in the layer conductivities; P/P_0 is the ratio of the partial vapour pressure of the organic compound to the total pressure in the system.

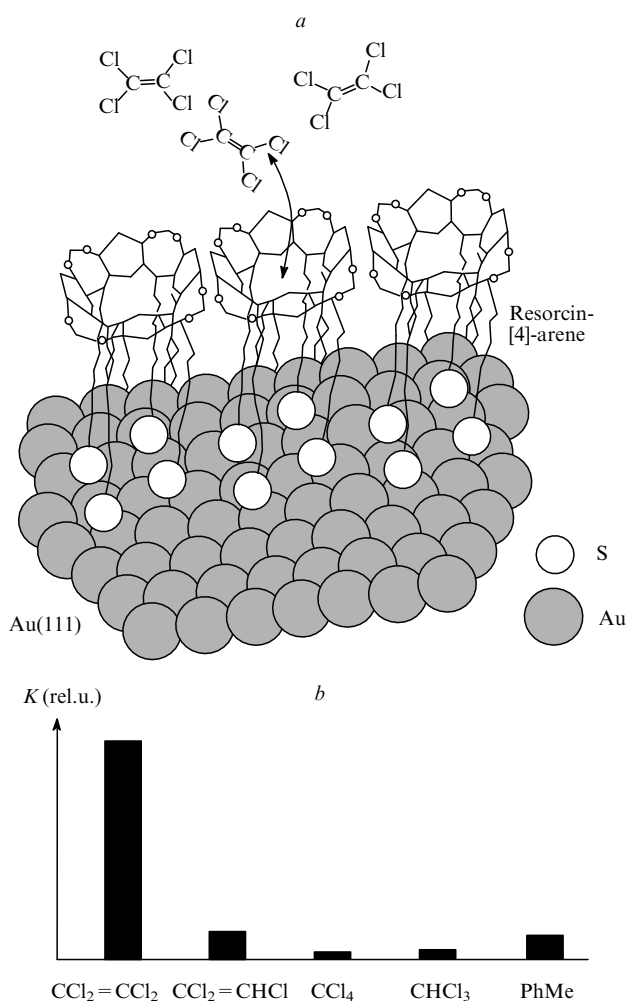


Figure 18. A scheme of organisation of resorcin-[4]-arene monolayers covalently bound to the (111) surface of gold single crystals and capable of selective binding of various organic molecules (a) and binding selectivity diagram for these molecules (b);²⁵⁷ K is the binding constant.

VIII. Conclusion

Cryochemistry allows one to investigate highly reactive particles, atoms, clusters, metal nanoparticles and their organised ensembles. At cryogenic temperatures, chemical interactions begin at the atomic level. Co-condensation and subsequent warm-up of samples are characterised by competition between aggregation and stabilisation of atoms and small clusters in matrices. Introduction of complexing ligands and reactive species into the system causes additional chemical and physicochemical processes resulting in unusual chemical compounds and complexes. Aggregation of atoms and their interaction with ligands occur almost barrierlessly. High reactivities of metal atoms, clusters and nanoparticles preclude establishment of correlations between the particle sizes (number of atoms in the particle) and their reactivities. This problem, as well as the problems of synthesis and stabilisation of atoms, clusters and nanoparticles can be solved only by carrying out spectroscopic studies at cryogenic temperatures.²⁶² Based on the results obtained thus far, the size of the reacting particle can be considered as a parameter which determines the state and chemical properties of a reaction system along with the temperature.²⁶³

At cryogenic temperatures, processes occur under strongly nonequilibrium conditions in metastable systems characterised by a broad reactivity distribution of the reacting species. This

manifests itself as peculiar features of the kinetics of low-temperature processes.

Operation at cryogenic temperatures allows preparation of small particles of size less than 1 nm. Potential applications of such species are related to the search for highly efficient stabilisers of nanoparticles. Novel catalysts and sorbents, optical and anti-corrosive coatings, pharmaceuticals and dyes, degassing agents and bioactive components can be prepared at cryogenic temperatures. High reactivities of small stabilised particles make it possible for them to be considered as chemical systems for energy accumulation and storage and as specific nanoscale chemical reactors. Such systems allow the carrying out of novel chemical reactions and unusual chemical transformations, which cannot proceed under normal conditions.

Currently, efficient cryochemical methods for stabilisation of nanoparticles in matrices and on various surfaces and procedures for fabrication of nanostructured film materials with prescribed optical, magnetic, electrophysical and mechanical characteristics are being developed. The future of these approaches is closely related to extension of the field of possible practical applications of nanosystems in nanotechnologies.^{264, 265} These are primarily creation of toxic gas sensors, highly selective and reactive catalytic systems, membranes and highly porous sorbents with large surface areas and prescribed pore sizes, novel ultrahard and superplastic materials, coating-protective nanoalloys, absorbing and reflecting ceramics, pharmaceuticals with improved bioavailability and controlled delivery, novel hybrid organometallic materials and bio-metallo-ceramic composites.

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^l — *Crystallogr. Rep.* (Engl. Transl.)

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Nucleation: theory and experiment

M P Anisimov

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Abstract. Various theoretical and experimental methods for studying nucleation are considered. Since theoretical methods have fundamental limitations, information is gained from experimental research. It is demonstrated that the nucleation theory is entering a new phase of development, which is going to be, in essence, semiempirical. A semiempirical method for constructing nucleation rate surfaces is described. The topology of these surfaces in the limit of the zero nucleation rate can be determined using phase equilibrium diagrams. This opens up possibilities for revising certain approximations employed in experiments and particular axiomatic statements of the classical nucleation theory. Examples of the practical use of nucleation essential for the development of modern technologies are given. The bibliography includes 396 references.

I. Introduction

In the last two decades, the problems of nucleation have attracted considerable interest. These problems are related to many disciplines and the vast majority of systems in which first-order phase transitions can occur. The available nucleation theories are arbitrarily divided into the so-called 'theories of original potential' and phenomenological theories. With the aim of simplifying the problem of determination of the nucleation rate, the authors who uphold the former line of investigation consider average fluctuations of a nucleating medium to find conditions under which the 'averaged' cluster evolves into a droplet.¹ The principle of detailed equilibrium is invoked to solve the kinetic problem of cluster growth. In doing so, one should specify the equilibrium distribution in such a way that the averaged clusters could, to a certain degree, simulate non-equilibrium clusters.¹

Generally, a method for describing nucleation follows, with some delay, after the development of approximate methods in the many-body theory (see, for example, Ref. 2). The non-equilibrium state of a macroscopic system can be indirectly taken into

account, using, in particular, the linear reaction theory. In this theory, the effects caused, for example, by thermal perturbations are expressed in terms of mechanical perturbations. Alternative methods employ the theory of stochastic processes and the Fokker–Planck equation or Onsager's hypothesis according to which the fluctuation damping follows the same law as the change in the corresponding macroscopic variables. There are also methods based on the use of a local-equilibrium distribution (*i.e.*, on the assumption that a near-equilibrium distribution occurs in small volumes in the case of moderate deviations from equilibrium) as the initial condition for the fulfilment of the Liouville equation. The methods of statistical Gibbs ensembles for non-equilibrium systems (for example, Zubarev's method of a non-equilibrium statistical operator based on the construction of local integrals of motion) as well as the method accounting for the effect of thermostatting by considering non-potential forces find wide application.

In recent years, certain advances have been made in the study of non-equilibrium processes in dense multiparticle systems. Thus, the Vlasov equation was derived for a multiparticle system involving the field $U(r)$, which depends on the nature of particles

$$\frac{\partial f}{\partial t} + \mathbf{v} \text{grad}_r f + \mathbf{a} \text{grad}_r f = 0.$$

Here f is the distribution function of single-particle states in the phase space of coordinates (r) and rates ($\mathbf{v}$), $\mathbf{a} = -\text{grad}_r U(r)/m$ (m is the particle mass). In the monograph,³ this equation was considered as a special case of the more general Vlasov–Uehling–Uhlenbeck equation allowing for the formation of coupled states. The Vlasov equation results from the averaging of the generalised equation in the lowest approximation, where the energy of quasiparticles is calculated in the self-consistent Hartree–Fock approximation and collisions can be ignored. Vlasov deduced this equation by assuming that particles are not localised and their properties are responsible for the state of the system. This eliminates the problem of field averaging.

Vlasov reasoned that this equation does not follow from the Hartree–Fock or Liouville equations because of the presence of the property of branching of solutions, whereas neither processes of crystal formation nor crystal structures can be described using equations of classical statistics and quantum mechanics. Hence, the problem of allowing for collective interactions in a multiparticle system is replaced by the problem of finding an interaction potential of non-localised particles, including its functional dependence on the characteristics of the macroscopic state of the

M P Anisimov Aerosol Nucleation Laboratory, G K Boreskov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, Moskovskii prosp. 41A, 650065 Kemerovo, Russian Federation.
Fax (7-383) 234 30 56.
E-mail: anisimovmp@mail.ru

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system (for example, on the temperature in the consideration of a crystallisation process). In other words, simplified relations were proposed for the description of physical systems, which allow one to obtain results consistent with experimental data. This is achieved due to the fact that many systems can be described in an approximation of noninteracting particles in a potential field.² Of methods employing this approximation, let us note first of all the effective (self-consistent) field methods. The idea is that a certain simplification is introduced, whereby the motion of a given particle can be considered as a motion in a potential field, which depends only on the coordinate of this particle and is independent of the coordinates of all other particles. If the properties of all particles in this effective field are known, the assumed potential can be calculated. If no consistency with the expected result is achieved, the effective field can be 'corrected' until the desired result is obtained.

In the approximation used in the classical nucleation theory, the cluster is considered as a liquid droplet of uniform density equal to the density of the macroscopic liquid; the droplet has a sharp boundary with the surrounding metastable phase. Using this model, one can calculate the free energies of real systems taking into account the translational degrees of freedom of the cluster.⁴ The droplet model describes only some of the possible configurations of the cluster consisting of a particular number of molecules, and there is no assurance that it is one of these configurations that plays a decisive role in the dynamic process.¹

The clusters under consideration can be divided into two types, *viz.*, stable clusters whose configurations are determined by their own structures and clusters whose structures depend on the results obtained in the context of a particular theory (for example, the density functional theory). The former type of clusters corresponds to the approximation of noninteracting particles, whereas the latter type corresponds to the approximation of interacting particles, which is similar to the self-consistent field approximation. It should be noted that by specifying *a priori* the type of the cluster (rather than determining it by analysing intermolecular interactions), we actually go from analytical theories to phenomenological approaches.¹

The best results, which are in quantitative or semiquantitative agreement with experimental data, were obtained using models based on the classical nucleation theory. In essence, such models are phenomenological rather than molecular.¹ The foundations of the classical nucleation theory were laid by Gibbs. In the 1940–1950s, this theory acquired its modern meaning after publications by Zeldovich⁵ and Frenkel.⁶

In recent years, many studies have been devoted to the development of molecular theories of nucleation. However, the applications of certain relations of statistical mechanics to nucleation were not always justified.^{2,3} The thermodynamic approach to the description of nucleation leads essentially to more than noting the introduction of additional terms to equations for the work of formation of critical nuclei of a new phase. For instance, Abraham⁷ took into account characteristic features of dipole–dipole interactions. Dillmann and Meier^{8,9} proposed various phenomenological coefficients. Overlapping of clusters was accounted for in the study.¹⁰

The correlation between the modern theoretical and experimental data can be judged from the curves shown in Fig. 1.¹¹ It should be noted that the agreement between the results can be substantially improved by varying a certain parameter of the theory, *e.g.*, the surface tension, within its experimental error. At the same time, out of numerous theories one can always choose a theory, which is best suited for the description of a particular series of experimental results. Therefore, a good agreement between theoretical and experimental data does not evidence the predictive force of the theory.

In the last five decades, the accuracy of experimental methods was substantially improved. It was expected that the classical nucleation theory would be experimentally confirmed. Actually, abundant experimental data, which have been accumulated, are

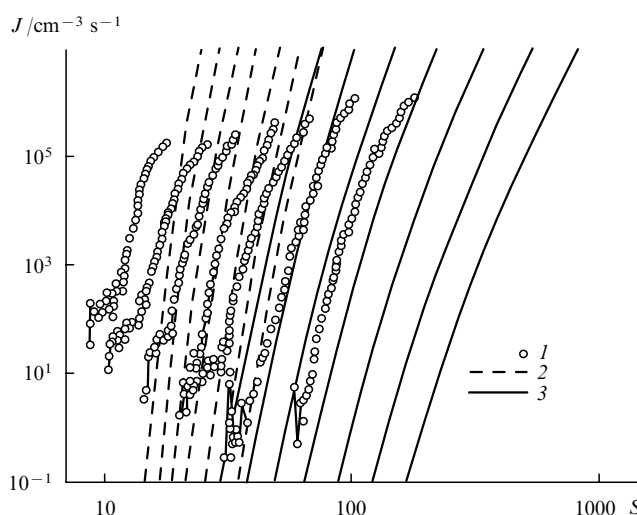


Figure 1. Experimental (1) plots of the nucleation rate J vs. supersaturation S of an octanol vapour in an octanol–sulfur hexafluoride system and analogous dependences calculated according to the classical theory (2) and the Dillmann–Meier theory (3).¹¹

Nucleation temperatures for each series of experiments /°C (from right to left): 261.8, 266.3, 271.2, 276.4, 281.5, 286.6, 291.7.

not contradictory with this theory. However, taking into account the ever-increasing accuracy of experimental results, it becomes more and more evident that the classical nucleation theory has limits of applicability. Presently, there is a pressing need to reveal these limits and develop new nucleation models, which can predict nucleation rates in various systems.

Approximately 10 years ago, semiempirical methods were proposed for constructing nucleation rate surfaces based on phase equilibrium diagrams.^{12,13} Based on this idea, nucleation rate surfaces were constructed for a series of simplest systems.¹⁴ Assuming this rather evident concept, it is apparent that the multitude of nucleation rate surfaces can be constructed from the multitude of phase equilibrium lines. In other words, 'multiple' nucleation rate surfaces are a rule rather than an exception. Hence, scarce experimental data on nucleation rates need analysis for 'singularity'. A direct experiment on the detection of two rate surfaces upon glycerol nucleation in the vicinity of its triple point was described in study.¹⁵ Each surface corresponds to its own nucleation channel. By contrast, the classical nucleation theory generally considers a singular nucleation rate surface. Of course, the multiplicity is implicitly embedded in the classical theory; however, no attention has been given to this fact until recently. Evidently, in the presence of many surfaces, attempts to describe the overall nucleation rate in the singular approximation of the classical theory are unjustified.

In the present review, attention is primarily given to studies published in the last 10–15 years. Earlier publications are considered, when the retrospective analysis of the problem is necessary. It may seem that the number of references relating to some problems, which have been covered in detail in scientific publications, is insufficient, whereas references relating to other problems, which are no less important but have not been adequately explored, are excessive. Some reviews devoted to rather narrow subject matters are mentioned with the aim of demonstrating the generality of approaches to the description of nucleation in different systems. The present review does not include particular details, for example, the preparation of sols for chemical syntheses in homogeneous solutions, micelles, vesicles, Langmuir–Blodgett films, polymers, glasses, zeolites, *etc.* Undoubtedly, the main conclusions are applicable to all systems in which nucleation takes place. The lines of investigation, which, in my opinion, show promise for the development of the

nucleation theory, are considered in most detail. Presently, it seems reasonable to focus efforts on developing individual parametric semiempirical theories for particular systems characterised by topologically similar (brought to a single topological form) phase equilibrium diagrams. Apparently, a combination of these theories based on the similarity criteria will be the next step in the development of concepts of nucleation. Progress in experimental methods gives promise that new unique results will be obtained in the nearest future, which will give impetus to further theoretical investigations of nucleation.

II. Nucleation theory

Nucleation accompanies first-order phase transitions. They occur in the initial metastable phase due to the fluctuation formation and nucleation (cluster formation) of a new phase.¹⁶ The formation of a macroscopic nucleus requires energy for the formation of an interface between the old and newly formed phases. A need for an excess energy gives rise to hysteresis phenomena, such as supercooling (or superheating) of melts and solutions relative to the equilibrium melting point, supercooling of gases, overvoltage upon electrodeposition of films, *etc.*

In 1878, Gibbs was the first to describe theoretically the formation of a new phase.¹⁷ He has provided a rigorous thermodynamic definition for critical nuclei of a new phase and laid foundations for the formalised description of nucleation rates. Almost five decades later, Volmer and Weber¹⁸ elaborated the Gibbs model in a study devoted to nucleation kinetics. Volmer considered the nucleation work as the activation energy and described qualitatively the nucleation of a new phase in the course of crystallisation.¹⁹ He also introduced the concept of three- and two-dimensional nuclei of a new phase and related their fluctuation appearance to the nucleation and crystallisation rates.

However, the proposed model has drawbacks. For example, the pre-exponential factor in the corresponding kinetic equations remains undetermined due to which the theory is only semi-quantitative. Further efforts by researchers were directed at searching for more rigorous theoretical foundations of the kinetics of the process. Farkas²⁰ solved a system of Szilard kinetic equations describing the formation of droplets from a vapour. The nucleation theory as applied to the stationary kinetics of the droplet formation from a supersaturated vapour was elaborated in studies by Kaischew and Stranski.²¹ Becker and Döring²² completed the study aimed at determining the constants in equations considered by Farkas. They created a general picture of various molecular events proceeding upon the formation of a new phase.

Becker and Döring's statistical theory considers a simplified stationary model according to which the average number of nuclei consisting of 2, 3, 4, ..., n molecules remains constant with time, although depends on external conditions. Clusters whose sizes are larger than the critical value are withdrawn from the system, and the vapour pressure is maintained constant due to the introduction of monomers (molecules, atoms). For nuclei of each size, the evaporation and condensation rates are in balance. By going from a discrete to continual problem and using integration, the authors estimated the nucleation rate (J). The latter is equal to the number of clusters, which are capable of growing and are formed in a unit volume (generally, in cubic centimeter) in a unit time (1 s). It was assumed that clusters containing n molecules are formed from nuclei containing $(n - 1)$ molecules.²² This theory was completed in the above-mentioned studies by Zeldovich⁵ and Frenkel.⁶ The specificity of formation of crystalline nuclei from liquid and gas phases and the problem of heterogeneous nucleation were discussed in Refs 6, 23 and 24. The theory, as it formulated by Zeldovich and Frenkel, is called the 'classical nucleation theory'.

Up to the early 1960s, it was believed that this theory adequately described homogeneous condensation of a supersaturated vapour. The predictions based on this theory were in good agreement with results of experimental measurements of critical

supersaturations using a Wilson chamber and studies of isentropic expansion of a gas in a nozzle or a turbulent vapour flow evaporated into a cold gas. However, in succeeding years, the determination of the dependence of the nucleation rate on supersaturation became possible and the principal foundations of the classical theory and its applicability to interpretation of experimental data were doubted. This gave rise to several tens of equations for the nucleation rate of a new phase.

1. Free energy of nucleation in the classical nucleation theory

For a metastable (according to the Gibbs definition¹⁷) system to become stable, energy sufficient for the creation of a phase interface is required. The free energy of cluster formation involved in a number of thermodynamic equations is one of the main parameters in the nucleation theory. The macroscopic approach, which employs concepts of thermodynamics and statistical physics developed for systems consisting of a large number of molecules, provides a quantitative description of nucleation. Below is given a brief derivation of the equation for the free energy of nucleation in approximations of the classical nucleation theory, which was described in detail in many publications (in particular, the latest versions were published in the book of collective works²⁵).

In the droplet approximation, a change in the Gibbs free energy (ΔG) upon the formation of a cluster consisting of n molecules in a closed system, which contains a vapour at the temperature T and pressure p , can be written as follows

$$\Delta G = n(\mu_l - \mu_v) + 4\pi r^2 \sigma, \quad (1)$$

where μ_l and μ_v are the chemical potentials of molecules in the liquid and vapour phases, respectively, r is the radius of the cluster and σ is the surface tension. Under isothermal conditions, the first component in the right-hand side of Eqn (1) can be estimated from the equation

$$d(\mu_l - \mu_v) = (v_l - v_v)dp_v, \quad (2)$$

where v_l and v_v are the specific volumes of molecules in the liquid and vapour phases, respectively, and p_v is the vapour pressure. If the vapour is considered as an ideal gas and the volume of the molecule in the condensed phase is ignored, the integration of Eqn (2) gives

$$\mu_l - \mu_v = -k_B T \ln S, \quad (3)$$

where k_B is the Boltzmann constant, $S = p_v/p_0$ is supersaturation (p_0 is an equilibrium vapour pressure over the planar interface at the temperature T). Assuming that nuclei of a new phase (clusters) retain the macroscopic physicochemical properties, the overall work of formation of rather large clusters in the droplet approximation can be expressed as a sum of surface ($4\pi r^2 \sigma$) and volume ($nk_B T \ln S$) changes in the Gibbs free energy.[†] Then, the change in the free energy upon cluster formation is

$$\Delta G = 4\pi r^2 \sigma - nk_B T \ln S, \quad (4)$$

where $n = (4/3)\pi r^3/v_l$. A liquid nucleus can grow to a droplet only when its size becomes larger than the critical radius r^* . The terms in Eqn (4) depend differently on r and have opposite signs at $S > 1$. Hence, the plot of ΔG vs. r passes through a maximum. The free energy of formation of a cluster with a critical size is

$$\Delta G^* = -\frac{4}{3}\pi(r^*)^3 \frac{k_B T \ln S}{v_l} + 4\pi(r^*)^2 \sigma. \quad (5)$$

[†] In the present review, the problem is considered in no more detail than follows from the early droplet model and determination of the surface and volume contributions. According to this model, a cluster is represented as an isotropic sphere covered with an infinitely thin film with a surface tension σ .

At a maximum, $r = r^*$ and $d(\Delta G)/dr = 0$. Hence, the radius of a critical nucleus can be easily determined as follows

$$r^* = \frac{2\sigma v_l}{k_B T \ln S}. \quad (6)$$

Equation (6) enables one to determine the equilibrium pressure of a saturated vapour over a droplet of radius r^* as a function of initial vapour supersaturation and cluster size. From Eqns (5) and (6), we have the following known equation

$$\Delta G^* = \frac{4}{3} \pi (r^*)^2 \sigma. \quad (7)$$

In the droplet approximation, ΔG^* is equal to one-third of the surface energy of the cluster. By excluding r^* , we obtain another form of the same equation

$$\Delta G^* = \frac{16}{3} \frac{\pi \sigma^3 v_l^2}{(k_B T \ln S)^2}. \quad (8)$$

The dynamics of droplet formation at pressures close to the equilibrium vapour pressure over the planar surface can be represented as follows. At $p < p_0$, the free energy of cluster formation rapidly increases as the cluster size increases. In the system occurring under these conditions, clusters of any sizes can, in principle, exist; however, the smallest clusters generally prevail in such systems. At $p > p_0$, the number of nuclei with a radius smaller than r^* undergoes random fluctuations. When the nucleus reaches a critical size, any favourable fluctuation leads to its infinite growth. Then the problem lies in estimating the rate (frequency) of formation of nuclei of the critical size.

The nucleation rate J is determined by the number of viable nuclei formed in a unit volume in a unit time. According to the classical theory,

$$J = \beta Z s^* c_{n^*} = 2v_l \zeta_c \sqrt{\sigma} \frac{N^2}{\sqrt{2\pi m}} \exp\left(-\frac{\Delta G^*}{k_B T}\right), \quad (9)$$

where β is a flow of condensing monomers, Z is the Zeldovich non-equilibrium factor; s^* is the surface area of the critical nucleus, c_{n^*} is the concentration of the critical nuclei, ζ_c is the condensation coefficient determined by the ratio of the number of molecules condensed on the nucleus surface to the total number of collisions between the molecules, m is the mass of the monomer and N is the concentration of the monomers. The Zeldovich non-equilibrium factor is determined as follows

$$Z = \sqrt{\frac{1}{2\pi k_B T} \left(\frac{\partial^2 \Delta G}{\partial n^2} \right)_{n^*}}. \quad (10)$$

The flow of condensing monomers can be expressed by the equation

$$\beta = \zeta_c \frac{p}{\sqrt{2\pi m k_B T}}, \quad (11)$$

where p is the partial pressure of the monomer.

As a result, the stationary growth rates are identical for clusters of any sizes.^{22, 25}

One of the most important problems of non-stationary nucleation kinetics is to determine the period (time) of non-stationarity. Zeldovich was the first to demonstrate that upon a sudden change in vapour supersaturation, a new stationary distribution of clusters follows the exponential law with a characteristic time constant τ called the time delay or relaxation time.⁵

According to the concepts proposed by Zeldovich, under conditions of a non-stationary process, the condensation rate is a function of time t (see Ref. 26)

$$J = J_s \left[1 - \exp\left(-\frac{t}{\tau}\right) \right],$$

where J_s is the stationary nucleation rate. Based on the results of the experimental investigation of the water vapour condensation in supersonic nozzles, Kantrowitz²⁷ found an empirical relationship between τ and vapour supercooling ΔT

$$\tau(\Delta T)^4 = 9.36 \times 10^3 \text{ (s K}^4\text{)}.$$

The simplest approximation, which allows one to estimate the time required for the achievement of constant amount of nuclei, was proposed in the study²⁸

$$\tau_s = \frac{25(n^*)^2 (2\pi m_1 k_B T)^{1/2}}{4\pi p (r^*)^2},$$

where m_1 is the mass of the monomer. According to this approximation, the time τ under standard experimental conditions of vapour nucleation (at $\zeta_c = 1$) is $10^{-5} - 10^{-7}$ s.

In the studies,²⁷⁻²⁹ it was assumed that clusters whose sizes are similar to the size of the critical nucleus are of kinetic importance. The time required for the achievement of 95%–99% of the stationary nucleation rate is often taken as the period of non-stationarity.^{30, 31} In principle, this level should be chosen depending on the accuracy of experimental measurements of the function $J(t)$ within the limits, where the change in the nucleation rate can be estimated. Knowing the dependence $J(t)$, the period of non-stationarity can be calculated.

In the investigation,³² it was demonstrated that the period of non-stationarity depends on the value and shape of the energy barrier to nucleation. The formation of a cluster consisting of two atoms is the slowest step of nucleation. Kantrowitz²⁷ quantitatively estimated the influence of cluster heating through the latent condensation heat on the nucleation rate. In a typical case of nucleation of a 2% water vapour in air, this effect leads to a fivefold decrease in J_s . In the study,³³ it was hypothesised that corrections for a non-equilibrium state are generally of little importance in the classical nucleation theory. Hence, such corrections are introduced only in extreme cases.

The condition of consistency of supersaturation in the system is a substantial limitation, which hinders the application of theoretical conclusions to the solution of practical problems, because nucleation most often occurs at variable temperature and supersaturation. It was demonstrated³⁴ that the rate of nucleation, which proceeds under conditions of a slow increase in supersaturation of the system, is lower than the rate calculated provided that the process is stationary. A decrease in the nucleation rate is proportional to a change in supersaturation, the time of non-stationarity and the size of the critical nucleus. The macroscopic nucleation theory includes certain unjustified assumptions and mathematical approximations. For example, it is assumed that small clusters can be considered as small portions of a macroscopic phase.

In principle, nucleus formation and growth should occur at any vapour supersaturation. The critical supersaturation is arbitrarily determined as a condition for rather fast nucleation. The nucleation rate changes with a change in the degree of supersaturation so rapidly that no significance has been attached to an error of even several orders of magnitude in the estimation of the pre-exponential factor in Eqn (9) (see, for example, Ref. 35).

Lothe and Pound^{36, 37} revised the classical nucleation theory and suggested an alternative scheme of condensation involving the following three steps:

- (1) nN_n molecules of a vapour are condensed into a liquid through isothermal compression;
- (2) this liquid is mechanically disintegrated giving rise to N_n droplets of equal size;
- (3) translational and rotational motion is imparted to all the droplets formed.

The authors of the cited studies introduced two additional multipliers, which were found based on the concepts of quantum statistics. Taking into account these multipliers, the nucleation rate increases by a factor of $10^{17} - 10^{20}$ (!). It should be noted that

the authors simply assumed that Eqn (8) is incomplete and should include a change in the translational and rotational entropy of the cluster. This question has been discussed in detail, for example, in Ref. 38. This problem was solved using statistical thermodynamic analysis. Finally, it was concluded that the correction for the translational and rotational motion of nuclei lacked experimental support (this problem was analysed in the review³⁹). It should be noted that the concept of formation of a stationary droplet in a vapour is a principal drawback of the classical theory because clusters execute, for example, Brownian motion.

Critics of the foundations of the classical nucleation theory primarily note that the properties characteristic of a macroscopic droplet (density, surface tension, saturated vapour pressure) cannot be extended to clusters consisting of only several tens of molecules. Since the properties of small clusters cannot be divided into volume and surface characteristics, the concept of surface tension seems to be artificial as applied to these clusters. To eliminate this problem, the excess free energy of the cluster can be, for example, determined as the difference between its free energy and the free energy of the same number of molecules present in a macroscopic volume of the condensate.

In the studies,^{40,41} the following dependence of the surface tension on the radius of the droplet was deduced:

$$\sigma(r) = \sigma_0 \left(1 - \frac{2}{kr} + \frac{2}{k^2 r^2} \right), \quad (12)$$

where σ_0 is the surface tension of the planar surface of the liquid, $1/k \approx (0.2-0.5) \times 10^{-7}$ cm.

When considering rather small clusters, not only the equation for σ but also the Kelvin equation [Eqn (6)] should be changed.⁴² However, the authors of the studies^{43,44} believed that the Kelvin equation is applicable to droplets of sizes ≥ 20 Å. This is contradictory to the Tolman equation. The latter equation relates the surface tension to the droplet size. According to the Tolman thermodynamic theory,⁴⁵ in the case of high surface curvature, a change in the surface tension should be described by the equation

$$\frac{\sigma}{\sigma_0} = \frac{1}{1 + 2\delta/r}, \quad (13)$$

where δ is 0.25–0.6 of the diameter of the molecule.

Until recently, the efforts of many researchers were directed primarily towards the improvement of the classical model by making it consistent with thermodynamics by introducing additional correction coefficients, which take into account individual factors. However, the theory did not become universal.

2. Modifications of the classical nucleation theory

In recent years, one of the versions of the classical theory, the so-called self-consistent theory (SCT) of nucleation, has gained acceptance.^{46–48}

From Eqn (1) describing the change in the free energy of a cluster in the classical nucleation theory, it follows that the work of formation of cluster consisting of one monomer is not equal to zero. By contrast, the change in the free energy of monomers in SCT is equal to zero due to the introduction of the corresponding corrections. According to this theory,

$$\Delta G = (4\pi r^2 - s)\sigma - (n - 1)k_B T \ln S, \quad (14)$$

where s is the area of monomer surface.

Using Eqn (14) written for the droplet approximation, we have a new equation for the nucleation rate

$$J_{\text{SCT}} = \frac{\exp(\sigma s/k_B T)}{S} J, \quad (15)$$

where J is the rate calculated in the context of the classical nucleation theory according to Eqn (9). It can be seen that this equation differs from the classical one by the presence of the

coefficient e^{Θ}/S (here $\Theta = \sigma s/k_B T$ is the surface energy of the monomer). The remaining physical assumptions in SCT are identical to those used in the classical nucleation theory.

The basis for the Dillmann–Meier theory is the semiphenomenological droplet model of the cluster formation.⁸ In this case, the expression for the free energy includes such vapour parameters as virial coefficients, pressure and density at the critical point. The Dillmann–Meier theory takes into account all significant (in the author's opinion) contributions to the energy of cluster formation. The agreement between experimental results and data obtained in the context of the Dillmann–Meier theory was discussed in the studies.^{8,49}

Dillmann and Meier modified Fisher's expression⁵⁰ for the free energy of cluster formation by adding the coefficient k_n , which reflects the difference between the surface energies of the cluster and macroscopic liquid droplet

$$\Delta G = k_n \sigma s n^{2/3} + \tau k_B T \ln n - k_B T \ln q_0 V - n k_B T \ln S, \quad (16)$$

where k_n , τ and q_0 are parameters of the model and V is the volume of the system. The first term corresponds to the surface energy of the cluster and the last term takes into account relaxation of the metastable state. It should be noted that the authors did not discuss the question as to how the surface tension should be specified. The remaining two terms take into account the contributions of the translational, vibrational and rotational degrees of freedom to the free energy of the droplet. Unlike Lothe and Pound,^{36,37} who calculated these contributions from the Boltzmann distribution, the authors of the cited study introduced the parameters τ and q_0 normalised to the experimental values. The configurational contribution to the overall sum is small and, hence, it is ignored.

The expression for the coefficient k_n was proposed by Tolman⁴⁵

$$k_n = f\left(\frac{\delta}{r}\right),$$

where δ is the submolecular length, which is smaller than the radius of the monomer. Using the approximation of a spherical cluster, Dillmann and Meier⁸ expressed the dependence of k_n on the cluster radius as the first terms of the power series

$$k_n = 1 + \alpha_1 n^{-1/3} + \alpha_2 n^{-2/3}, \quad (17)$$

where

$$\alpha_1 = \frac{(k_2 - 1) - (k_1 - 1)2^{-2/3}}{2^{-1/3} - 2^{-2/3}}, \quad (18)$$

$$\alpha_2 = -\frac{(k_2 - 1) - (k_1 - 1)2^{-1/3}}{2^{-1/3} - 2^{-2/3}}. \quad (19)$$

These authors obtained the expressions for k_1 and k_2
first two derivatives of the density with respect to pressure

$$k_1 = -\frac{1}{\Theta} \ln \left(\frac{p_s}{q_0 k_B T} \right), \quad (20)$$

$$k_2 = -\frac{1}{2^{2/3} \Theta} \ln \left[-\left(\frac{p_s}{q_0 k_B T} \right)^2 2^{\tau-1} q_0 B \right], \quad (21)$$

where B is the second virial coefficient. The parameters τ and q_0

the state of the liquid
 ρ

$$c = q_0 \xi(\tau - 1), \quad (22)$$

$$p_c = q_0 k_B T_c \xi(\tau).$$

Here, ρ_c , p_c and T_c are the critical density, pressure, respectively, and ξ is the Riemann function.

The nucleation rate in the Dillmann–Meier theory is calculated by the equation:

$$J_{\text{DM}} = \frac{1}{3} \sqrt{\frac{\Theta}{\pi} \left[1 + \alpha_1 (n^*)^{-1/3} + \frac{9\tau}{2\Theta} (n^*) \right]^{-2/3} \frac{s_1 p_v}{\sqrt{2\pi m k_B T}}} \times \quad (23)$$

$$\times q_0 \exp[-k_n \Theta (n^*)^{-2/3} - \tau \ln n^* + n^* \ln S],$$

where p_v is the vapour partial pressure and m is the molecular mass.

The size of the critical nucleus (the number of atoms or molecules in this nucleus) n^* is determined by finding the real root of the cubic equation

$$\tau x^3 + \frac{1}{3} \alpha_1 \Theta x^2 + \frac{2}{3} \Theta x - \ln S = 0.$$

Here

$$x = (n^*)^{-1/3}, \quad \Theta = \frac{\sigma s_1}{k_B T}.$$

The Dillmann–Meier theory is consistent with the classical nucleation theory at $\tau = 0$, $q_0 = p/k_B T$ and $k_n = 1$. The contradictions in the Dillmann–Meier theory were discussed in the study,⁴⁹ where corrections for the imperfectness of a vapour were introduced. However, the calculations performed with consideration for these corrections resulted in even poorer agreement with experimental observations.

Frenkel⁶ introduced the concept of heterophase fluctuations in a vapour, which are small density fluctuations and do not disturb a particular aggregate state of the system. According to this concept, Frenkel assumed that the system is not quite homogeneous, *i.e.*, it contains prenuclei of a new phase already before the onset of the phase transformation.

The fluctuation mechanism of nucleation of a supersaturated vapour was developed in the publications.^{51–53} It was suggested that in small subsystems isolated from a large system, fluctuations could occur such that their density reaches the value corresponding to conditions of spinodal decomposition, *i.e.*, of activationless nucleation of the condensate. The conditions of spinodal decomposition were considered using nonane as an example. For this purpose, the Peng–Robinson equation of state (see references in the study⁵¹) was rearranged to give

$$P = \frac{RT}{v-b} - \frac{a_T}{v(v+b) + b(v-b)} - \frac{d(\sigma s/n)}{dv}, \quad (24)$$

where P is the pressure in the subsystem, v is the molar volume of the cluster consisting of n molecules, a_T is a temperature-dependent constant, b is a constant, s is the surface area of the fluctuating volume. In this case, the Gibbs potential takes the form

$$G = A + PV = A - v \left(\frac{dA}{dv} \right),$$

where A is the Helmholtz potential. The latter term in Eqn (24) describes the contribution of the bubble pressure within the microvolume.

A change in the Helmholtz potential due to a fluctuation of a small subsystem is described by the equation

$$\Delta A_s = v_s(P_s - P_p),$$

where the index s signifies the spinodal conditions and P_p is the pressure in the starting phase. Following the well-known Landau–Lifshits approximation, the frequency of cluster formation (J) was determined^{51–53} as the density fluctuation

$$J = \Omega \exp\left(-\frac{\delta n_0 \Delta A_s}{k_B T}\right) \exp\left(-\frac{t}{\tau}\right),$$

where Ω is the coefficient corresponding to the number of fluctuations in the starting phase in a unit volume in a unit time; $\Omega = \Omega_0(1 - T_r)^{3.57}$ ($\Omega_0 \approx 10^{23}$, $T_r = T/T_c$, T_c is the critical temperature); δn_0 is the fluctuation of the number of molecules in the cluster. The second exponent describes relaxation of fluctuation

$$\frac{t}{\tau} = \beta^{-1}(1 - T_r)^3,$$

where β^{-1} is the constant associated with the diffusion coefficient within the fluctuating bulk. As a result, the expression for the nucleation rate takes the form

$$J = \Omega_0(1 - T_r)^{3.57} \exp\left[-\alpha \frac{(1 - T_r)^5}{T^4} (\ln S)^{-3}\right] \times \quad (25)$$

$$\times \exp[-\beta(1 - T_r)^{-2}],$$

where α is a constant. It was assumed⁵¹ that the nucleation begins when the size of the cluster reaches a size larger than the size of the classical critical nucleus. For such clusters, the condition of equality of the surface and volume contributions to the Gibbs free energy is fulfilled. The pre-critical nucleus has a lower density. At the pre-critical nucleus–vapour interface, the pressure jump is absent. Finally, as applied to the Peng–Robinson equation of state, nucleation is considered as local spinodal decomposition to give the Ostwald nucleus and supersaturated mother phase. In this case, the nucleation rate (like in the classical nucleation theory) is described by the exponential equation but with a different pre-exponential factor at the logarithm of supersaturation. According to the classical nucleation theory [see Eqn (8)], the logarithm of the nucleation rate should be a linear function of the value reciprocal to the square of the logarithm of supersaturation. By contrast, according to Eqn (25), this value is inverse to the cube of the logarithm of supersaturation. However, the linear regressions of the experimental nucleation rates both as the functions $(\ln S)^{-3}$ and $(\ln S)^{-2}$ give equally good approximations.

It was noted⁵² that within the framework of the fluctuation model, the effect of the total pressure in the system on the nucleation rate, which is not predicted by the classical theory, can be attributed to compression of a nucleus under the action of a carrier gas. The limitation of the fluctuation model is that it assumes the independence of the density (or supersaturation) fluctuations. The fluctuation lifetime should be sufficient for spinodal decomposition giving rise to a pre-critical nucleus. At high temperatures and large supersaturations, the independence of fluctuations can be disrupted due to an increase in the coherence length. The above-considered approach has not been further developed, but can be mentioned as one of examples of possible theoretical models.

The theory of heteromolecular (binary) nucleation, as noted by Volmer,⁵⁴ began to be developed after the publication by Flood, who used the thermodynamic method, calculated the critical vapour supersaturation for aqueous-alcoholic mixtures and studied experimentally this supersaturation in a Wilson chamber. The experimental data were in qualitative agreement with the theoretical results. This theory was further elaborated in the investigation,⁵⁵ where the work of formation of two-component critical nuclei with different compositions and of different sizes was examined.

The solution of a differential equation describing the nucleation kinetics⁵⁶ made it possible to reveal the characteristic features of the free-energy surface of clusters as a function of the cluster composition, *viz.*, n_1 and n_2 , where n is the number of molecules of the corresponding component (1 or 2) in the cluster. The equation for the homogeneous nucleation rate in a binary system is analogous to Eqn (9) for one-component nucleation

$$J = C \exp\left(-\frac{\Delta G}{k_B T}\right), \quad (26)$$

where the pre-exponential coefficient C depends only slightly on the external conditions and ΔG is the energy of formation of a critical nucleus. For binary nucleation, the coefficient C was first determined by Reiss.⁵⁶ Stauffer⁵⁷ studied nucleation in an analogous system without considering the direction of nucleation in the bulk (like in the studies^{56,58,59}) and obtained a self-consistent expression for the growth angle.

A quantitative simulation of vapour nucleation in a binary water–ethanol system,⁶⁰ which was carried out as a continuation of the study,⁵⁶ made it possible to calculate the critical supersaturations and achieve good qualitative agreement with experimental data.¹⁸

The correct determination of a saddle point on the free-energy surface of clusters is of great importance for an adequate prediction of the binary nucleation rate. This point can be determined by solving two equations:

$$\left(\frac{\partial \Delta G}{\partial n_1}\right)_{n_2} = 0,$$

$$\left(\frac{\partial \Delta G}{\partial n_2}\right)_{n_1} = 0.$$

Generally, it is assumed that the cluster retains a homogeneous composition throughout the bulk. The equations include the derivatives of the surface tension

$$\left(\frac{\partial \Delta G}{\partial n_1}\right)_{n_2} = \mu_{1l} - \mu_{1v} + \frac{2\sigma v_1}{r^*} - \frac{3X^* v}{r^*} \frac{\partial \sigma}{\partial X} \Big|_{X=X^*} = 0, \quad (27)$$

$$\left(\frac{\partial \Delta G}{\partial n_2}\right)_{n_1} = \mu_{2l} - \mu_{2v} + \frac{2\sigma v_2}{r^*} - \frac{3v(1-X^*)}{r^*} \frac{\partial \sigma}{\partial X} \Big|_{X=X^*} = 0, \quad (28)$$

where μ_l and μ_v are the chemical potentials of the liquid and vapour phases, respectively; v_1 and v_2 are the partial molar volumes of components 1 and 2, respectively; $v = (1-x)v_1 + xv_2$ is the molar volume of the solution; $X = n_2/(n_1 + n_2)$.

However, it was demonstrated^{60–63} that the coordinates of the saddle point cannot precisely be determined using Eqns (27) and (28) because of the insufficiently correct description of the clusters. Various numerical methods have been proposed for calculating saddle points. In particular, it was postulated⁶⁴ that σ is constant at a particular composition of the nucleus. However, this assumption excludes, for example, the dependence of the excess energy on the cluster size and, hence, the coordinates of the saddle point cannot be accurately determined. An example of the practical use of these calculations is the study,⁶⁵ where the nucleation rate of a mixture of water and sulfuric-acid vapours was determined. More recently, analogous calculations were carried out at different supersaturations.⁶⁶

A two-channel mechanism of nucleation in a binary system was considered in the study.⁶⁷ Two-channel nucleation occurs, when two saddle points appear on the surface of the Gibbs free energy. The relative contributions of individual channels to the nucleation process were estimated by thermodynamic methods.⁶⁸ Binuclear nucleation of vapours as liquids with limited mutual solubility was investigated.^{69–71} Besides, binuclear nucleation of miscible liquids was also studied.⁷²

A mixture of a vapour and a carrier gas is a special case of a binary system. Nucleation of propane-1,2- and -1,3-diols in carbon dioxide and sulfur hexafluoride was studied.⁷³ A phase transition in the condensate was observed for each propane-diol–gas pair. An increase in the concentration (pressure) of the carrier gas was accompanied by a shift in the phase transition temperature toward the critical temperature of this gas. By changing the carrier gas (for example, from CO₂ to SF₆), the temperature of the phase transition in nuclei of the condensate can be changed by 15–20 °C. It should be noted that phase transitions

in equilibrium propane-1,2- and -1,3-diols do not occur in the temperature range in which the nucleation rates were measured. The appearance of phase transitions in the condensate upon the addition of a carrier gas is indicative of the involvement of its molecules in the formation of critical nuclei of the condensate. The composition of the nuclei was determined from the slopes of isotherms of the nucleation rate and it was found that they contained up to 20% of carrier-gas molecules.

Experimental and theoretical studies often do not take into account the fact that a carrier gas can act as a nucleating component (see, for example, Refs 74 and 75), and vapour nucleation in a gas atmosphere is considered in the approximation of a one-component vapour. In this case, the gas is considered as a medium providing thermostatic control of nucleation. This assumption, which has been accepted in early experimental studies of vapour nucleation, should be revised.

It was demonstrated⁷⁶ that two different methods of calculations of nucleation rates in heteromolecular systems in a stationary state, which have been proposed in the studies,^{57,77} are virtually equivalent. One method⁵⁷ is based on the classical theory of binary nucleation, whereas an alternative method⁷⁷ is based on the solution of the Fokker–Planck equation. Although calculation by these two methods gave the same binary nucleation rates, the latter are inconsistent with the experimental data.⁷⁵ Analysis⁷⁷ of different conclusions⁴³ of the classical theory of binary nucleation^{62,78,79} demonstrated that the methods under consideration give different estimates of the size and composition of critical nuclei. It should be noted that the solution of the Fokker–Planck equation requires the introduction of coefficients accounting for evaporation and accommodation of molecules in the cluster, and their uncertainty leads to a substantial decrease in the reliability of the results of calculations. The use of different values of these coefficients enables one to find numerical and sometimes even analytical solutions, which are nevertheless only of qualitative importance.

The parametric model considered in the study⁸⁰ was based on the equation reduced as applied to the nucleation rate of a one-component vapour (26) and the following assumptions were made: (1) the cluster grows (decreases) through condensation (evaporation) of monomers; (2) the probability of fixation of the molecule on the cluster surface upon collision is equal to unity; (3) clusters have a spherical shape; (4) interactions between clusters are absent. The authors of the cited study believed that incorrect results were obtained primarily because of the use of surface tensions measured for a planar interface. Hence, following Tolman,⁴⁵ the excess energy of clusters was calculated using expansion in a series

$$\sigma_{\text{micro}} = \sigma_0(1 + \alpha_\sigma n^{-1/3} + \alpha_\sigma^2 n^{-2/3} + \dots),$$

where σ_0 is the surface tension coefficient for the planar interface; $\alpha_\sigma = 2\delta/r_1$ is the so-called Tolman length (δ is the length of the order of the molecular size; r_1 is determined from the equation $r_n = r_1 n^{1/3}$, r_n is the radius of the cluster consisting of n monomers). The work of formation of the cluster was determined using Eqn (16) converted to the parametric form

$$\beta\Omega_n = \beta\sigma_{\text{micro}}sn^{2/3} + \tau \ln n - \ln q_0 V_c.$$

The parameters of this equation are as follows: $\beta = (k_B T)^{-1}$, $2.1 < \tau < 2.2$, $q_0 \sim \rho_c/5$, where ρ_c is the density at the critical point.

The equilibrium density (ρ_n) of clusters is calculated assuming the Boltzmann distribution

$$\rho_n = \frac{1}{V_c} \exp(-\beta\Omega_n),$$

where V_c is the volume of integration for the determination of the configuration integral for the cluster. The parameters are normalised by extrapolation to the critical point.

A comparison of the nucleation rates calculated within the framework of the classical and parametric theories demonstrated

that the difference is very small in the case of water. In the study,⁸⁰ the nucleation rate predicted by different theories was compared with the published experimental data for vapours of different compounds. It appeared that the use of the parametric model gave the best results.

In the study,⁸¹ the influence of an increase in the pressure of a carrier gas as a perturbing parameter was taken into account. The properties of the nucleating vapour vary depending on this parameter. The authors believed that this fact leads to reduction of binary nucleation to nucleation of a one-component vapour. The criterion characterising the perturbing action of the pressure of a carrier gas should meet the condition $x_g \ll (S - 1)/S$, where x_g is the solubility of the carrier gas in the liquid phase at supersaturation S . Another parameter was introduced to compensate the effects of a decrease in the surface tension and an increase in the saturating vapour density. This modification of the nucleation theory is consistent with the model proposed in the study⁸⁰ as well as with the density functional theory.⁸² Evidently, the introduction of additional parameters can lead to agreement between the theory and experiment. In the study,⁸³ multicomponent nucleation was described for a ternary system using a one-component model and introducing the effective parameters of the process.

Apparently, such approaches can be applied to the parametric description of practically important systems. However, these approaches seem to hold little promise from the viewpoint of the development of the theory because they have poor predictive ability even with respect to the model system under consideration. It is more correct to refer to this type of parametrisation as interpolation of experimental data. This parametrisation has no predictive potential outside the range of experimental characteristics parametrised and there is little likelihood that it will be correct even if only one family of nucleating systems is treated.

Below are considered models in which the intermolecular interaction potential is introduced in an explicit form, *i.e.*, through parameters determining the force interaction and geometric arrangement of molecules in the system. A simplified consideration of collective interactions can be, in particular, performed by introducing the dependence of the distribution function on a particular macroscopic parameter, for example, on the distribution density of molecules (density functional theory), which, in turn, includes the effect of collective interactions. The classical theory takes into consideration the fluctuation character of the exchange of substance between a nucleus and its environment. The number of molecules in the nucleus is a variable characterising the state of the system, all other parameters being equal to their average values.

In a number of studies (for example, in the study⁸⁴), the influence of the pressure of a carrier gas on vapour nucleation was considered. It was demonstrated that the gas can either accelerate or decelerate the nucleation frequency. This depends on the sign of the second virial coefficient. If a carrier gas is absent, the different degrees of freedom of the cluster and particles forming the cluster can correspond to different temperatures.^{85,86} This effect is observed in experiments with molecular beams expanding into vacuum. In experiments with a monosilane–argon mixture, nucleation was observed in a pulse supersonic jet.⁸⁷ In addition to clusters, mixed argon–silane complexes were detected for the first time and conditions for their formation in a flow were determined. The existence of mixed clusters is direct evidence for the involvement of the carrier gas in the nucleation of a new phase. The dependences of the concentrations of monomers and cluster ions on the stagnation pressure indicate that condensation in a flow at low stagnation pressure gives rise only to individual monosilane clusters, whereas condensation at high pressure affords monosilane–argon clusters. It is advantageous to analyse the nature of this phenomenon using phase diagrams of the system.

The determination of the nucleation rate by solving the one-dimensional Fokker–Planck equation for the probability density

of the size distribution of nuclei is justified if rather rapid relaxation of all degrees of freedom takes place in the cluster. The necessity of taking into account relaxations and, correspondingly, using the multidimensional Fokker–Planck equation appears only when the above-mentioned condition is violated. Admittedly, the classical theory, which has made it possible to solve the fundamental problem of the formation of a new phase in the first approximation, is characterised by a high degree of completeness and can serve as an example of a reasonable combination of the approximations and the minimum necessary complexity of the mathematical apparatus used. At the same time, it is evident that the classical nucleation theory should give way to a theory possessing an essentially different axiomatic basis, whose foundations are already being developed.

The density functional theory holds considerable promise.[‡] In this theory, only a part of collective interactions responsible for the attraction energy of molecules is taken into account in an explicit form. Short-range interactions are determined in the approximation of rigid spheres. This approach enables one to consider interactions between molecules in the pair-additive terms for which good approximations based on experimental data are available.

Oxtoby and co-workers^{88–91} considered the nucleation process using the density functional theory. Unlike Vlasov,³ who introduced the concept of a collective interaction from the very beginning (*i.e.*, he assumed that weak collective interactions between molecules lead to the existence of the system as an organic whole and cause a phase transition at particular parameters), Oxtoby believed that the presence of a gas–liquid interface is a manifestation of weak density inhomogeneity of the system. The profile of the equilibrium average density is determined from the condition of equality of the thermodynamic potential to zero. In this case, the expression for the free energy functional takes the form

$$\Omega_V(\rho) = \int \{f[\rho(r)] - \mu\rho(r)\}dr + \frac{1}{2} \iint \phi(|r - r_1|)\rho(r)\rho(r_1)drdr_1,$$

where f is the free energy of the unit volume of a liquid in the approximation of rigid spheres,⁸⁸ which was assumed to be known. Here, it is assumed that the potential of interactions can be represented as the sum of repulsion forces (in the approximation of rigid spheres) and attraction forces. This sum is denoted as ϕ . The functional derivative of this equation is an integral equation for the critical density profile.

In the study,⁸² the pre-exponential factor used in the equation for the nucleation rate is identical to that in the classical nucleation theory. At the same time, it was noted that it is improper to use the classical pre-exponential factors in other theories. The description of the dynamics of the first-order phase transition presented in the study⁹² is still of great interest.

The density functional theory was applied^{93,94} to the investigation of gas–liquid nucleation in binary mixtures consisting of Lennard-Jones atoms in the approximation of one-point (monomers), two-point (dimers) and three-point (trimers) rigid spheres. The temperature dependence of the nucleation rate calculated within the framework of this theory is similar to the corresponding experimental dependence. At the same time, the results of calculations are not always consistent with the data obtained by other methods, for example, by numerical simulation. Numerical simulation (based on the Lennard-Jones potentials) was carried out for homogeneous gas–liquid nucleation in a binary mixture⁹⁵ and the dependences of the size and composition of critical nuclei on the composition and supersaturation of a vapour were studied. Growing nuclei are characterised by bifurcation of the composition. In the case of non-ideal systems, components cease to be soluble and droplets enriched with a particular component

[‡] In 1998, W Kohn (Austria) was awarded the Nobel Prize in Chemistry for his development of the density functional theory.

appear. However, in studies using the density functional theory, the researchers did not reveal fractionation of phases within the critical nucleus.^{96–98}

The theory of molecular homogeneous nucleation in a vapour phase¹ includes a minimum number of assumptions and parameters. Preliminary calculations carried out for argon by the Monte Carlo method⁹⁸ demonstrated that the free energy varies within two orders of magnitude. The authors of the cited study believe that areas of application of this method to the description of real processes of homogeneous nucleation in a vapour will be extended as the method is improved. One can partially agree with this statement, because it seems plausible that a reasonable simplification of the model of a nucleating system will allow one to obtain results, which can be verified experimentally.

The average values of the main parameters of an equilibrium system are determined by the conditions of its contact with the environment. To describe the non-equilibrium state, it is necessary to introduce additional parameters characterising the deviation of this system from equilibrium. The number and character of additional parameters required for the determination of the non-equilibrium state depend on a particular model.

The irreversibility can be described by equations for random processes, for example, by the Fokker–Planck kinetic equation or the Langevin equation. It should be noted that the area of application of such equations can be narrowed under certain conditions. As an example, let us consider the kinetic equation, which, on the one hand, serves for the description of transitions between the states of the system and, on the other hand, was derived using methods of non-equilibrium statistical mechanics in the approximation of noninteracting particles.^{2,3} In the absence of memory effects, the time dependence of the probability $[p_n(t)]$ of the system occurring in the state n is determined by the frequency of its transitions (w_{nm}) from the state m

$$\frac{dp_n(t)}{dt} = \sum_m w_{nm} [p_m(t) - p_n(t)].$$

According to the principle of detailed equilibrium, the frequencies of direct transitions are equal to those of reverse transitions, *i.e.*, $w_{nm} = w_{mn}$. Taking into account the identical relation $\sum_n p_n(t) = 1$, we find the time derivative of entropy

$$\frac{dS(t)}{dt} = \frac{1}{2} k_B \sum_n \sum_m w_{nm} [p_m(t) - p_n(t)] [\ln p_m(t) - \ln p_n(t)] \geq 0.$$

Therefore, if the states, between which transitions are allowable, are equiprobable, *i.e.*, $p_n(t) = p_m(t)$, the process under consideration is an equilibrium. The deviation from the identity of the conditions of stationarity and equilibrium of the process (which follows from the above-given equations) can take place only if the principle of detailed equilibrium breaks down. Consequently, if this principle is fulfilled, the kinetic equation in stationary conditions is inapplicable to the description of irreversible processes, in particular, of nucleation. It should be noted that the description of processes of the appearance and growth of clusters in a non-equilibrium system presents problems related to the non-equilibrium thermodynamics and the kinetic theory of rarefied gases (see, for example, the review⁹⁹).

Roldugin¹⁶ described the nucleation process in the context of concepts of non-equilibrium thermodynamics and analysed the symmetry of the diffusion tensor in the generalised parameter space of the process. He hypothesised that in the case of, for example, a one-dimensional system, the nucleation rate should be several orders of magnitude lower than that predicted by the classical theory. It should be noted that these conclusions may be influenced by a popular error in overestimating the reliability of experimental data. The above-discussed inconsistency between experimental data obtained by different researchers could be explained quite prosaically taking into account that many important problems associated with experimental procedures for per-

forming nucleation remain to be solved. For example, there is a pressing need for the determination of an absolute error of experimental measurements.

In the classical kinetic theory of gases, collisions are taken into account only in short-range interactions. The question of whether it is possible to improve the description of long-range interactions in an ensemble of particles by successive inclusion of double, triple, quaternary, *etc.* collisions remains to be answered. Moreover, the kinetic equations include terms related to both the flow and collisions, which cannot be separated from each other.^{99–101} An approach was developed as applied to non-equilibrium processes in non-ideal gases. This approach allows one, in principle, to derive closed kinetic equations provided that the initial correlations between two, three, *etc.* particles are weakened. However, it appeared that collision integrals, which determine dissipative processes in kinetic equations, become divergent when interactions of four and larger numbers of particles are taken into account¹⁰² and only summation of the infinite number of multi-particle processes eliminates the divergence.

3. Use of the formal apparatus of quantum mechanics for the description of nucleation

First studies of nucleation at temperatures close to absolute zero using the formal apparatus of quantum mechanics were carried out as early as 1972.^{103,104} In these investigations, relaxation of a metastable state was associated with tunnelling of a nucleus of a new phase through a potential barrier in the configuration space. The nucleus passes through a series of local inhomogeneous states. In the phenomenological description of nucleation accepted in early studies, the problem of growth of a new phase was separated from the quasiclassical problem of the determination of a spectrum of cluster sizes. Later on, the quantum-mechanical description was proposed.¹⁰⁵ This approach includes quantum fluctuations, which lead to the tunnel transition of virtual clusters.

As an example, let us consider a brief scheme of quantum calculations of the nucleation rate.¹⁶ A change in the nucleus radius r in the potential

$$V(r) = 4\pi r^2 \sigma - \frac{2}{3} \frac{4\pi \sigma}{r}$$

can be described by the Schrödinger equation

$$\left[-\frac{\hbar^2}{2m} \nabla^2 + V(r) \right] \psi(r) = E \psi(r),$$

where $\psi(r)$ is the wavefunction and E is the set of energies of quantum states.

Assuming spherical symmetry, the variables of the wavefunction $\psi(r) = [Z_n(r)/r] Y(\theta, \varphi)$, where $Y(\theta, \varphi)$ is a spherical function, can be separated. Hence it follows that the motion equation can be deduced for $Z_n(r)$ in the potential

$$U(r) = V(r) + \frac{l(l+1)\hbar^2}{2mr^2},$$

where l is the quantum number of the angular moment. At $l \neq 0$, there is an additional barrier, which noticeably decreases the probability of nucleation. Hence, the main contribution to nucleation is provided at $l = 0$. The probability of tunnelling P_t is determined by the equation

$$P_t \propto \exp \left\{ -\frac{2}{\hbar} \int_0^{r^+} [2m(r) V(r)]^{1/2} dr \right\},$$

where $r^+ = (3/2)r^*$ (r^* is the radius of the critical nucleus) and $m(r)$ is the effective mass determined by the relation

$$m(r) = \frac{4\pi}{\rho_v} (\rho_l - \rho_v)^2 r^3,$$

where ρ_l and ρ_v are the liquid and vapour densities, respectively.

A somewhat different approach was used in the studies.^{106, 107} According to the corrections^{108, 109} to the Lifshits–Kagan theory,^{103, 105} clusters are considered to be spherical and consist of an incompressible liquid whose energy depends on the cluster size. It is assumed that the centre of gravity of the clusters is at rest, whereas the surface layer and vapour environment move. The authors of the cited studies^{106, 107} examined the possibility of tunnelling from all energy levels, except for the ground level.

To summarise, it should be noted that the quantum theory of nucleation is still being developed. However, this is the only theory, which may be useful for the interpretation of the results of experiments, for example, on binary nucleation in the ^3He – ^4He system at temperatures close to 10^{-3} K,¹¹⁰ from the quantum standpoint. The quantum-mechanical approach to the description of ion-induced nucleation was employed in the investigation,¹¹¹ where the nucleation rate of a water vapour on Na^+ ions was estimated. The results of this investigation are comparable with the results following from the classical nucleation theory. In particular, the free energy minima and the sizes of the corresponding clusters are identical to within experimental error. The free energy maxima are also virtually identical, but the size of the critical cluster evaluated by the classical theory is 20% larger.

A system of noninteracting particles can be considered with the use of conventional methods of statistical mechanics, where the Hamiltonian of the system is represented as a sum of the Hamiltonians of individual particles. The applicability of these methods is limited by the region, where the Boltzmann statistics is fulfilled. Systems consisting of many particles obey the Boltzmann statistics.⁸

In the classical nucleation theory, molecules of a metastable phase and the nuclei formed in this phase are also treated as a mixture of noninteracting particles. In the thermodynamic consideration, the frequency of collisions of molecules with the cluster consisting of n molecules is calculated in the ideal gas approximation, *i.e.*, without regard for their interactions. In the kinetic consideration, an analogous approach was used for determining the frequencies of transitions of nuclei from one size to another, *i.e.*, the dependence of these frequencies on interactions of a nucleus with other molecules and clusters of the mother phase are ignored.

Phenomenological theories describing states of solutions (for example, the theory of regular solutions), which employ equations for a particular average state of the system consisting of many particles, can be assigned to the same type of theories. Since these equations are, generally, empirical, it is more correct to refer to these theories as empirical theories. One of the simplest phenomenological theories of equilibrium phase transitions taking into account the co-operative effect is the van der Waals theory of condensation.¹⁰⁰ It should be noted that the Kac potential (as an effective potential) used in the study¹⁰⁰ is not a realistic value and the extension of the results thus obtained to real (in a physical sense) potentials is still an open problem. Certain progress in the use of the models under consideration is attributable not to the validity of their main concepts but to an appropriate choice of additional factors, which, in turn, allows one to consider these models as phenomenological.

III. Experimental methods for studying nucleation

Experimental studies of nucleation were carried out for various objects, *viz.*, from a mixture of the ^3He – ^4He isotopes at temperatures of several thousandths of Kelvin up to a plasma. Complex processes, such as the formation of solid-phase nuclei from cooled molten metal and metal boiling upon superheating, formation of exciton drops and cavitation, for example, in a screw propeller or

in the case of nuclear reactor accidents, *etc.*, were also investigated.

Experimental investigation of bulk nucleation is a complicated problem, because the parameters of the formation of a new phase rapidly vary with time and space, which substantially complicates their measurements. Hence, experimental publications on nucleation are scarcer than theoretical studies. Experiments on nucleation are hindered due to the lack of well-developed algorithms for the determination of parameters for many nucleating systems. Procedures for studying bubble frequencies in liquids and nucleation in a supersaturated vapour have been best elaborated. These methods can be extended to other systems.

1. Thermal effects of condensation

The non-isothermality of a real nucleation process is the subject of considerable attention. However, the classical theory assumes that nucleation is an isothermal process. In other words, a mixture of clusters and monomers is treated as if it were in a thermostat. In real systems, an inert gas, which is not condensed under the experimental conditions, plays a role of such a thermostat. The energy transfer occurs due to collisions of molecules of an inert gas with a vapour and clusters, and the final number of gas molecules as well as the final rate of this process are such that the system is transformed into the state in which the average temperature of clusters is higher than that of the vapour–gas mixture. This leads to a decrease in the efficiency of elementary events of the addition of vapour molecules to small clusters. According to an estimate made in the study,³⁹ the effect of non-isothermality should be manifested at nucleation rates higher than $10^2 \text{ cm}^{-3} \text{ s}^{-1}$. More recent data obtained by methods of non-equilibrium thermodynamics¹¹² demonstrated that the influence of non-isothermality should decrease as the vapour supersaturation is increased, *i.e.*, at high nucleation rates.

The thermal effects of condensation were considered in a series of studies by Kuni and co-workers.^{113–124} The data on a stationary flow and stationary distribution of near-critical droplets, their temperatures and characteristic sizes, rates of free-molecular and diffusion growth of overcritical droplets, the spectrum of their sizes and time of formation as well as information on the conditions of applicability of a macroscopic approach to the kinetics of condensation were surveyed in the study.¹¹³ The final step of non-isothermal condensation was discussed in the publication.¹¹⁴ Non-isothermal condensation at moderate concentrations of an inert gas was considered in the investigation.¹¹⁵ A two-dimensional description of the material and heat balance of particles of a nucleating liquid phase in a vapour–gas medium was published and the effect of the quasi-isolated state of a nucleus of a liquid phase under non-isothermal conditions was examined in the studies.^{116, 117} The two-dimensional Zeldovich–Frenkel equation in the kinetics of non-isothermal nucleation of a liquid phase was considered.¹¹⁸ Problems of thermal relaxation of particles of a nucleating liquid phase were discussed in the study.¹¹⁹ The effect of the temperature of particles of a liquid phase on the rate of non-isothermal nucleation and other effects associated with heat exchange were investigated in a series of studies.^{120–124}

The theoretical problem of thermal effects of condensation seems to be solved, but the predictions of the theory remain to be experimentally confirmed.

2. Nucleation in electrochemical processes

Let us consider an electrochemical process as an example of practical application of the nucleation theory.[¶]

A substrate plays a very important role in such processes. The effect of the substrate state on the nucleation kinetics was

§In this case, the motion of each particle in the field of surrounding particles is considered as a motion in the averaged field, which is independent of the local arrangement of the particles.

¶Problems of nucleation in electrochemical processes were surveyed in detail in the review.¹²⁵

studied.^{126–129} In particular, chemical interactions upon adsorption and the role of the real surface in crystallisation of a new phase were discussed in detail.¹²⁷ The concept of nucleation on active centres of the substrate surface, which have a high free energy, was developed.^{128,129} If the effect of shielding zones occurring around growing nuclei is ignored,¹³⁰ the activity distribution function of the centres can be determined based on experimental dependences of the number of nuclei on supersaturation.¹³¹

When describing the nucleation in electrochemical systems, it is generally assumed that

— in the presence of a double electric layer and electric charges on particles that arrive at the electrode surface, it is necessary to take into account the kinetics of charge transfer at the electrode;

— adsorption of water molecules, cations, anions and organic compounds on the electrode leads to a change in the work of nucleation and influences the discharge kinetics of ions;

— diffusion is of importance: the lower is the activation energy of surface diffusion and the stronger are the interactions of the adsorbed atoms with the substrate, the higher is the nucleation rate on the electrode surface.

The heterogeneous nucleation theory assumes that a liquid nucleus on the surface of a solid substrate has a shape of a spherical segment. A change in the energy of the system upon the formation of a liquid nucleus is proportional to the work of homogeneous nucleation

$$\Delta G_{\text{het}} = \Phi \Delta G_{\text{hom}},$$

where Φ is the shape factor, which depends on the wetting angle and is equal to the ratio between the volume of the spherical segment of the liquid phase on the substrate surface and the volume of the sphere of the same radius.

In this case, the supersaturation can be characterised by the overvoltage at the cathode η . The dependence of the stationary nucleation rate J_0 on the work of nucleation has the form

$$J_0 = D_c Z(1) \exp\left(-\frac{\Delta G}{RT}\right) = K_1 \exp\left(-\frac{K_2}{\eta^2}\right), \quad (29)$$

where D_c is the flow of atoms that add to the critical nucleus; $Z(1)$ is the concentration of individual atoms; K_1 and K_2 are constants. Equation (29) adequately describes experimental data within a narrow range of the overvoltage at the cathode.¹²⁵ This is not surprising because the use of the classical theory is most efficient for describing simple nucleation processes in electrochemical systems, *viz.*, vapour nucleation or cavitation.

The experimental results obtained within narrow ranges of supersaturation were discussed in the publications.^{126,132–137} Analysis of the data obtained within the framework of thermodynamic and atomistic models led to virtually the same conclusions. In the model representations used in the cited studies, interactions between the nuclei formed are ignored.

In broad overvoltage ranges, the step of charge transfer assumes great importance. Hence, it is necessary to take into account the kinetics of ion discharge.^{138–143} In this case, the $\ln J_0 - (1/\eta^2)$ or $\ln J_0 - \eta$ dependences are linear and the constant K_2 in Eqn (29) can be determined from their slopes. Experimental investigations of the nucleation kinetics within broad ranges of supersaturation present considerable problems. At high supersaturations, coalescence of nuclei giving rise to aggregates is highly probable. The surface curvature of nuclei influences the activation energies of both the cathodic and anodic processes.^{142–144} The expressions for the stationary nucleation rate are deduced based on the Becker and Döring kinetic method.²²

Nucleation requires an expenditure of work proportional to the electrochemical potential difference.^{126,132,135,140,145,146} This work characterises the deviation of the system from equilibrium (values with the subscript 0 belong to a stable state and the

corresponding values without the subscript belong to a metastable state)

$$\Delta \bar{\mu} = \bar{\mu} - \bar{\mu}_0 = zF(\psi - \psi_0) = zF(E - E_0) = zF\eta,$$

where $\bar{\mu}$ is the thermodynamic potential, z is the ion charge, F is the Faraday number and E is the electrode potential. The potential of a metal nucleus is equal to the electrode potential E . The nucleus formation requires an expenditure of work

$$\Delta G = \Phi \frac{16\pi\sigma^3 V^2}{3(zF\eta)^2} = \frac{1}{2} n_c zF\eta.$$

In this case, Eqn (6) takes the form

$$r_c = \frac{2\sigma V}{zF\eta}.$$

It is assumed that the nucleation energy is determined by the amount of metal atoms deposited on the electrode surface rather than by the electrochemical potential difference.^{138,139,147–150} This approach corresponds to the assumption that the ion discharge giving rise to adsorbed atoms is independent of nucleation in a medium of neutral atoms on the substrate surface.

In electrochemical nucleation processes, the nucleus formation proceeds most probably by the direct insertion mechanism.^{151,152} In the gas phase, heterogeneous nucleation through the direct insertion of atoms or molecules into a nucleus is highly improbable.¹⁵³ The concentration of surface atoms has an effect only on the pre-exponential coefficient in the equation for the rate of the process. The work of nucleation is determined by the cathode overvoltage.¹⁵⁴

It should be noted that the work of nucleation is generally treated¹⁴¹ as a continuous function of the number of atoms in the cluster n , although this function is actually discrete. It is assumed that the nucleus is in metastable equilibrium with the mother phase and has a size at which the probability of further growth is equal to the probability of dissolution. In the case of fluctuation formation, the maximum work corresponds to the critical nucleus. The nucleus size depends on the structure of the cluster and the interaction forces between the atom and substrate.

It was believed¹²⁵ that the changes in the surface energy and the kinetic factor can be ignored in the consideration of nucleation processes within narrow ranges of supersaturation. Hence, the number of molecules (atoms) in the critical nucleus can be determined from the slope of the experimental dependence of the nucleation rate on supersaturation according to the equation

$$n_c = RT \frac{d \ln J}{d \Delta \mu}.$$

This equation was first proposed in the study devoted to nucleation of supersaturated vapours. Below the deduction of this equation is considered in detail. It should be noted that this equation enables one to determine the critical nucleus size regardless of the nucleation model used as well as to find the dependence of this size on supersaturation $\Delta \mu$.

In the review,¹²⁵ it was stated that a decrease in the nucleation rate in an electrochemical process following the stationary region in a voltammogram is attributed to an exhaustive consumption of the active centres of the substrate, overlapping of shielding zones or coalescence of growing crystals. In the nucleation theory, it was assumed that in the case of electrodeposition, active centres of the substrate can appear during the action of a nucleation pulse, the rate of their formation being dependent on the degree of supersaturation. The nucleation kinetics in various systems can be studied experimentally, in particular, by determining the time of formation of the first nucleus. Methods for calculations of the space and time distributions of nucleation events upon electrodeposition, which have been developed in the studies,^{126,132,151,154} allow one to perform more detailed analysis of the mechanism of nucleation. The magnetic properties of electrodeposited amor-

phous Fe–Cr melts were investigated, for example, in the study.¹⁵⁵

Adsorption of surfactants has an effect on the work of nucleation and the critical size of nuclei due to changes in the surface energy at nucleus–electrolyte and nucleus–substrate interfaces accompanied by changes in the wetting angle and shape factor.^{156, 157} The effect of surfactants on the initial steps of electrocrystallisation is manifested in the redistribution of the rates of formation and growth of nuclei of a new phase due to blocking of active centres of the substrate and inhibition of ion discharge on the surface of growing crystallites. On the whole, the effect of surfactants on nucleation is poorly known. Experimental studies are generally aimed at solving applied problems. In these studies, the frequencies of nucleation of a new phase are, as a rule, not measured. Scarce data on the measured nucleation rates in the presence of surfactants cannot as yet be systematised. A more detailed discussion of this problem is beyond the scope of the present review.

The phase formation upon electrodeposition was studied by analysing the time dependences of the current under potentiostatic conditions. The theory of growth of two-dimensional layers and formation of three-dimensional crystals was developed in the investigations.^{151, 158} In the last decade, the structures of various electrode materials, primarily, of atomic- and molecular-modified single-crystalline electrodes and electrodes including isolated nanoparticles have been established with very high accuracy by high-precision X-ray diffraction methods. These data enable one to reveal the characteristic features of a nucleation process giving rise to a particular structure. Evidently, coalescence and agglomeration, which accompany nucleus growth in the solid phase, hinder calculations of the number of nuclei of a newly formed phase.

Much less progress has been made in studying the structures of electrodes acting as catalysts, which are characterised by a large specific surface and a broad size distribution of particles (or blocks). Examples of such systems are electrolytic deposits of platinum metals on polycrystalline substrates. The dependence of the activity of platinum and palladium electrolytic deposits on the deposition potential is one of the prominent manifestations of the so-called 'structural effects' in electrocatalysis.^{159, 160} Multilayer deposits, for example, of platinum metals on polycrystalline foils, are very complex systems characterised by a multi-level structural hierarchy. It is hardly probable that their structures could be established at the nanostructural level. However, it is of great interest to reveal factors responsible for the reproducible formation of nanostructural fragments and find reliable correlations between the macroscopic properties of materials and structural characteristics as the first step of such investigations.

Measurements of copper *K* X-ray radiation made it possible to observe co-deposition of copper and chloride ions from an electrolyte solution on the Au(111) surface. These results are indicative of a high degree of statistical disorder of molecules in the deposit, the Cu–Cl, Cu–Au and Cu–Cu bond lengths and the corresponding bond angles varying within narrow ranges. These data are very useful in simulating nucleation and subsequent film growth by molecular dynamics methods. Chronocoulometric measurements provided information on the film composition and the number of electrons crossing the interface per copper ion. Electrocrystallisation on dislocation-free faces of silver single crystals was studied experimentally.¹⁵¹ The formation of anodic films was investigated.¹⁶¹ The results of studies using mathematical simulation (see, for example, Refs 162 and 163) are consistent with the classical nucleation theory. A model of two-dimensional nucleation and subsequent three-dimensional crystal growth was proposed in the study.¹⁶⁴

However, the seemingly good situation, which is manifested in the agreement between the results of theoretical studies of electrochemical nucleation and experimental data, resembles a situation, which has been observed in the field of investigation of vapour nucleation, when high-precision data have been lacking. Begin-

ning in the 1980s, the necessity of developing a universal theory of vapour nucleation and a need for searching new ideas for the elaboration of this theory became evident because a rather large number of systems were studied and experimental data were obtained with a sufficiently high accuracy.

3. Nucleation in dense ion plasma

Atomic and molecular systems are traditionally studied by approximate methods based on expansion of a small parameter in a series (for example, virial expansions in statistical physics, the non-linear perturbation theory in non-equilibrium statistical mechanics, the perturbation theory in quantum mechanics, *etc.*). In the review,¹⁶⁵ it was emphasised that a small system follows the Gibbs distribution law provided that interactions with the environment are weak. Hence, the choice of such a system from a statistical ensemble should be the subject of the special consideration. There are different ways of isolating a small system from a macroscopic one.

It should be noted that the time it takes for the equilibrium to be established within a cluster is much shorter than the time interval between collisions of the cluster with gas particles. Hence, the cluster can be considered as an isolated system during a certain (short) period of time. The properties of the cluster as a small system influence the behaviour of the macrosystem as a whole. The thermodynamic properties of critical nuclei are responsible for the nucleation rate. A nonideal gas is considered as a mixture of clusters of different sizes, *viz.*, dimers, trimers, *etc.*

The description of clusters of charged particles in the region of a substantial deviation from the ideal state is hampered by the necessity of taking into account long-range Coulombic interactions. The collective effects are not weakened as the plasma density decreases. By contrast, this effect increases because the radius of the Debye shielding sphere increases. For ionic systems, the main results are obtained with the use of integral equations. A macrosystem is divided into clusters and the phase space of the system is divided into the corresponding regions. When estimating the equilibrium properties, the statistical integral reduces to the configuration integral over the coordinates of the molecules.

Nucleation in an ion plasma is associated with shielding of Coulombic interactions of ions in a liquid phase due to which the long-range Coulombic potential becomes an efficiently short-range potential. Investigations of the equilibrium properties of a model of charged spheres by the Monte Carlo method demonstrated that the shielding typical of a macrosystem is also observed in systems consisting of several tens of ions at the same temperatures as those in the macrosystem.

The fact that supersaturation cannot be attained in a cooled ionic system, *i.e.*, the fact that metastable thermodynamic states cannot occur, is associated with the absence of an energy barrier to the formation of microdroplets. The charge symmetry breaking in plasma causes a change in the nucleation mechanism. Of all possible orientations of triplets, only one type of orientation at which the symmetry axes of the triplets are mutually orthogonal leads to their mutual attraction. This result was obtained only by computer simulation.

The thermodynamic stability of a dense phase in ion plasma is determined by short-range attractions and medium-range repulsions between the molecules. Repulsions are changed to attractions as the temperature decreases. The formation of a stable dense phase is attributed to the appearance of a short-range orientational order. In a macroscopically homogeneous system, a short-range orientational order occurs at higher temperatures compared to those in a small system because surface particles in the former system are absent and the average number of the nearest neighbours in the former system is larger than that in the latter system. Mutual repulsions between ionic triplets can be interpreted as an additional internal pressure equilibrating the external pressure of the macrosystem. Hence, in the approximation of charged spheres microdroplets of a particular radius are formed at higher pressures and lower temperatures compared to

those in a neutral system. Due to a competition between Coulombic attraction and repulsion forces, emission of charged particles from the cluster can take place. The inhibition effect of microcondensation due to repulsions between ionic triplets is most pronounced in the case of microdroplets consisting of 10^2 – 10^3 ions. The mechanism of nucleation inhibition was studied by different methods, including numerical simulation by the Monte Carlo method, the lattice approximation and the approximation of physical groups.

4. Growth of critical nuclei in solid solutions

Coalescence in solid solutions is described using the Lifshits–Slezov theory,^{166,167} which considers a change in the size of a spherical nucleus with time. It is assumed that there are weak interactions between nuclei and the nucleus size is a small fraction of the average distance between these nuclei. Based on this theory, spinodal decomposition of a binary system upon coalescence in solid solutions was studied.¹⁶⁸

In the course of spinodal decomposition, it can happen that upon rapid removal of a system outside the spinodal, interactions between nuclei cannot be considered as weak. Using a nonlinear equation for the free energy of a two-component solution,¹⁶⁹ all steps of spinodal decomposition can be described. Nonlinear members of this equation take into account interactions between nuclei. The nonlinearity restricts the exponential growth of fluctuations in the region of thermodynamic instability and gives rise to the coalescence effect.

In the study,¹⁶⁸ a truncated equation for spinodal decomposition was used for estimating a change in the nucleus size in the ordered structure formed. The equation describing a change in the wavenumber as a characteristic of the structure was deduced using asymptotic methods. In the long-time limit, rather simple relationships were obtained, whose form depends on the size of the decomposition region d ($d = 1$ corresponds to coherent platelet-like structures, $d = 2$ corresponds to cylindrical structures and $d = 3$ corresponds to nearly spherical three-dimensional structures).

Upon nucleation and nucleus evolution of a new phase on solid substrate surfaces in closed multicomponent and multiphase systems, film formation proceeds through several steps.¹⁷⁰ First, dispersed particles appear on the substrate surface (generally, on its defects). Then the substance is redistributed between these particles. Evolution of ensembles of dispersed particles is accompanied by latent heat release and an increase in the temperature of the system. One mode of redistribution of the substance between dispersed particles involves coalescence.¹⁷¹ Due to a decrease in the free energy upon interface reduction, the average particle size increases as a result of mass transfer from smaller to larger particles.

Interactions between dispersed particles upon crystallisation of one-component melts associated with the occurrence of a heat field is called ‘heat coalescence’.^{172,173} A consideration of the evolution processes occurring in multicomponent closed dispersed systems in the general form demonstrated that in the asymptotic limit, the concentrations of components and the equilibrium temperature on the particle surface are independent of the nature of the particles. The distribution functions of phases depend only on the heat and mass transfer. The types of phases formed are determined by the ratios between the amounts of compounds dissolved, temperature and rate constants of chemical reactions. The time dependence of the size distribution function of new phases was found.

Investigations of evolution processes in ensembles of multicomponent and multiphase dispersed particles were continued in the study.¹⁷⁴ The phase formation in closed systems has also been examined.¹⁷⁵ Real systems are open, and the heat and mass transfer can take place in such systems. Dispersed particles on a substrate, the generalised field of adsorbed atoms and mass and heat flows interact with each other.

The effect of heat, which is evolved in chemical reactions proceeding under adiabatic conditions, on the dynamics of decomposition and crystallisation of multicomponent multiphase solid solutions and melts was examined.¹⁷⁶ The final step of decomposition and crystallisation of solutions involves coalescence accompanied by heat evolution. Under adiabatic conditions, the temperature of the system increases and the equilibrium concentrations of the components change. As a result, some phases decompose. It should be noted that the phase co-existence regions differ from analogous regions occurring upon isothermal decomposition. The condensed phase grows as a result of two concerted processes, *viz.*, diffusion and heat exchange. The system of equations proposed in the study¹⁷⁶ describes evolution of phase isolation in the step of coalescence in an N -component solid solution, where both the temperature and composition fluctuations can be ignored. This system consists of K continuity equations, N equations of the law of conservation of matter, $(N - K)$ stoichiometric relations for flows, K equations of the law of mass action, the heat balance equations and an equation relating the characteristic size of the phase deposited to the matter flow. The dependence of the equilibrium constants of chemical reactions on the temperature and sizes of the phases being deposited was taken into account and an additional equation for the rate of their growth was introduced. The asymptotic solution of the above-mentioned system of equations allows one to determine the boundaries of the co-existence regions of all possible K phases in the space of the initial amounts of components and temperature. The authors of the publications^{174–176} believed that their results can be considered as laws, which can enable one to control evolution of ensembles of multicomponent dispersed particles in the course of the growing of films with desired structures and compositions.

5. Boiling of stretched liquids

An adequate theoretical description of the boiling process of the so-called stretched (superheated) liquids based on high-precision experimental studies was published in the studies.^{177–179} Phase transitions in systems occurring in the vicinity of the boundary of thermodynamic stability (the so-called spinodal) were analysed in the review.¹⁸⁰ These transitions of the critical type are characterised by a strong space–time correlation of perturbations and a high degree of fluctuations. In the case of rapid liquid–vapour phase transitions, one or both co-existing phases are outside the region of stable states.

Spinodal decomposition is a special case of the initial step of a phase transition whose occurrence requires that the system be initially transformed into a labile state. The system relaxation is accompanied by an increase in the number of random inhomogeneities, which may give rise to modulated relaxation structures. Propagation of small perturbations is characteristic of a system occurring in an unstable state, whereas perturbations dissipate in the case of stable states.

At high supersaturations, metastable states occur at the boundary of the region of absolute instability. In rapid processes, a labile state can occur along with a metastable stable; the compound rapidly loses the spatial homogeneity and acquires a cellular granular structure. Unlike the phase transition from a metastable state, spinodal decomposition does not require activation. Nuclei of a new phase appear if a stable surface layer is formed. In this case, certain portions of the system can be located in a metastable region. If the stability condition is violated, a stable layer between two phases cannot occur. As the spinodal is approached, the mechanism of phase transition changes. Spinodal decomposition and nucleation are the initial and final steps of a continuous process of instability propagation.

In a one-component system, the rate of spinodal decomposition is limited by heat exchange between the contracting and expanding volume units.¹⁸¹ The time of formation of an unstable state should be shorter than the characteristic time of spinodal decomposition.

In multicomponent systems, the region of unstable homogeneous states is limited by the critical liquid–vapour conditions. The diffusion instability is characterised by the negative diffusion coefficient (ascending diffusion). In the case of two-component systems, diffusion instability is preceded by mechanical instability.¹⁸² The diffusion mass transfer is determined by the chemical potential gradient. In the case of stable states, the approach to the stability boundary is characterised by deceleration of the diffusion transfer (the diffusion coefficient D tends to zero). For unstable states, $D < 0$.

The phenomenological theory of spinodal decomposition was first presented in the study.¹⁶⁹ The use of the Fourier representation for analysis of the stability of a two-component isotropic solution made it possible to determine the critical wavenumber k_c and the critical wavelength $\lambda_c = 2\pi/k_c$. Within a spinodal, the solution is unstable with respect to relatively small fluctuations in composition with the wavelengths $\lambda > \lambda_c$. The plot of the amplification coefficient R , which characterises a change in the amplitude of the concentration wave, vs. the wavenumber k has a sharp maximum at

$$k = k_m = \frac{k_c}{\sqrt{2}}.$$

This indicates that all concentration waves, except for those characterised by the wavenumber k_m , can be ignored within a time interval after the onset of decomposition. At $k < k_c$ [$R(k) > 0$], the concentration waves are exponentially amplified. At $k > k_c$, these waves are exponentially attenuated [$R(k) < 0$]. The Cahn theory¹⁶⁹ is based on the self-consistent field theory. In the vicinity of a spinodal, there are strong interactions between fluctuations due to which the concept of the free energy may appear to be inapplicable. The usual linearised equation for diffusion is valid only in the initial steps of decomposition, when deviations of the composition from the average value are small.

The Cahn theory was further elaborated by Cook,¹⁸³ who considered thermal fluctuations in composition. This made it possible to explain the fact that the experimental critical wavevector k'_c is larger than the theoretically predicted wavevector k_c .

The work of formation of a near-critical bubble plays an important role in phase transitions to which decomposition of a gas-supersaturated solution belongs.¹⁸⁴ Under isothermal conditions, which occur at high thermal conductivity of a solution, two variables are required for the description of a nucleus of a stable phase. The work of formation of a near-critical bubble was approximated by the equation

$$F = F^* - x^2 + y^2,$$

where F^* is the work of formation of a critical bubble; $x = (V - V^*)/\Delta V^*$; $y = (P - P^*)/\Delta P^*$; V^* and P^* are the volume of the critical bubble and the pressure in this bubble, respectively.

The work of bubble formation includes the squares of variables with opposite signs. Hence, the activation barrier F has a saddle. The variable x is unstable (therefore, the bubble volume can increase infinitely), whereas the variable y is stable. On going from the variables x and y to variables characterising the bubble state, which are specified by the number of molecules in the bubble v and a series of critical parameters, the bilinear approximation is retained.

The intensity of the phase transfer is proportional to the normalising coefficient C corresponding to the equilibrium distribution of the clusters. After integration of a two-dimensional equilibrium distribution with respect to the stable variable v , we obtain a one-dimensional distribution of bubbles over this variable

$$g_c(v) = \frac{C\pi^{1/3}}{\Delta v_c} \exp[-F(v)],$$

where $F(v) = F_c - (v - v_c)^2/(\Delta v_c)^2$. The correction ΔF for the work of accommodation of a gas molecule was found thermody-

namically, which made it possible to refine the normalising coefficient

$$C = \frac{P_c[2v_c(1 - \varepsilon^2)]^{1/2}}{\pi^{1/2}\varepsilon k_B T},$$

where $\varepsilon = [2\sigma/(3r^*p^*)]^{1/2}$ (r^* is the radius of the critical bubble).

The normalising coefficient in the thermodynamic equation was refined in the study.¹⁸⁵

The above-considered theory can be applied to solutions supersaturated by an increase in their concentration by gas pumping or a decrease in the concentration upon a change in the temperature or pressure. The rate of formation of a metastable state in a gas-supersaturated solution influences all variables describing solution decomposition.¹⁸⁶ Conditions were found for attaining the maximum intensity of the formation of overcritical gas bubbles and supersaturation of a solution, and all characteristics of solution decomposition at this instant were studied. The size spectrum of overcritical bubbles in the stage of their formation was determined.

The work of formation of a critical bubble is a function of solution supersaturation. The metastability of a solution is described by the law of increase in ideal supersaturation with time, the time being measured from the instant when the ideal supersaturation is equal to zero. The coordinate z of the maximum of the overcritical bubble distribution over the excess free energy increases with time at a rate dependent on the supersaturation, temperature and some other parameters of the solution. The variable x , which is the deviation of the coordinate z from the size of the overcritical bubble, is introduced to characterise the size spectrum of overcritical bubbles $f(x)$. Throughout the growth process, each overcritical bubble is characterised by its own value of x . At $x = 0$, the spectrum $f(x)$ has a maximum. The material balance equation for a solution includes the function g corresponding to the difference between the ideal and real supersaturations. The dependence $g(x)$ and the related spectrum $f(x)$ are found by an iteration method.

Most researchers reasoned that the classical nucleation theory adequately describes experimental data on the frequency of formation of gas nuclei upon liquid boiling. Presumably, this is associated with rather large sizes of critical nuclei, although this assumption is evidently unjustified in the case of spinodal decomposition.

Skiprov and co-workers^{177–179} have achieved much success in experimental investigations on boiling of stretched (superheated) liquids. Since the elementary event of bubble formation can be observed experimentally, it is possible to demonstrate that the nucleation process is accidental. Thus, the expectation time cannot be predicted, and only the time of the elementary event of formation of the first bubble can be estimated at the probability level. Experimental studies showed that the expectation time is determined by the distribution of random values.

It should be noted that nucleation rates in any system are only certain average values. To determine these rates, it is necessary to carry out a statistically sufficient number of individual tests, like in studies of stretched liquids and investigations of the boiling of superheated metallic wires. Another way is to observe the appearance of numerous nuclei of a new phase. Apparently, the latter approach allows one to reduce the experimental time. Generally, researchers, who use this approach, do not measure elementary nucleation events and observe only average values. In the case of an insufficient number of parallel nucleation events, fluctuations of nucleation events can be observed. To obtain reliable average values, it is generally necessary to increase the time of observation. In the case of a statistically sufficient number of measurements (with the variance in average values of $\sim 1\%$) and a rather high relaxation rate, the experiment can be quasistationary, *i.e.*, one of the parameters of the system can slowly (compared to the relaxation rate of the system) change. In this case, one can obtain

more experimental data than in the case of accumulation of the results of individual tests.

One of the main schemes used in experimental investigations of boiling of stretched liquids (in particular, of the cavitation phenomenon) involves stretching of a column of a temperature-controlled liquid by relieving pressure. Several tens of experiments are already sufficient for the determination of the average expectation time for the breaking (boiling) of a liquid (the value inverse to the expectation time normalised to the volume unit is the nucleation rate). Hence, it is necessary to carry out several hundreds of tests of the system to obtain 10–20 points for the construction of one isotherm.

In an alternative scheme, a metastable state is achieved by superheating, which is provided by passing an electric current through a conductor. This scheme allows one to attain high degrees of superheating when heterogeneous boiling centres no longer play an essential role. This way of performing experiments allows the use of electronic means of automation and control. If relaxation of a system is achieved in a short period of time, a statistically reliable data set can be collected in an automatic mode rather rapidly. For example, the bubble formation in liquid nitrogen on a conducting film surface was studied,¹⁸⁷ and the kinetics of bubble formation in glassy methyl methacrylate and polycarbonate containing dissolved carbon dioxide was investigated.¹⁸⁸ In the latter case, the bubbling was monitored using a light beam. The light-transmission factor served as a quantitative measure of the concentration of pores formed in the polymers. Pressure jumps and surface tension at the boundary of critical bubbles at different temperatures and concentrations of dissolved CO₂ were determined. In some cases, these values corresponded to parameters typical of homogeneous nucleation, otherwise they corresponded to those of heterogeneous nucleation. It should be noted that it is possible to carry out a more detailed interpretation of results. For this purpose, one should use phase diagrams of a polymer–gas system, because some characteristic features of nucleation rate surfaces may be associated with the characteristic features of phase equilibrium diagrams of the systems under study. Nevertheless, the conclusion that the nucleation properties of a polymer–gas solid solution vary with saturation with gas is beyond question. This result confirms the generality of the concept (which was considered using vapours as an example) that the nucleation rate depends on the total pressure in a medium.

The bubble nucleation can also be studied using a two-piston chamber.¹⁸⁹ A constant negative pressure pulse is applied to a liquid sample during several milliseconds after which stretching is decreased by 10%–20%. As a result, the formation of new nuclei ceases and the bubbles grow to sizes, which can be observed by an optical method. The advantage of this scheme is that several bubbles can be formed simultaneously, which allows one to obtain abundant data in a single experiment, thus accelerating measurements of elementary events of bubble formation a hundred times.

In a study of the boiling of polymers,¹⁹⁰ the thermal stability of a polymeric liquid was estimated using a controlled pulse heating technique. The average lifetime of the polymeric liquid before its boiling was determined from a temperature plateau in a thermogram of the process. A correlation was found between the thermal stability and the slope of the plot of the average lifetime of superheated liquids *vs.* the temperature. A distinct relationship between the average time of bubble nucleation and the total pressure was revealed.

Cavitation in binary systems has long attracted the attention of researchers. The kinetics of phase transitions in binary solutions of several systems based on hydrocarbons and water was examined¹⁹¹ in the vicinity of critical stratification points. The stratification was detected by photomicrography. Corrections for the equations describing the growth of a new phase volume were found. It was demonstrated that at the late step of the process, the dependence of the reduced average radii of the droplets of a new phase on the reduced time is described by an exponential equation with the exponent of 0.81.

Achievements in the field of research of liquid boiling under the action of a current pulse have not gained wide acceptance. Some researchers concerned, for example, with the boiling of metallic wires, did not employ the concepts of the nucleation theory at all. For instance, in the study¹⁹² devoted to the dynamics of microplasticity of whisker single crystals under the action of a current pulse, the nucleation of dislocations in single crystals and their propagation were investigated. However, the experimentally observed incubation period determined by the plasticity delay time of the initially dislocation-free silicon whisker crystal¹⁹² is nothing else as the expectation time for nucleation of dislocations. The nucleation of dislocations is a nucleation process involving all inherent metastable states and accident events. The delay time should be a random value and be characterised by the distribution, which was not discussed in the cited study. The evident drawback of this study is that the authors did not use the formal apparatus of the nucleation theory, which could substantially change the direction of investigation and interpretation of the results.

To summarise, it should be noted that the methods for studying nucleation in vapours and cavitation in liquids have gained most acceptance. However, these methods are not rigorously justified and need a thorough validation of the assumptions used for the interpretation of experimental data. Thus, in spite of a rather reliable verification of the dependence of the vapour nucleation rates on the total pressure in a nucleating system (see, for example, Refs 73 and 81), some researchers traditionally, like a quarter of a century ago, reject the effect of gas pressure as such.¹⁹³ These researchers use a variable pressure in a two-piston chamber to maintain both the nucleation temperature and initial composition of the vapour–gas mixture constant. Undoubtedly, this makes experimental studies with adiabatic cooling easier, but leads to an error associated with the dependence of the nucleation rate on the total pressure in the nucleating system. In other words, experiments are carried out under isothermal conditions but at a variable total pressure. For the results to be interpreted correctly, the experimental data are necessary to recalculate as applied to the constancy of the total pressure. For example, such a procedure should be carried out in calculations of the compositions of critical nuclei from the slopes of nucleation isotherms. In the investigation,¹⁹³ one variable in the parameter space was ignored and, in actuality, a particular section from different subspaces was measured without an adequate description of the trajectory in this space.

The nucleation, for example, of a binary vapour can be described in a five-dimensional space including the nucleation rate, the composition of the initial vapour, the composition of the nuclei of the condensate, the total pressure in the system and the nucleation temperature. It should be noted that the level of description of the experimental processes is not sufficiently high to give an estimate of the changes in the state of a nucleating system in the above-mentioned space. Different trajectories in this space give different projections onto subspaces, which is one of the factors responsible for the disagreement in the results obtained by different methods. The common aim of researchers is to develop experimental techniques for obtaining more precise and reliable data in the well-determined conditions of nucleation.

6. Nucleation in condensed phases

Nucleation in condensed phases assumes the existence of transformations from one condensed phase to another. Experiments on crystallisation of supercooled liquids were surveyed in the review.¹⁹⁴ The rate of crystalline phase formation was estimated using the maximum supercooling with respect to the temperature of the equilibrium melting–crystallisation process. The nucleation begins to proceed at a substantial rate once a sufficiently high supersaturation is attained. Generally, the supercooling limit is determined by the rate of heterogeneous nucleation on the walls, the presence of a liquid surface and heterogeneous nuclei in this surface, *etc.*, rather than by a homogeneous process. In emulsions and on substrates, the liquid breaks into droplets. To weaken

interactions, droplets are coated with surfactants or salt melts. When droplets are rather large, many of them do not contain heterogeneous nuclei. The supercooling maximum is generally taken as a homogeneous limit. Container-free methods of investigations are of considerable interest. In the falling drop method, a molten drop falls in a tube, which is filled with an inert gas (or evacuated) and whose walls are cooled. By hanging a drop in an electromagnetic field, one can more easily control the phase state of a sample. In this case, observations can be more prolonged and measurements are more accurate. In the case of metals, the maximum supercooling is $\sim 20\%$ of the melting point.

In the study,¹⁸⁵ homogeneous nucleation was treated as a heterogeneous process in which individual molecules serve as nuclei. This approach enables one to introduce a correction in the equation for the work of nucleation under different conditions.^{195–197} The type of the correction is determined by the presence or absence of a thermal equilibrium between the nucleus and the medium. The work of nucleation depends on the external conditions of the nucleation process. The equation was derived for the work of nucleation upon homogeneous nucleation in the absence of an equilibrium between the nucleus and the medium in the case of an isentropic isochoric process. Under other conditions, this work can be evaluated by removing the corresponding terms from the equation for the potential of a critical nucleus. In the case of a complete equilibrium between the nucleus and the medium, the results correspond to the classical theory. The Gibbs equation describing the work of nucleation in the case of a heterogeneous process includes the work of wetting. To determine the work of wetting, one should consider an ensemble of macroscopic nuclei, which are in equilibrium between the mother and new phases. Each nucleus is considered as a dispersed particle and its chemical potential is taken into account.¹⁹⁸

Studies of glass relaxation are of great technological and scientific interest. Here the question arises as to the existence of the limit of liquid supercooling.¹⁴ Liquid supercooling gives rise to an increase in viscosity, the possible spinodal transformation of the liquid to a crystalline state being 'diffused'. At the same time, it is common practice to treat a glass as a liquid occurring in a metastable state, which is reasonable to regard as one of the states of the supercooled liquid. In any case, investigations of glass relaxation rates provide a unique possibility to answer the above question. The maximum glass relaxation rate is observed at low temperatures. Samples are kept at a low temperature until nucleation of crystals starts and then the samples are annealed at higher temperatures. In this process, the rate of formation of new nuclei is low, whereas the rate of cluster growth is much higher compared to those under the conditions of nucleation. The clusters grow to sizes such that their amount can be measured by simple methods. In metallic glasses, nucleation and nucleus growth are often not separated. Investigations of metallic glasses did not provide new information compared to that obtained in studies of well-known silicate glasses. In studies of a series of metallic glasses, including Zr–Ti–transition metal, Al–Fe, Ni–rare-earth metal and Fe–Si–B systems, anomalously high nucleation rates (which sometimes approach $10^{17} \text{ cm}^{-3} \text{ s}^{-1}$) were observed.^{199–202}

Investigations of nucleation in condensed phases are of importance for both fundamental knowledge and the solution of applied problems. Tauer and Padtberg²⁰³ devised a system for computer collection of data on conductivity and haziness (transmission of light) of aqueous solutions. The authors of the cited study believed that this system is a universal tool for investigating nucleation in such systems. The onset of nucleation in solutions is determined from the discontinuity of the first derivative of the conductivity and the appearance of a bend in the curve of the transmitted light intensity vs. the composition. These experiments closely resemble the initial stage of investigation of aerosol nucleation, in which aerosol was observed, whereas the nucleation rate has not been measured. Emulsion polymerisation was studied in a similar way.²⁰³

Nucleation in chemically reacting systems is of great interest. The theory of this process was developed within the framework of classical notions of nucleation as early as the 1980s. The effect of surfactants on nucleation was simulated in the study.²⁰⁴ It was demonstrated that due to the presence of surfactants, clusters can occur before the onset of phase transition. The addition of surfactants is equivalent to an increase in the deviation from the equilibrium state because the term proportional to the concentrations of the introduced compounds is added to the equation for the thermodynamic potential. The energy of cluster formation passes through a minimum, which provides the occurrence of metastable states. Due to anisotropy of the surface energy, the adsorption pressure is different on different crystal faces and the latter grow at different rates. This fact can account for the formation of dendrites in the presence of surfactants.

Recently, a general model was proposed for nucleation in chemically reacting systems.²⁰⁵ This model is based on the Becker–Döring kinetic scheme²² according to which clusters grow and decompose due to one-step aggregation and fragmentation processes. The model takes into account the catalytic effect of the already formed clusters on the rate of appearance of other clusters. The role of precursors (or specific reagents), which spontaneously decompose to form relaxing metastable states, and inhibitors, which hinder the cluster growth to sizes larger than a particular value, was discussed. The model includes several key equations describing the experimentally observed macroscopic behaviour of a system. Based on these equations, the most important components of the reacting system can be revealed and the steps of the process dependent on the rate can be determined. One of the versions of this model was used for the description of cement hydration. The problem was solved in the asymptotic mode. The results of calculations were consistent with the experimental data.

In the scientific literature, the problem of spontaneous formation and the existence of dimers in a nucleating system is actively discussed. In the theoretical investigation of the drop growth in a medium of an inert gas containing monomers and dimers of the agent condensed,²⁰⁶ analytical equations were proposed for estimating the effect of dimerisation of vapour molecules on the rate of growth in an isothermal approximation. The growth of cesium drops in a helium atmosphere was calculated as an example. At high supersaturations, the rate of drop growth increases substantially due to formation of dimers.

The kinetic molecular mechanism of the onset of snowballing condensation from a supersaturated vapour with a high concentration of dimers was described in the general form.²⁰⁷ The possibility of cluster growth due to the presence of dimers was taken into account. The enthalpy effects were taken into consideration by fitting the parameters of the model to the experimental values. This model can be used for calculating the total entropy of the clusters. At high pressures, the rate constants of condensation are corrected for the restriction of diffusion of monomers and dimers involved in the growth process. The description of the nucleation process in the density functional approximation was extended to condensation in an associated liquid. The theory of associated liquids in a system of spherical molecules with one associated bond was used for this purpose. Calculations demonstrated that the use of the classical nucleation theory led to a substantial overestimation of the activation barrier to nucleation in these systems. This deviation can be to a large degree compensated using the model proposed in the study.²⁰⁸

The investigation of nucleation in a benzene vapour giving rise to dimers in the temperature range of 15–123 K is of obvious interest.²⁰⁹ For the range of 15–88 K, the coefficient of the rate of dimer formation was calculated. The formation of benzene dimers was proved by studying the reactions of hydrocarbons with C_6H_6 and analysing the optical spectra of the products. Model calculations showed that the systematic error of measurements is low. The coefficients of the dimerisation rate calculated on the assumption of free rotation of dimers are in good agreement

with the experimental values for the temperatures above 30 K at which decomposition effects should be small.

Agglomeration of nanosols can be considered as a model of a phase transition without long-range interactions. The activation energy of restructurisation of agglomerates from nanoaerosols was determined *in situ*.²¹⁰ In experiments with agglomerates of silver and copper nanoparticles, the height of the activation barrier to the rearrangement of particles in the agglomerate was determined. Agglomerates are formed due to collisions of several tens of the initial nanoparticles. The structures of the agglomerates can be described by the exponential law relating the number of the initial nanoparticles to the radius of the agglomerate. The exponent including the radius is generally referred to as the fractal dimensionality. This exponent is determined from electron microscopic images.

Interactions between nanoparticles can be of a different nature from van der Waals forces to ionic or covalent bonds. Agglomeration in which strong bonds are formed gives rise to rigid (generally, porous) structures. Agglomeration characterised by weak bonds affords clusters with more compact structures, the number of nanoparticles involved in the clusters being increased. The temperature dependence of the restructuring rate is described by the Arrhenius equation whose exponent includes the activation energy of the process. The pre-exponential factor has the dimensionality of frequency. To estimate the bond energy of nanoparticles in an agglomerate, it is necessary to know how the coordination number of the nanoparticles changes with time and to determine the fractal dimensionality at a particular instant of time. The initial particles interact only with the adjacent closely located particles. The activation energy of this process is an order of magnitude lower than the bond energy calculated with the use of the Hamaker constant,²¹⁰ for example, for silver and copper. In the range of the nanosol sizes under study, the energy of activation for silver is similar to that for copper. The maximum activation energy corresponds to the particles with a diameter of ~ 18 nm. This energy decreases as agglomerates grow. The addition of oxygen before the onset of agglomeration of the initial nanoparticles leads to a twofold increase in the activation energy, the maximum energy corresponding to the particles with a diameter of 15 nm.

In the review,²¹¹ it was mentioned that the development of theories of solid-state nucleation allowing for the thermodynamic aspects of nucleation and cluster growth is presently underway. To detect nuclei and determine their phase states, Rayleigh scattering of Mössbauer radiation and Mössbauer spectroscopy are used. Diffusion of clusters in pores is investigated using the microprobe method. Generally, studies are accompanied by investigations of the catalytic activity of clusters.

7. Photonucleation

Based on the results of the investigation of photonucleation,[†] a new procedure was developed for the determination of ultralow concentrations of molecules.^{212,213} The high level of analytical sensitivity is attained by exciting molecules with UV radiation. Upon vapour supersaturation, particles of photonucleation products (radicals, ions, *etc.*) grow to sizes, which can be easily detected by simple methods. Due to high spectral sensitivity of photo-detection, the desired compound can be selectively excited and detected. For example, resonant excitation made it possible to detect nitrotoluene vapours at such a low concentration that their pressure is 50 000 times lower than the saturated vapour pressure.^{212,213} As a result, the sensitivity with respect to the concentration of ~ 10 particles per billion was achieved.

The explanation for the photoactivation effect was put forward, for example, in the publications,^{214,215} where the distribution of vibrational energy in a binary reacting gas mixture after

optical excitation was theoretically analysed. Stationary optical pumping gives rise to a distortion of the equilibrium distribution function of molecules with resonant levels, the distribution of vibrational degrees of freedom of other molecules remaining unchanged. In a two-component system, the vibrational temperature of both components differs substantially from the translational one. These effects open up the possibility of performing experiments on nucleation upon relaxation of the levels pre-excited with resonant electromagnetic radiation.

Advances in the studies of photographic processes were made largely due to intuition and practical skills of researchers and are to a lesser extent associated with theoretical studies. In studies of the mechanisms of spectral sensitisation of silver halides with dyes, it was concluded²¹⁶ that the primary event of electron transfer from the photoexcited dye and the secondary dark reactions involving an oxidiser (silver) play a decisive role. In these processes, numerous various nucleation phenomena take place. Unfortunately, these phenomena have not been considered in the context of the nucleation theory. For example, AgBr crystals are formed in an emulsion, and the sizes of these crystals influence the quality of photographs. The formation of aggregated cyanine dyes on the surface of silver halide crystals is also associated with nucleation. Such dyes are used for spectral sensitisation of photomaterials.

Knowing the mechanism of photoprocesses at the molecular and atomic levels, one can follow the dynamics of changes in the electron density and the course of chemical reactions associated with photoactivated electron jumps. In studies of the formation, for example, of photoaerosols, researchers often restrict themselves to the detection of the photoeffect with no investigation of its kinetics and mechanism. Among a few exceptions are the investigations,^{217,218} where the mechanism of atmospheric nucleation upon photoactivation of the simplest aldehydes was proposed. When studying the mechanism of formation and growth of an aerosol upon photolysis of tungsten hexacarbonyl, the authors gave particular attention to the time range during which vapours leave the irradiation zone. The generation of the condensed product was discontinued to measure the concentration and evaluate the size distribution of the aerosol formed. The kinetics of aerosol formation was simulated by numerical methods using the Smoluchowski equation. The rates of monomer formation were calculated at different photolysis rates, which were varied by changing the irradiation time. These calculated values were in good agreement with the measured photolysis rates. It should be noted that some methodological problems remain unresolved, which hinders the quantitative determination of the frequency of aerosol formation upon photoactivation.

The translational energy release upon multiphoton dissociation of organometallic compounds was studied.²¹⁹ The results were discussed from the viewpoint of expenditure of energy in aerosol formation from photolysis products of $W(CO)_6$. The processes of the preparation of aerosols and thin films were controlled by a laser. The properties of semiconducting CdSe nanoparticles with a diameter of 2–15 nm were examined.²²⁰ It was assumed that the addition of butylamine to a colloidal solution of nanoparticles excludes the radiation path for their luminescence. An observation of interactions between nanoparticles and a hole acceptor (to which butylamine belongs) allows one to detect electron transitions in surface atoms of nanoparticles.

8. Search for similarity criteria

Many researchers are concerned with a search for similarity criteria allowing one to carry out rescaling of the results of studies of nucleation (see, for example, Ref. 221). The asymptotic limit of the activation energy on going from heterogeneous to homogeneous nucleation was determined depending on the contact angle.²²² This value is consistent with the results of numerical simulation. The possibilities of scaling as applied to the properties of molecules in the critical cluster and then to nucleation were

[†] Atmospheric nucleation giving rise to morning fog, which appears with the first sunbeam, is an example of photonucleation.

analysed.²²³ The scaling properties of nuclei were treated based on the Kelvin equation. Analysis was carried out using the formal apparatus of the density functional theory and the molecular dynamics method. The concept of the reduced height of the barrier to nucleation was introduced. It was demonstrated that both modes of scaling are related to each other by the nucleation theorem and, hence, can be combined.

The model of scaling invariance for binary nucleation in ideal systems³⁵ was used for analysing experimental data on nucleation rates in a hexanol–ethanol system.²²⁴ Nucleation in a water vapour was simulated by the Monte Carlo method²²⁵ and the results were presented in a criteria form. The results of simulation are in agreement with the data from the experimental study.²²⁶ Based on scaling, corrections applicable to the results obtained by other researchers were proposed.

9. Adiabatic expansion method

Homogeneous vapour nucleation can occur upon rapid adiabatic expansion of a vapour–gas mixture. First data on this type of nucleation were obtained already in the late 19th century. In early experiments (see, for example, Ref. 227), the critical supersaturation S_c , to which the nucleation rate $J = 1 \text{ cm}^{-3} \text{ s}^{-1}$ corresponds, was determined. The construction of a Wilson chamber used for studying homogeneous nucleation has gradually been improved.^{71, 228–231} Apparatus was devised to maintain a constant nucleation temperature over a long period of time, which made it possible to control the changes in the concentrations of the particles formed and their size distribution with time.^{228, 232} The nucleation rates were measured with high accuracy in different systems using an adiabatic two-piston expansion chamber.^{224, 233–235} Presently, a Wilson chamber is used most generally for studying different processes associated with volume nucleation.

In a number of studies (see, for example, Refs 236–238), condensation was examined in a shock tube. A shock tube is a device, where a vapour is heated and rapidly cooled due to generation of shock waves in a vapour–gas mixture. Generally, a tube consists of two cells separated by a diaphragm containing a vapour (gas) at high (driving chamber) and low (driven chamber) pressures. Once the diaphragm is broken, the shock wave propagates to the section containing the low-pressure vapour and rapidly heats the latter. The high-pressure gas is simultaneously cooled under the action of a rarefaction wave. Heating can cause decomposition of a chemical compound into non-volatile components,²³⁶ while cooling leads to vapour supersaturation.²³⁷

The construction of a tube with two diaphragms made it possible to extend substantially the range of compounds under study.²³⁹ In this tube, the vapour is compressed by a shock wave after breaking of the first diaphragm and then the vapour is expanded into vacuum after breaking of the second diaphragm. This tube can be used for studying compounds characterised by a high vapour pressure at room temperature (for this purpose, these compounds are mixed with an inert gas). Compounds occurring in the solid state at room temperature are introduced as aerosols. The shock wave causes evaporation of aerosols and the vapour formed is condensed in the expansion cycle.

The studies of nucleation of different systems at high pressures using a shock tube are of great interest.^{240–242} The authors of the cited studies were among the first who concluded that nucleation under an atmosphere of a carrier gas should be considered as a binary process.²⁴²

A shock tube is extensively used in studies of nucleation at pressures of 70 atm.^{243–245} The kinetics of formation of methane hydrates was the main subject of investigation. For example, nucleation of water in methane was studied at pressures up to 40 bar²⁴³ and an *n*-nonane–methane system was investigated in the pressure range from 10 to 40 bar.²⁴⁴ In the latter case, the dispersion in experimental measurements was much smaller than that achieved, for example, in the study.²⁴⁵ The scheme was proposed for the use of a shock tube in studies at high temper-

atures.²⁴⁶ The geometry of a shock tube was devised so that the reflected wave again increases the pressure after the expansion cycle, thus preventing the appearance of new nuclei and providing conditions for the growth of the already formed nuclei.

The processes occurring in the systems under consideration are non-stationary, which hinders interpretation of experimental results. A spontaneously formed aerosol can be prepared in experiments using a supersonic flow of a vapour or a vapour–gas mixture through Laval nozzles. The state of the gas throughout the length of the nozzle can be precisely determined with the use of the gas dynamics equations.^{247–249}

Interesting results were obtained in the studies of nucleation of light and heavy water in nozzles.^{250, 251} It appeared that the compositions of the aerosols thus prepared correspond to the initial compositions of the samples. These experiments were carried out with the use of computer simulation. The experimental results were more similar to the values calculated on the assumption of isothermal conditions of the process rather than non-isothermal conditions. Analogous results were obtained in parallel measurements in a two-piston chamber.²⁵²

Nucleation in Laval nozzles cannot be described on the basis of the isothermal theory because the process under consideration is non-isothermal. The nucleation theory at high supersaturations³⁹ (including the theory of processes occurring in nozzles) has not been developed in sufficient detail. The difference in the temperatures corresponding to different degrees of freedom was observed in experiments using high-intensity molecular beams.^{253, 254} However, a theoretical description of these results is lacking. The developed methods for diagnostics of molecular beams enable one to study directly critical nuclei and distributions of clusters in a vapour expanded into a vacuum. These methods are very useful for quantitative studies of non-stationary non-isothermal nucleation.

10. Method for turbulent mixing

Studies of homogeneous condensation of a vapour by turbulent mixing of a hot vapour–gas mixture with a cold gas are of considerable interest.^{255, 256} Up to the 1960s, qualitative studies were primarily carried out. The main results were systematised by Amelin in the monograph.²⁵⁷ First data obtained by Friedlander were presented in the publications.^{258, 259} The method under consideration was widely used in the investigations.^{260–262} In spite of the simplicity, this method enables one to investigate nucleation processes in broad ranges of temperature, supersaturation and nucleation rate under stationary conditions due to which it has advantages over methods in which an adiabatic expansion chamber is used in a cyclic mode.

Similar apparatus were used in the studies^{257–259} devoted to the determination of the critical vapour supersaturation at which the aerosol formation began. A gas flow heated to a particular temperature is ejected at high velocity through a nozzle into a surrounding atmosphere moving at a certain velocity²⁵⁷ or into a resting gas.²⁵⁸ The flow was initially saturated with a vapour of the compound under study and its cooling with the surrounding flow leads to vapour supersaturation to give an aerosol. To detect the aerosol, the flow is illuminated with a collimated light beam and photographed. A common drawback of the cited studies is that the presence of an aerosol is determined in an arbitrary way and the beginning of the particle detection depends on the point in time at which the critical vapour supersaturation is attained. However, these studies provided qualitative insight into the transformations that occur in this process.

In subsequent studies, the parameters of an aerosol formed in a turbulent flow were measured quantitatively. The aim of the study²⁶³ was to validate the homogeneous nucleation theory proposed by Becker and Döring.²² In the investigation,²⁶³ the concentrations of particles formed in a generator were determined (unlike the above-considered studies) using a photoelectric counter.²⁶⁴ A comparison of the calculated and measured concentrations of the particles demonstrated that the best agreement

between these values was achieved for dibutyl phthalate. There was a substantial discrepancy between the experimental and calculated concentrations of the particles of ethylene glycol, octadecane and sulfur.

A similar problem was solved in the studies.^{265, 266} Octadecane and heneicosane were used as working compounds. At that time, the discrepancy between the calculated and experimental data of four orders of magnitude was considered to be satisfactory.

Procedures were developed for determining the concentrations and disperse compositions of aerosols formed by turbulent mixing of a vapour–gas mixture. The aerosol concentrations up to 10^7 cm^{-3} can be measured using a flow-through ultramicroscope constructed by Deryagin and Vlasenko.²⁶⁷ Besides, the concentration can be determined with lower accuracy but then rapidly from light scattering. After enlargement in a vapour of an organic compound, an aerosol can be considered as monodispersed and its concentration can be easily determined using a nephelometer.²⁶⁰

Time scales of nucleation under turbulent conditions were simulated by Barrett.²⁶⁸ He studied the temperature and concentration distributions with no account for condensation. An increase in the rate as the nucleation peak is approached and a decrease in the rate after passing the peak were evaluated. The value inverse to time corresponds to the pulse rate. The number of the particles formed was estimated from the nucleation rate multiplied by the peak duration. The results of calculations were verified by comparing the results of more precise calculations performed on a computer and with the data obtained in a real turbulent flow containing water vapour. Under laboratory conditions at a temperature below 90°C , condensation has only a slight effect on the number of droplets along the flow axis. However, condensation noticeably suppresses nucleation at temperatures above 95°C . Barrett believed that the proposed model can be useful for the construction of systems in which nucleation and particle growth occur simultaneously.

In investigations of condensation under turbulent conditions, it is very important to estimate the amount of particles which are deposited on walls limiting the flow. Simulation of the particle motion in a near-wall turbulent layer²⁶⁹ is based on analysis of the flow stability in a channel. The equation of motion includes the Stokes, gravitational and lifting forces. In the cited study,²⁶⁹ the efficiency of particle deposition from a flow was analysed by considering trajectories ending in particle deposition. The precipitation rates predicted by the model were in good agreement with the available experimental data. Particle deposition on a small-disc target was studied.²⁷⁰ The deposition effects associated with convection, diffusion, sedimentation, electrification and thermophoresis were investigated. It was found that thermophoretic purification from particles can be reduced to zero because of very weak attractions between charges.

The turbulence effect on the rate of particle formation in a vapour flow was studied experimentally.²⁷¹ The authors of the cited study investigated nucleation in a flow with the temperature of 400 K , which was injected into air at 298 K and 1 atm . To simplify calculations, the Levi number was taken equal to unity. The temperature fluctuations in an axis-symmetric flow were estimated and local rates of particle formation averaged over fluctuations were calculated. Turbulent pulsations substantially decrease the nucleation rates at local maxima and increase the nucleation volume. In the cited study, particle distribution fields were reported.

In the last two decades, the scheme using a turbulent flow was virtually not used for studying the rate of vapour nucleation because there was no assurance that homogenisation of a system occurs before nucleation. The data on nucleation at large temperature and concentration gradients remain to be adequately interpreted. However, it can be expected that this ‘drawback’ will soon become an advantage because this approach can be used for the quantitative determination of the delay times of nucleation

under gradient conditions. This field of investigation is of importance because such processes often take place in practice.

11. Methods based on molecular diffusion

Of all the apparatus used for studying nucleation, a thermodiffusion chamber is of most interest from the viewpoint of accuracy of measurements, because only in this chamber (unlike a Wilson chamber, Laval nozzles and shock tubes), condensation proceeds in a stationary mode. This provides the possibility of measuring the parameters of the process with high accuracy. A thermodiffusion chamber was first proposed by Langsdorf.²⁷² The action of this chamber is based on the use of vertical diffusion of the vapour under study through a light carrier gas. A compound evaporates from a hot plate and diffuses through an inert carrier gas to a cold plate. The temperature and pressure of the vapour between the plates change approximately linearly, whereas the saturation pressure depends exponentially on the temperature which gives rise to supersaturation. At a supersaturation higher than the critical value, homogeneous condensation with the formation of droplets is observed.

There are two types of thermodiffusion chambers, which differ by the direction of vapour diffusion. Langsdorf evaporated the compound under study from an upper (hot) plate. However, this construction was rejected at a later time, and researchers used chambers in which the hot plate was located under the cold one.²⁷³ The convenience of such chambers is that the condensate from the upper plate drains down and compensates the volume of the liquid that evaporates from the lower plate due to which the cycle becomes closed and the stationary mode is maintained during many hours. Due to the stationarity of the process, self-purification of the chamber from heterogeneous nucleation centres becomes possible. Relatively rare nucleation events caused by solar beams can be excluded from the statistics. A diffusion chamber was used for studying the dependence of the nucleation rate on supersaturation in different systems,^{273–279} including those occurring at high pressures (up to $40–100 \text{ bar}$).^{273–275}

In detailed studies of homogeneous nucleation of higher alkanes, critical supersaturations and nucleation rates were measured,²⁸⁰ the relations between the corresponding states were found and the dependences of the critical supersaturation of hydrocarbons on the number of carbon atoms and the number of molecules in the critical nuclei were revealed.²⁸¹ In the investigation,²⁸² ion-induced nucleation of vapours of six compounds was examined in a thermodiffusion chamber. Ions were generated using an α emitter. Either positive or negative ions were generated by varying the electric field. Experiments were carried out both in the presence and absence of an electric field in the nucleation zone. In the presence of the field, nucleation on positive and negative ions proceeded differently.

Interesting experiments on nucleation were carried out using photoactivated ions.^{212, 213, 283} Dose amounts of ions were produced with the use of small additives of 4-fluoroaniline or hexamethyldisilazane, which can be ionised upon resonance excitation. A resonance excitation pulse from a tunable UV laser initiated the generation of ions in the region below the point of maximum vapour supersaturation. Ions with the required sign were shifted to the nucleation zone by applying an electric field.

Diffusion chambers enable one to measure the frequencies of nucleus formation within $10^{-2}–10^2 \text{ cm}^{-3} \text{ s}^{-1}$. The lower limit is determined by the long expectation time for the appearance of a viable nucleus, whereas an upper limit is determined by the fact that at nucleation rates higher than $10^2 \text{ cm}^{-3} \text{ s}^{-1}$ the droplets that appear substantially disturb the diffusion and heat flows. The dependences of the distribution of vapour and temperature in a thermodiffusion chamber as well as of the nucleation rates on both the stationary homogeneous vapour condensation on droplets and the release of the phase transition heat were examined, for example, in the study.²⁸⁴ Moderate changes in supersaturation and temperature in a chamber caused by the release of phase transition heat and a decrease in the concentration of a vapour

upon its condensation on droplets lead to a substantial decrease in the nucleation rate as compared to the rate which should be observed (according to the nucleation theory) provided that the vapour is not consumed and the condensation heat is not released.

Distortions of the results obtained in flow diffusion chambers may be a consequence of particle deposition on walls. With the aim of estimating this effect experimentally, thermodiffusiophoresis of growing droplets of dioctyl phthalate formed in a supersaturated vapour upon homogeneous nucleation was studied.²⁸⁵ It appeared that the thermodiffusiophoresis theory, which was developed as early as the 1970s, gives an adequate prediction of results obtained in real conditions. This theory allows one to estimate the effect of thermodiffusiophoresis on the overall nucleation rate in a flow diffusion chamber. The first experiments with the use of this chamber have already demonstrated²⁸⁶ that an aerosol column formed along the flow axis does not virtually spread out during the period (several tenths of a second) of the presence of particles in the chamber. A noticeable (at the error threshold) effect can be observed if the number of particles decreases by a factor of 2–3 due to thermodiffusiophoresis. Such a decrease has not yet been observed in flow diffusion chambers. In investigations of nucleation of chemical compounds under conditions of a high vapour pressure (> 30 Torr), it is necessary to estimate additionally the effects under consideration.

In experiments on nucleation, there is a probability that aerosol particles undergo aggregation due to which their number and size distribution can change. This problem is most pressing in experiments with the use of adiabatic expansion methods, where high concentrations of aerosols are produced in the nucleation volume. This problem is rather easily solved based on the assumption that substantial coagulation cannot be observed in a fraction of a millisecond required for the particle detection. In studies with the use of a flow chamber, tenths of a second are required for the detection, the maximum concentrations of particles being four orders of magnitude lower than those in the case of adiabatic expansion methods, which also eliminates the problem of aggregation. In experiments with the use of a static diffusion chamber, this problem does not occur at all because the maximum concentrations of particles are too low to influence coagulation. A certain insight into the effect of aerosol aggregation on the nucleation rate was offered in the study.²⁸⁷ A model of coagulation of a two-component aerosol was described in the investigation.²⁸⁸ Coagulation occurring at different compositions and sizes of particles was examined in the publication.²⁸⁹

In experimental studies, the question as to the effect of vapour depletion on the nucleation rate is of importance. In a real system, only a limited amount of a vapour can be used and, hence, nucleation occurs inevitably on the background of a varying supersaturation. This fact is often ignored and the results of studies are related to average parameters of the system or conditions at which the maximum nucleation rate is achieved. In the study,²⁹⁰ the nucleation rates and nucleus growth were examined under conditions of a limited amount of a vapour. The equations were derived for the particle growth and changes in the concentration of a vapour due to its condensation under conditions corresponding to a combination of continuous and free-molecular modes. The characteristic times for these modes were found depending on the particle sizes and these times were compared with the characteristic times of nucleation, coagulation and chemical reactions. The vapour concentration decreases as the number of particles in the system increases. The authors of the study²⁹⁰ believed that an estimate of characteristic times is an efficient method for the determination of the relative importance of condensation compared to other competitive processes.

The idea of a thermodiffusion chamber was used in the study²⁸⁶ of spontaneous vapour nucleation in a flow. A flow diffusion chamber was constructed such that two coaxial flows with different temperatures, *viz.*, a heated gas saturated with the vapour of the compound under study and a cold blowing gas flow free from the vapour, move in a laminar mode. Supersaturation of

the vapour of the condensed compound is achieved as a result of equalisation of the temperature and concentration through thermal conductivity and molecular diffusion. Under conditions of a laminar flow, the temperature and concentration distributions of a vapour in the bulk of a tube can be calculated using the standard heat-conduction and diffusion equations. Simplified examples of such calculations in vapour–gas laminar flows were given, for example, in the monograph.²⁵⁷ The influence of perturbations occurring at the interface of hot and cold flows was studied in detail²⁸⁶ and conditions at which these perturbations have virtually no effect on the nucleation rate were found experimentally.

In the study,²⁹¹ the nucleation and growth of aerosols in a laminar axis-symmetric flow were analysed theoretically, problems of heat and mass transfer were considered and the dynamics of the establishment of the size distribution of particles was investigated. Nucleation of one- and multicomponent condensation aerosols was studied using an experimental apparatus with a laminar axis-symmetric flow.²⁹² The measured aerosol concentrations were compared with those calculated within the framework of the classical nucleation theory. Nucleation of a dibutyl phthalate vapour as a function of temperature and supersaturation was studied in a flow diffusion chamber.^{293, 294} An algorithm was proposed for solving the two-dimensional problem of heat and mass transfer.²⁹⁵ It was demonstrated²⁹⁶ that a carrier gas affects the nucleation rate of alcohols at atmospheric pressure. This result is of great importance because it provides independent evidence in support of the thesis about the influence of a carrier gas on nucleation, which I proposed earlier.²⁹⁷

In a modified version of a flow diffusion chamber,²⁹⁷ a gas together with a vapour first go from a saturating reactor to a heated tube, where the flow becomes stationary and laminar, and then it passes to a condenser. Laminarisation of the starting vapour–gas flow facilitates substantially the specification of the boundary conditions for the flow rate distribution and vapour concentration distribution, which simplifies the solution of the stationary problem of heat and mass transfer in a chamber. Experience of the use of a flow diffusion chamber is being gradually accumulated. For example, reproduction²⁹⁸ of earlier experiments²⁹⁹ on nucleation of a dibutyl phthalate vapour gave results, which differ from the earlier data by a factor of 2–3. This is quite satisfactory for the initial stage of investigation.

Experimental methods for studying vapour nucleation are being extensively developed. Information on nucleation rates under precisely fixed conditions of nucleation can be gained in different ways. However, the method of a laminar axis-symmetric flow or a flow diffusion chamber holds, apparently, most promise. The simplicity of this method and the possibility of measuring a large number of experimental points in a rather short period of time enable one to observe, for example, a change in the phase state of critical nuclei.⁷³ Undoubtedly, this approach will be further elaborated and will find wide application in studies of processes of aerosol formation. It should be noted that different experimental methods complement each other. These methods can be arranged in the following order of increasing measured nucleation rates: a static diffusion chamber ($10^{-2} \div 10^{-3} \text{ cm}^{-3} \text{ s}^{-1}$), a flow diffusion chamber ($10^{0 \div 1} \div 10^{6 \div 7} \text{ cm}^{-3} \text{ s}^{-1}$) and adiabatic expansion methods ($10^1 \div 10^5 \text{ cm}^{-3} \text{ s}^{-1}$). The employment of a flow diffusion chamber can be supplemented by the method for turbulent mixing ($10^{5 \div 7} \div 10^{9 \div 12} \text{ cm}^{-3} \text{ s}^{-1}$). The adiabatic expansion methods assume the use of apparatus such as a Wilson chamber, shock tubes and nozzles.

IV. Excess energy of clusters. Experiment

It is known that the behaviour of a thin layer of a compound at the interface, in particular, at the vapour–condensate interface differs substantially from the behaviour of each of the homogeneous phases in the bulk. The theoretical representation of a surface layer as an inhomogeneous film, which separates homoge-

neous or virtually homogeneous substances, has been proposed already by Gibbs. The surface energy and, as a consequence, the surface tension are among the main thermodynamic characteristics of the surface layer. The available surface tension theories are far from being perfect and are, generally, applicable to only a narrow range of compounds (see, for example, Refs 8 and 80).

The excess (surface) energy of clusters plays a key role in the nucleation theory because it determines the activation energy of the nucleation process. Since our knowledge about complex systems are scarce, it is advantageous to use a simplified approach involving similarity methods and analysis of dimensionalities. The fundamental similarity criteria characterising microdisperse systems were found.²²¹ Calculations based on reference data for 38 liquids (condensed inert gases, alkanes, alkenes, dienes, aromatic hydrocarbons, alcohols, liquid metals) indicated that these criteria are temperature-dependent. The authors of the cited study believed that two systems are thermodynamically similar if their similarity numbers have (their pairs) close values. Presently, it is difficult to evaluate the importance of this approach for the nucleation theory because the proposed criteria need further verification with the use of a greater body of data for various chemical compounds. However, a search for similarity criteria undoubtedly belongs to classical problems of thermodynamics. It seems likely that the application of this or an analogous approach will pave the way to considerable progress in the development of the nucleation theory. It should be noted that a search for scale invariance requires that as much data should be used as possible and has need for intuition or research. Successive theoretical approaches are more unlikely to give a reasonable set of axiomatic statements favourable for the development of the parametric theory as compared to an essentially semiempirical search for scale invariants.

The importance of the determination of the excess energy of critical clusters was illustrated in the investigation,³⁰⁰ where the size distribution of clusters was estimated in a broad range (from dimers to macroscopic drops). In the cited study, the ratios between the equilibrium constants of dimers and the surface tension coefficients were determined and the correction for the surface tension coefficient in the Frenkel equation was found. The chemical potential of a cluster is written as a linear function of the number of 'inner' and surface molecules. The author of the cited study believed that his semi-phenomenological model and data on the size distribution of clusters can explain, for example, the experimentally observed abnormally high nucleation rate of a mercury vapour.

In the study,³⁰⁰ a vapour was treated as an ideal mixture of clusters with different sizes. The state of the atom in the cluster is characterised by the coordination number, which is similar to its value N for the corresponding condensed phase. The coordination number of the surface atoms is smaller than N . The surface tension of clusters can be described by the equation

$$\frac{\sigma}{\sigma_0} = 0.414(n-1)n^{-2/3},$$

where n is the number of molecules in an arbitrary cluster.

If the size of the critical nucleus $n^* < 30$, the surface tension of the cluster σ is much smaller than σ_0 . Consequently, the Frenkel model substantially underestimates the nucleation rate as if nucleation had occurred at high supersaturation S . Nucleation of a mercury vapour proceeds, for example, at $S \approx 10^5$ at an abnormally high rate.³⁰¹

The study³⁰² is yet another example of a search for an adequate description of the excess energy of critical nuclei. The authors introduced a correction to the equation for the surface tension and intermolecular interaction, which takes into account the second virial coefficient thus modifying the Fischer droplet model.⁵⁰ This leads to changes in the average area of the cluster surfaces and the number of molecules in the clusters. The authors of the cited study believed that their approach is applicable to any temperatures below the critical point, which was supported by the

fact that the calculated values were consistent with experimental data.

The study³⁰³ was concerned with nucleation in gases. The surface tension was described by modified McLeod's equation

$$\sigma(w_g, w_l, \theta) \simeq \Theta(\theta)(w_l^{-1} - w_g^{-1})^\delta,$$

where $w_{g,l} = v_{g,l}/v_c$ is the ratio of the specific volume of gas (or liquid) molecules to the specific critical volume; $\Theta(\theta) = (A/v_c)^4(w_{l,eq}^{-1} - w_{g,eq}^{-1})^{4-\delta}$, where A is a constant, $w_{l,eq}$ and $w_{g,eq}$ are normalised specific volumes corresponding to bimodal conditions; $2 \leq \delta \leq 4$; in most calculations, it was taken that $\delta = 2.5$.

It is assumed that as the system approaches the conditions for spinodal decomposition, the work of formation of a critical cluster decreases more rapidly than is expected from the classical nucleation theory. The authors of the cited study reasoned that their approximation combines the simplicity of the classical theory and the ease of its use. In the region of small supersaturations (like in the limiting case), the results of the classical theory are reproduced. This is attributed to the fact that the surface tension of clusters in the case of slow nucleation is close to the equilibrium value corresponding to the planar surface and high supersaturation; the surface tension deviates from the reference data and approaches the dynamic values corresponding to the appearance of new interfaces. Therefore, the surface tension is inconsistent with its macroscopic value. Hence, the application of the classical theory to systems with high supersaturations leads to substantial errors. It can be readily seen that this approach includes a useful but rather trivial parametrisation, which is present in an indirect form as the consideration of the notion of dynamic surface tension. Hence, the calculation possibilities of this approach are no higher than those of other theories. The parametrisation enables one to describe correctly the behaviour of a series of nucleating systems. However, this parametrisation does not solve the problem of the development of a universal theory.

The drawbacks in the procedures for the determination of the excess energy of critical clusters were discussed in the study.³⁰⁴ Concepts of statistical mechanics were employed for the development of the nucleation theory based on the determination of the potential energy of clusters, which is independent of the space distribution of molecules. It is assumed that the excess energy of the cluster consisting of one molecule should be equal to zero. Using the potential constants from models of macroscopic samples, one can calculate the latent heat and surface tension of clusters.

It was proposed to use a fractal model and the corresponding kinetic equations for the description of cluster formation.³⁰⁵ Clusters formed due to coalescence can be characterised by a lognormal size distribution. The results obtained with the use of the Smoluchowski equation and different theories describing a cluster size spectrum are similar to those obtained in experiments with the use of molecular beam expansion into a vacuum and in the laser chemistry of organometallic compounds. The authors of the cited study believed that the model provides a statistically perfect basis for the interpretation of data on the distribution of clusters synthesised by different methods.

In the study,³⁰⁶ a semi-phenomenological correction was proposed, which made it possible to refine the surface energy taking into account the curvature of a spherical drop known as the 'Tolman length'.⁸⁰ The following equation of state was derived with the use of Fischer's droplet model:⁵⁰

$$\frac{P_{\text{sat}}}{q_0 k_B T} = \sum_{n=1}^{\infty} n^{-\tau} \exp[-\theta_0(1 + \alpha_\sigma n^{-1/3})n^{2/3}],$$

where P_{sat} is the saturated vapour pressure, $\theta_0 \equiv \sigma_0 s_1 / k_B T$ is the dimensionless surface tension at the planar interface and $\alpha_\sigma \equiv -2\delta_T / r_1$. At low temperatures, the surface tension is high and the Tolman length is, as expected, small ($|\alpha_\sigma| \ll 1$). In this case, the solution of the equation of state takes the form

$$\alpha_\sigma = -\frac{1}{\theta_0} \ln \left(\frac{P_{\text{sat}}}{q_0 k_B T} \right) - 1.$$

In the general case, the equation of state for different nonpolar compounds is solved by numerical methods. Away from the critical temperature, the Tolman length is positive and, according to the Dillmann–Meier model, is equal to $\sim 20\%$ of the surface tension of the droplet. The Tolman length becomes negative as the critical temperature is approached and its change is consistent with that predicted by the density functional theory.

The problem of the excess energy of clusters is closely related to the question about the limits of applicability of the droplet model to small clusters. A model, which is alternative to the droplet model used for small clusters, was suggested for the description of atomic chains spontaneously formed at rather high temperatures.³⁰⁷ Analytical estimates were made on the assumption that the atom interacts only with the nearest neighbours. The interaction potential is additive and short-range. A model with a minimum number of bonds and a statistical model of a macroscopic droplet represented as many linked chains are two limiting models of the cluster. In the study,³⁰⁷ the authors used both an analytical equation for the statistical sum of a gas-like cluster, which was derived within the framework of simplified model representations of the interaction potential of particles and the cluster structure, and numerical simulation of the cluster evolution in a supersaturated vapour by molecular dynamics.³⁰⁸ The equilibrium size distribution of clusters was found by discrete methods. This distribution made it possible to calculate the homogeneous nucleation rate in a supersaturated vapour.

Studies by molecular dynamics and the Monte Carlo method demonstrated that in the first steps of cluster formation, the generation of branched chains (fractals) is energetically favourable. The latter are folded into a sphere as the size becomes rather large. A computer simulation showed³⁰⁹ that the formation of chain clusters is typical of a polar Lennard-Jones liquid. The chain length increases with increasing number of dipoles in the cluster. As a particular size is reached, the fractal is broken to form a compact spherical cluster. At the boundary of spherical clusters, chain fragments still persist. The authors of the cited study stated that the interface of spherical clusters differs substantially from a planar boundary. Collapse of fractals occurs when the number of dipoles is as much as ~ 200 .

The fact that atoms tend to be combined into clusters as energetically favourable structural units is evidenced by the results of mass spectrometric measurements. Dark-blue crystals of clusters with composition $\text{Na}_{48}[\text{H}_x\text{Mo}_{368}\text{O}_{1032}(\text{H}_2\text{O})_{240}(\text{SO}_4)_{48}] \cdot (\sim 1000 \text{H}_2\text{O})$ were prepared.³¹⁰ In these clusters, 368 molybdenum atoms form a virtually spherical shell with two open mouths on the opposite sides and the inner cavity of size $\sim 2.5 \times 4 \text{ nm}$. This structure was called a ‘nanohedgehog’ because of the presence of numerous protruding (like hedgehog hair) $\text{Mo}=\text{O}$ bonds. The ‘nanohedgehog’ has a diameter of $\sim 6 \text{ nm}$. Regions with both positive and negative curvatures are present on the cluster surface thus breaking the ‘monotonicity’ of symmetry within this nanoobject comparable in size to proteins. It is assumed that the nanocluster possesses catalytic properties. In addition to this surprising cluster, families of fullerenes and carbon nanotubes, huge nanoclusters, supramolecular compounds, *etc.* are known.

The idea that diamonds can be prepared by impact loading or rapid deposition of carbon onto a substrate followed by cooling was put forward rather long ago. Investigations of deposition on substrates have been successfully performed by Russian researchers. The results of these studies were generalised in papers and monographs.^{311,312} It was demonstrated³¹³ that meteorite diamonds are key objects, which can help in elucidating the nature of impact-wave cosmic phenomena. Studies of meteorite diamonds provided a reliable interpretation of impact recrystallisation of silicate minerals in meteorites.

Calculations by the Monte Carlo method³¹⁴ demonstrated that spheroidal silicon clusters consisting of more than 36 atoms are stable and showed that the bond energy rapidly increases as the cluster size increases. Such an increase in the bond energy is not observed if clusters are described in the droplet approximation. Calculations using the Hartree–Fock approximation for the icosahedral Si_{60} cluster gave similar results.^{315–317} In the review³¹⁸ devoted to the computer simulation of nanotubes, it was noted that the synthesis of the first carbon nanomaterials was carried out virtually simultaneously with a series of studies on simulation of their electronic structures and almost all nanotube compounds and many of their properties were predicted based on the results of calculations. Due to the unique properties of nanomaterials, the latter attract great interest, which, in turn, causes an increase in the number of investigations.

Theoretical problems of nucleation as applied to nanotube materials remain to be solved. The practical realisation of the process has not yet sufficiently developed. Hence, the quantitative determination of the nucleation rate is not a problem to be solved. Nanostructures are prepared predominantly in an arc discharge using graphite electrodes. This method was used for the synthesis of structurally different clusters.

The results of the above-considered studies provide arguments in favour of the fractal model of critical nuclei. The formation of a nucleus of a new phase can be represented as a series of successive fluctuation transformations from one relatively stable configuration of the cluster to another one. Obviously, the problem of calculating the excess energy of clusters for the description of the nucleation kinetics without resorting to the droplet model becomes more complex. However, as will be demonstrated below, this problem can be resolved.

Presently, in spite of the complexity of the experimental determination of the size (and all the more, the shape) and the excess energy of critical nuclei, such attempts are made. The surface tension at the crystal–melt interface at atmospheric pressure was calculated based on experimental data on the kinetics of spontaneous crystallisation of a supercooled liquid.³¹⁹ The region where the surface tension was determined was extended beyond the triple point. Calculations were carried out with the use of a dimensionless parameter relating the surface tension, entropy of melting and specific volume of the crystal.

In the study,³²⁰ the excess energy of the cluster formed upon crystallisation was determined using a computer experiment with the Lennard-Jones approximation, whereas other calculations were carried out using the density functional theory in the rigid-sphere approximation. In a parallel direct experiment, the nucleation and growth of crystalline nuclei was observed using a laser confocal microscope. The results of the study were compared with the results of computer simulation. Apparently, a combination of experimental investigations with theoretical methods has the most chance of making progress in studies of the nature of nucleation.

Based on generalisation of the results of experiments on nucleation, algorithms were developed for the determination of the numbers of molecules (atoms) in critical nuclei^{228,321–324} and evaluation of the surface tension.^{323,325–328}

It is known that the nucleation rate is expressed by an exponential relation analogous to Eqn (26). In the classical nucleation theory and its different modifications, the pre-exponential coefficient C is a weak function of supersaturation. In the general form, this factor can be written as

$$C = \frac{1}{\rho} \sqrt{\frac{2\sigma m}{\pi}} \left(\frac{p_0}{k_B T} \right)^2 S^{n_0}, \quad (30)$$

where ρ and σ are the density and surface tension of the condensed phase, respectively, m is the molecular mass, p_0 is the equilibrium vapour pressure under given conditions, n_0 is the exponent equal to 1 or 2. The size of the critical nucleus n^* can be calculated from the dependence of the nucleation rate on the supersaturation at constant temperature

$$\left(\frac{d \ln J}{d \ln S_i}\right)_T = \frac{d \ln C}{d \ln S_i} + n_i^* - \frac{\partial f(n, p)}{k_B T \partial \ln S_i}, \quad (31)$$

where the subscript i is the ordering number of the component. In the study,³²⁴ it was demonstrated that this equation is applicable to multicomponent nucleation. In the study,³²⁰ the possibility of determining the size of a critical nucleus upon non-isothermal nucleation under conditions of crystallisation was substantiated. The assumption that there is a relationship between the nucleation rate J , supersaturation S_i and the nucleus size n^* was made, for example, in the publication.²²⁸

It should be noted that Eqn (31), which has gained wide acceptance, has one term less than the thermodynamically exact equation derived for one-component nucleation,^{326, 327}

$$\left(\frac{d \ln J}{d \ln p}\right)_T = \frac{d \ln C}{d \ln p} + \frac{n_i^*}{k_B T} (v_v - v_l) - \frac{\partial f(n, p)}{k_B T \partial \ln p} \bigg|_{n^*}, \quad (32)$$

where v_v and v_l are the molar volumes of the vapour and liquid, respectively. In the general case, v_v and v_l should be considered as the molar volumes of the initial and equilibrium phases, respectively. In the case of nucleation in a vapour, the vapour serves as the initial phase and the volume of the liquid away from conditions for spinodal decomposition and critical conditions can be ignored. In the case of cavitation, the volume of the initial liquid phase is ignored for the same reason, and the volume of the equilibrium phase, *viz.*, the vapour, is considered.

Equation (31) for a one-component system was independently derived in the study,³²³ where it was called the nucleation theorem. The difference between the chemical potentials of phases $\Delta\mu$ was used instead of the variable $\ln S_i$; however, judging from the estimate of the summands, this difference is described in the ideal gas approximation, *i.e.*, $\Delta\mu \equiv k_B T \log S$. This immediately excludes the term associated with the specific volume v_v with the result that Eqn (31) becomes inapplicable in the region of critical and spinodal conditions, where these volumes are virtually identical. Oxtoby and Kashchiev⁷⁹ discussed the possibility of determining the number of molecules in a nucleus from the slopes of experimental isotherms of nucleation rates on the assumption that the first and third terms in Eqn (32) make only small corrections. In normal conditions, the situation is saved because the first and third terms have opposite signs, which provides their virtually complete compensation, and the specific volume of the vapour in the second term is three orders of magnitude larger than the specific volume of the condensate. However, in the case of transitions in condensed phases or in the vicinities of the critical or spinodal points, the difference between the specific volumes virtually vanishes and, hence, it is necessary to take into account all terms.

It should be noted that the exact solution of the problem of the determination of the critical nucleus size, *viz.*, Eqn (32), exists only for a one-component system. Such a problem for multicomponent systems remains to be solved. As mentioned above, the use of the ideal gas approximation leads to a loss of significant terms. Hence, it is hardly probable that Eqn (31) can be considered as the nucleation theorem. The term 'nucleation theorem' has already gained acceptance. However, it should be remembered that this term is arbitrary. Presumably, this idea will be developed to the level of the theorem in the future.

Undoubtedly, the above-considered equations extend the possibilities of studying nucleation. However, the problem of the description of multicomponent nucleation calls for further analysis. This problem is being debated in scientific literature (see, for example, Ref. 79), which, undoubtedly, will help in gaining more precise insight into the fields of application of Eqns (31) and (32). These equations can be used for considering all first-order phase transitions. The specificity of the transition can be refined by calculating a change in the Gibbs thermodynamic potential corresponding to the formation of a critical nucleus of a new phase. The study of electrocrystallisation¹²⁵ provides an example.

The usual error is to use these equations for the description of two-channel nucleation without separation of the channels. An example is the study,¹⁹³ where the estimation of the composition of critical nuclei from the slope of the nucleation rate surface in the case of two-channel nucleation was not substantiated.

Let us attempt to justify the possibility of determining the excess energy of clusters upon nucleation in a one-component system.

The necessity of taking into account such factors as the ambient pressure and, particularly, the radius of surface curvature in the deduction of an equation for the surface energy (or surface tension) requires a careful thermodynamic analysis. In the studies,^{326–328} the method for the determination of the excess energy of critical nuclei in the case of homogeneous nucleation was theoretically validated. Let us consider the deduction of the corresponding equation.

The derivative of the change in the thermodynamic potential of nucleation ΔG takes the form³²⁸

$$\frac{d\Delta G(n, T)}{dT} = \left(\frac{\partial \Delta G}{\partial T}\right)_n + \left(\frac{\partial \Delta G}{\partial n}\right)_T \frac{dn}{dT}.$$

The condition for the formation of a critical nucleus is met when the second term in the right-hand side of the equation is equal to zero. At constant pressure,

$$\frac{d\Delta\mu}{dT} = -\Delta s,$$

where Δs is the difference between the entropies of the old and new phases per molecule. Without any assumptions about the shape of the cluster, the work of its formation ΔG can be written as follows

$$\Delta G(n, \Delta\mu, p, T) = n\Delta\mu + \Theta(n, \Delta\mu, p, T), \quad (33)$$

where $\Delta\mu$ is the difference between the chemical potentials in the macroscopic volume of the liquid and in the gas phase; p is the total pressure; T is the temperature; Θ is the energy of the cluster determined by the presence of the phase interface. Then the final equation for the surface (excess) energy of the critical nucleus Θ^* with consideration for Eqn (26) takes the following form:^{70, 325, 326}

$$\frac{d}{dT} \left(k_B T \ln \frac{J}{C} \right) = n^* \Delta s - \left(\frac{\partial \Theta^*}{\partial T} \right)_n. \quad (34)$$

The solution of this equation includes the known values determined by the boundary conditions. An additional theoretical study is required to determine the multipliers in the expression for the pre-exponential coefficient C (which depends on the temperature).

Another way of estimating the surface (excess) energy of a critical nucleus was developed by Ford.^{325, 329} The excess energy can be determined using critical supersaturation; however, another equation was also derived³²⁵

$$\left(\frac{\partial \ln J}{\partial T}\right)_S = \frac{\Delta H - k_B T + \Theta^*}{k_B T^2},$$

where ΔH is the heat of vapour formation per molecule. Ford did not report data sufficient for reproducing his results [in particular, it is necessary to know how the derivative of Θ in Eqn (34) was determined] and comparing these results with the data published in the literature. It should be noted that the monotonicity and continuity conditions of $J = J(S, T)$ as a function of independent variables, *viz.*, the temperature T and supersaturation S , are not fulfilled in the vicinity of the phase transition temperature in the condensate

$$\left(\frac{\partial \ln J}{\partial \ln S}\right)_T \left(\frac{\partial \ln S}{\partial T}\right)_J \left(\frac{\partial T}{\partial \ln J}\right)_S = -1.$$

This can be attributed to the fact that the temperature dependence of the critical nucleus size in the nucleation isorate curve has a bend in the vicinities of the phase transition points.^{330, 331} Evidently, the surface energy should also undergo certain changes. These changes can be found using the criteria for singularity of nucleation surfaces.

Let us consider the experimental method for the determination of the surface energy of a critical nucleus³³² with the constraint $p = \text{const}$. Assuming that the behaviour of a vapour is described by the equation of state of an ideal gas, *i.e.*,

$$\Delta\mu = -k_B T \ln S,$$

let us go to new independent variables in Eqn (33)

$$\Delta G(n, \ln S, T) = -n k_B T \ln S + \Theta(n, \ln S, T). \quad (35)$$

For a critical nucleus, the following equation is valid

$$\left(\frac{\partial \Delta G}{\partial n} \right)_{n=n^*, S, T} = 0.$$

The number of independent variables in Eqn (35) for the work of formation of a critical nucleus decreases by unity because the nucleus size is unambiguously determined at fixed temperature and supersaturation. Let us choose S and T as independent variables. Then

$$\Delta G^*(\ln S, T) = -n^*(\ln S, T) k_B T \ln S + \Theta(\ln S, T). \quad (36)$$

After differentiation of Eqn (36) with respect to T at a constant supersaturation, we obtain

$$\left(\frac{\partial \Delta G^*}{\partial T} \right)_S = -n^* k_B \ln S - k_B T \ln S \left(\frac{\partial n^*}{\partial T} \right)_S + \left(\frac{\partial \Theta^*}{\partial T} \right)_S.$$

Let us consider this equation as applied to nucleation. The exponential dependence of the rate of formation of a new phase J on the work of nucleus formation of this phase ΔG^* described by Eqn (26) is beyond question. However, the pre-exponential coefficient C was not unambiguously determined. According to the classical nucleation theory, the factor C is proportional to the square of supersaturation. However, in more recent studies (self-consistent theory),^{46–48} this coefficient was reduced. While staying within the framework of the classical nucleation theory, the pre-exponential coefficient can, in the general case, be represented by Eqn (30).

By differentiating Eqn (26) with respect to T at a constant supersaturation, we have

$$\left(\frac{\partial \ln J}{\partial T} \right)_S = \left(\frac{\partial \ln C}{\partial T} \right)_S + \frac{\Delta G^*}{k_B T^2} - \frac{1}{k_B T} \left(\frac{\partial \Delta G^*}{\partial T} \right)_S. \quad (37)$$

Taking into account Eqn (30),

$$\left(\frac{\partial \ln C}{\partial T} \right)_S = \frac{1}{2} \frac{\partial \ln \sigma}{\partial T} - \frac{\partial \ln \rho}{\partial T} + 2 \frac{\partial \ln p_0}{\partial T} - \frac{2}{T}. \quad (38)$$

In the analysis of the temperature dependences of the surface tension and density for a series of compounds (water, glycerol, pentanol, *etc.*), the first two terms in Eqn (38) are two orders of magnitude smaller than the third term and, hence, they can be ignored. Equation (37) can be rearranged to Eqn (39) using the Clausius–Clapeyron equation

$$\begin{aligned} \left(\frac{\partial \ln J}{\partial T} \right)_S &= \frac{2(\Delta H - k_B T) + \Theta^*}{k_B T^2} + \ln S \left(\frac{\partial n^*}{\partial T} \right)_S - \\ &- \frac{1}{k_B T} \left(\frac{\partial \Theta^*}{\partial T} \right)_S. \end{aligned} \quad (39)$$

The latter equation reduces to the first-order linear differential equation

$$y' + f(x)y = g(x), \quad (40)$$

where $y = \Theta^*$, $x = T$. If the functions $f(x)$ and $g(x)$ are continuous, the integral curve passing through the point $(x, y) = (\xi, \eta)$, provided that $y(x) = \eta(\xi)$ is known, is described by the following equation

$$y = e^{-F} \left(\eta + \int_{\xi}^x g(x) e^F dx \right), \quad (41)$$

$$F(x) = \int_{\xi}^x f(x) dx.$$

Therefore, to solve Eqn (40), it is necessary to know at least one point at which the required parameters of the system are determined. The dependence of $\ln p_0$ on the inverse temperature specified by the Clausius–Clapeyron equation can be considered to be linear at a vapour pressure corresponding to a constant supersaturation up to the conditions for spinodal decomposition.³³³ At fixed supersaturations, an increase in the temperature of a system leads to the state at which the vapour pressure is equal to the pressure of spinodal decomposition. According to Eqn (36), the following equation should be fulfilled at the spinodal decomposition point

$$\Theta_{sp}^* = k_B T_{sp} n^* \ln S.$$

The use of this equation for solving Eqn (41) with consideration for Eqn (39) leads to the following expression for the surface energy of a critical nucleus:

$$\frac{\Theta^*}{k_B T} = n^* \ln S + 2 \frac{\Delta H}{k_B T} \left(\frac{T}{T_{sp}} - 1 \right) - 2 \ln \frac{T}{T_{sp}} - \ln \frac{J}{J_{sp}}. \quad (42)$$

It can be seen that it is necessary to know the number of molecules in a critical nucleus n^* and the temperature T_{sp} at the spinodal decomposition point to determine the surface energy. The critical nucleus size is calculated from the slope of the curve of the isothermal nucleation rate in double logarithmic coordinates. The temperature of spinodal decomposition T_{sp} at a constant supersaturation is found from the equation of state for a one-component mixture on the condition that $(\partial P / \partial V)_T = 0$. The corresponding nucleation rate J_{sp} is determined by linearisation of experimental data followed by the linear extrapolation of the temperature dependence of the nucleation rate to the point T_{sp} .

The applicability of the method proposed for the determination of the surface energy of critical nuclei was tested using supersaturated vapours of polyhydric alcohols (propanediols and glycerol) under an atmosphere of carbon dioxide and sulfur hexafluoride.³³² These experiments were preceded by detailed investigations of the effect of the parameters of systems on the characteristics of critical nuclei.⁷³ For example, the phase transition was observed in critical nuclei in the investigation of nucleation of a supersaturated propane-1,3-diol vapour under an atmosphere of sulfur hexafluoride at different temperatures and pressures. The isotherms of nucleation rates at a total system pressure of 0.30 MPa are shown in Fig. 2. The isotherm measured at a nucleation temperature of 334 K corresponds to the transformation from one nucleation rate surface to another. At the temperature corresponding to a change in the phase state in critical nuclei, the isotherm of the nucleation rate becomes non-monotonic. The temperature dependence of the surface energy of nuclei should also have some characteristic features indicative of the discontinuity of the first derivative of the thermodynamic potential, which is a direct condition for the first-order phase transition.

The experimental investigation of nucleation of glycerol under an atmosphere of CO₂ in the temperature range of 310–320 K demonstrated that the parameters of critical nuclei undergo a jump caused by a first-order phase transition in the vicinity of the critical line of a binary glycerol–carbon dioxide system.⁷³ In the

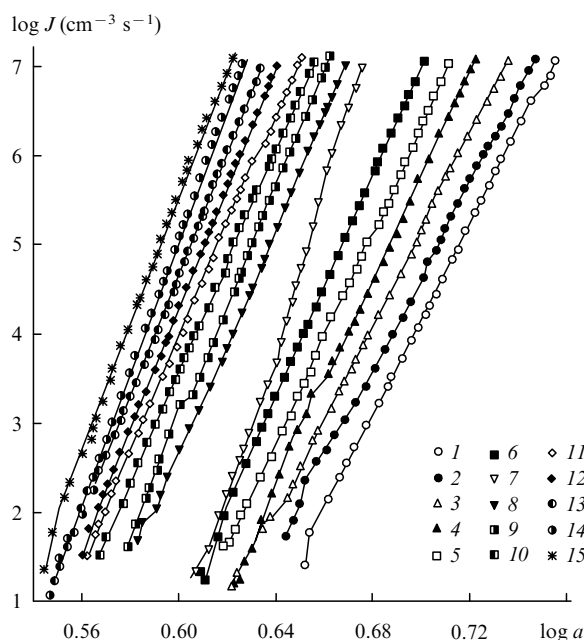


Figure 2. Nucleation rates vs. the activity of a propane-1,3-diol vapour under an atmosphere of sulfur hexafluoride at different nucleation temperatures.⁷³

T/K : (1) 320.92, (2) 323.17, (3) 325.29, (4) 327.63, (5) 329.88, (6) 332.31, (7) 334.25, (8) 336.45, (9) 338.62, (10) 340.84, (11) 343.16, (12) 345.48, (13) 347.54, (14) 349.75, (15) 351.90.

melting-temperature range of glycerol (295 K), the cluster surface energy shows anomalous behaviour.

The temperature dependences of the size and surface energy of critical nuclei of propane-1,2-diol, propane-1,3-diol and glycerol under an atmosphere of carbon dioxide and sulfur hexafluoride were found.³³² The surface energy was calculated using Eqn (42) at a constant nucleation rate ($10^3 \text{ cm}^{-3} \text{ s}^{-1}$).

Figure 3 shows the experimental dependence of the excess energy on the nucleus size and presents the results of calculations of the surface energy of critical nuclei that appear (using the droplet model in a one-component approximation) in an octa-

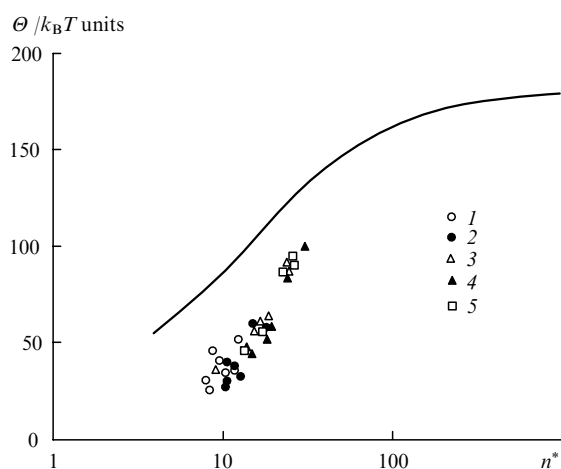


Figure 3. Surface energy vs. the critical nucleus size of octanol under an atmosphere of sulfur hexafluoride. Points correspond to the experimental data; the solid line indicates the data calculated using the droplet model. The total pressure in a vapour–gas system /MPa: (1) 0.10, (2) 0.15, (3) 0.20, (4) 0.25, (5) 0.30.

nol–sulfur hexafluoride system.³³² It can be seen that a decrease in the excess energy depending on the number of molecules in the nucleus is more rapid than that predicted according to the droplet model. Extrapolation to larger numbers allows one to estimate the critical nucleus size at the energies found according to the proposed algorithm which are identical with those determined using the droplet model. Beginning with this size, the droplet model of a nucleus becomes applicable. In the case under consideration, a nucleus should contain ~ 100 –140 molecules.

To extrapolate the dependence under consideration to the size of the nucleus consisting of one molecule (atom), it is necessary to define such a notion as the surface (excess) energy of the molecule. Langmuir proposed (using some simple compounds as examples) that the heat of evaporation of one molecule could be considered as an analogue of the surface energy.³³⁴ This assumption is rather arbitrary in spite of the fact that the evaporation energy and surface energy depend on the same factors, *viz.*, intermolecular interactions. The inconsistency is attributed to the differences in the distribution of intermolecular bonds in the bulk of a macroscopic object and in the cluster.

The order of the dependence of the surface energy of critical nuclei on the cluster radius is higher than two.³³⁵ This fact confirms the conclusion, which was made based on the results of computer simulation, that clusters have a fractal structure in the initial step of condensed phase growth. By extrapolating the logarithmic dependences of the energy on the nucleus size, the ‘surface’ energy of one molecule can be determined. A comparison of the surface energies of critical nuclei of polyhydric alcohols with the reference data³³⁶ on the heats of evaporation of individual compounds demonstrated that, for instance, the heat of evaporation of the glycerol molecule is two times larger than its surface energy. Apparently, this difference can serve as the characteristic (in energy units) of the excess energy accumulated in the cluster. Another reason for this discrepancy is the presence of the dissolved gas in the cluster.

The method proposed for the determination of the surface energy of critical nuclei based on experimental results can, undoubtedly, be a convenient tool for the quantitative estimate of this very important physicochemical parameter. However, the incorrect interpretation can be made, for example, based on the results of measurements of the overall rates in the presence of two nucleation surfaces. A lack of reliable methods for the measurement of the nucleation rates corresponding to each individual surface hinders a comparison of theoretical and experimental data. The application of the theory developed for single-channel nucleation to the interpretation of the results of measurements of the overall rates in the presence of two (or more) nucleation surfaces leads to a deadlock situation. It becomes apparent that there is a need to elaborate on the experimental methods for separate measurements of nucleation rates for each surface.

The development of procedures for examining experimental methods is of great importance. An *n*-pentanol–helium mixture can be used as a testing system.³³⁷ Evidently, the approximate dependence of the nucleation rate on the total pressure in this system has some errors, but the parameters of the approximation can be refined with more reliable data.

To test large sets of experimental data, it is advised to use differential values,³³¹ which formally characterise the conditions for monotonicity and continuity of the function. Therefore, one can achieve higher accuracy in the analysis of data and reveal inflections in the corresponding experimental curves.

The available analytical methods do not meet modern requirements. When performing theoretical analysis, one has to make initial assumptions about phase transitions and their kinetics rather than obtain the corresponding parameters based in more general laws. Experimental results often serve as a source of new theoretical ideas. For example, the possibility of using phase equilibrium diagrams for the development of the nucleation theory was not considered until recently. Taking into account that these diagrams (or their cross-sections) given in various

handbooks are lines of zero nucleation rates, the topology of the nucleation surface can be represented in the limit of its zero rates. By performing a few experimental measurements, one can determine the slope of the linearised nucleation rate surface thus estimating the rate with an accuracy, which is obviously higher than the accuracy of any theoretical calculations. This simple idea provided the basis for semiempirical methods for the construction of nucleation rate surfaces^{14, 338} considered below.

V. Semiempirical methods for constructing nucleation rate surfaces

It is not always possible to determine nucleation rates in practically important systems using theoretical models. A method for the semiempirical construction of nucleation rate surfaces was described.¹⁴

It is known that the chemical potential surface of one phase as a function of temperature and pressure in a system can intersect the chemical potential surface of another phase. The intersection of these surfaces is a phase equilibrium line. If the first derivatives exhibit discontinuities along this line, the first-order phase transition occurs. In the case of the vapour–liquid equilibrium, the equilibrium line consists of numerous points of first-order phase transitions with the phase transition temperature T_p (Fig. 4). The critical point corresponding to the second-order phase transition with the temperature T_c is at the end of this line. At the critical point, the chemical potential and its first derivative for the liquid phase are identical with those for the vapour phase. An individual phase is ‘insensitive’ to the equilibrium line. The phase can cross this line and reach the region, where the chemical potential of this phase is higher than that of another phase. These metastable states are denoted by V_m and L_m for the vapour and liquid, respectively. The lines of spinodal decomposition serve as metastable state boundaries. Figure 4 gives the lines of spinodal decomposition having projections cs_1 and cs_2 onto the PT plane. The projection of the equilibrium line of chemical potentials forms a vapour–liquid equilibrium line $T_p c$. This pattern can be readily generalised to multicomponent systems.

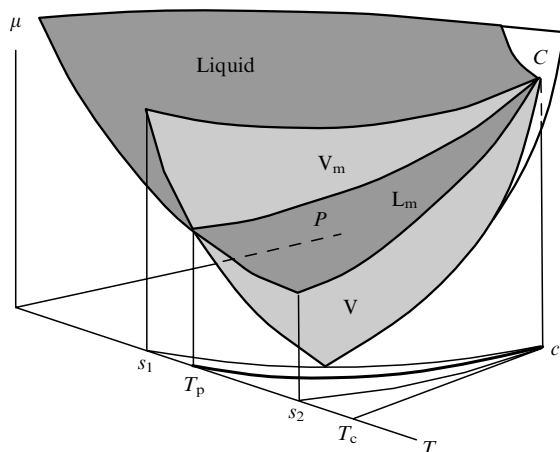


Figure 4. Chemical potential surface μ for the vapour–liquid equilibrium as a function of the pressure P and temperature T .^{12, 14}

Metastable states appear upon first-order phase transitions due to the necessity of expending energy for the creation of the interface of critical nuclei. The lifetime of a metastable phase depends on the depth of penetration of one phase into the region of another co-existing stable phase, *i.e.*, on the degree of supersaturation of the initial phase. The diagrams of metastable states in processes of melting and cavitation have been discussed many times (see, for example, Refs 339–342). A diagram of a metasta-

ble state of a vapour and a nucleation rate surface were proposed and analysed in the study.³³⁸

1. Phase PT diagram of unstable equilibria

The basic knowledge about the topology of the nucleation rate surface can be gained by analysing a simplified PT diagram of a one-component system with a critical point.¹⁴ Regions of metastable states, which exist for each phase, are shown in Fig. 5.

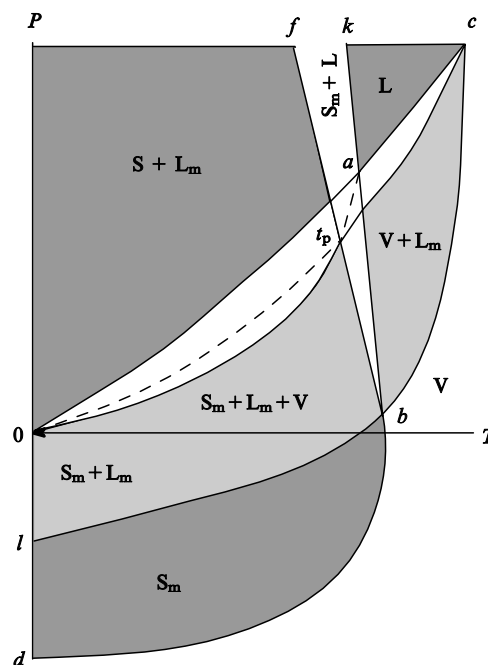


Figure 5. Simplified PT diagram of metastable states.¹⁴ The zero temperature limit is indicated by an arrow; the liquid, solid and gas states are denoted by L , S and V , respectively; the subscript m signifies the metastable state.

It is known that the phase equilibrium lines never end in a triple point. For this reason, the S – L equilibrium line intersects with the line of spinodal decomposition (kbd) of a superheated (stretched) crystal and with the line of spinodal decomposition (cbl) of a stretched (supercooled) liquid. The point b is the point of critical instability¹⁴ at which the S – L equilibrium line intersects with the spinodal for cavitation cbl . At the point b , the line of labile states of a liquid cbl intersects with both the line of labile states of a crystal kbd and the line of liquid–crystal unstable equilibrium $ftpb$.

The viscosity of a supercooled liquid increases as the temperature decreases and this liquid can exist at as low temperatures as is wished,¹⁴ the liquid being able to occur in the liquid or glassy state. The glassy state is not an independent phase because it has no equilibrium lines with other phases. In the degree of order, the glassy state is closer to the liquid in which the long-range order is absent. It seems reasonable to consider glassy states as metastable states of a liquid. However, glasses are sometimes (see, for example, Ref. 341) treated as individual phases and lines of spinodal decomposition of a liquid are passed to the region of existence of crystalline states. In this connection, it should be noted that the transformation of a liquid into the glassy state does not mean the glass–supercooled liquid equilibrium and it cannot be characterised by the equilibrium transition temperature. Hence, a glass cannot be considered as an individual phase. Nevertheless, the region of existence of a glass was approximated³⁴¹ by a line and it was assigned to conditions for spinodal decomposition of the liquid, the end of this line being called the critical point. In my opinion, the concept of the absence of a

temperature limit for spinodal decomposition of a liquid (see the line *cbl* in Fig. 5) up to the limiting temperature, *viz.*, absolute zero, is preferable.

The *S*–*V* equilibrium line passes from the point *a* to the point 0. It is essential that this line begins at the point *a*, where the spinodal line for crystals *kb* intersects with the spinodal line for a vapour *ca0*. This indicates that the vapour–crystal equilibrium line extends upward to higher temperatures. The point *a* corresponds to the highest temperatures and pressure at which the solid–liquid–vapour metastable state can occur over a short period of time. The crystalline state is spontaneously transformed into the liquid state. It was stated that¹⁴ the point *a* is not the crystal–vapour critical point, like the point *c*, because both phases at the point *a* occur at the same temperature and pressure, although they differ in density, structure and other properties and cannot be transformed into each other without activation. It should be noted that the difference in the density can be insignificant because the vapour supersaturation in an experiment can reach several hundred units. In the case of spinodal decomposition, it is reasonable to expect the vapour supersaturation to be as great as several thousand units, which is similar to the ratio between the densities of the condensed and vapour phases, *i.e.*, the difference in the densities of the crystal and vapour can appear to be vanishingly small. The possibility of a continuous change in the order parameter when going round the point *a* remains an open question.

In experiments on the generation of aerosols, it is possible to produce crystalline particles at moderate supersaturations. At high supersaturations, particles with a non-crystalline structure, *i.e.*, a supercooled liquid or an amorphous solid, are predominantly formed. Under the conditions for spinodal decomposition, the nucleation rate of a metastable liquid should be higher than the rate of crystal formation due to kinetic limitations. The above-mentioned limitations result from the fact that the formation of a nucleus with a crystalline structure requires that molecules (atoms) be able to migrate to sites of the crystal lattice formed. Evidently, in the case of a large flux of molecules that appears under conditions for spinodal decomposition, there can be not enough time for jumps of the molecules, which occupy crystal lattice sites and form a crystalline nucleus. Correspondingly, the probability (and the rate) of formation of droplets (or glasses) should be higher than the probability (and the rate) of formation of crystalline nuclei.

2. Examples of construction of nucleation rate surfaces

A nucleation rate surface can be constructed¹⁴ above a simplified *PT* diagram with a triple point (see Fig. 5). Nucleation rates are considered to be steady. Transient phenomena upon the establishment of a stationary nucleation rate or effects of vapour depletion are ignored. Nucleation rate surfaces are constructed using the following assumptions.

1. An individual phase can exist behind the line of interphase equilibrium in a metastable state. The equilibrium line can be extended to the region of an equilibrium state of another phase as a line of unstable equilibrium.
2. Equilibrium lines in the phase diagram are lines of zero nucleation rate.
3. Under conditions for spinodal decomposition, the highest nucleation rate is achieved at a constant pressure or constant temperature.
4. Under conditions for spinodal decomposition, the nucleation rate giving rise to less stable states is higher than the rate of nucleus formation of a more ordered stable phase.
5. The nucleation rate at the critical point is equal to zero.

The first three assumptions correspond to known empirical results of studies of first-order phase transitions. The fourth assumption seems to be reasonable taking into account data on the kinetics of phase formation. Thus, under conditions for spinodal decomposition, molecules do not have time to be incorporated into crystal lattice sites and, hence, form amorphous

particles with high probability. The fifth assumption is a consequence of the fact that the critical point corresponds to the second-order phase transition, where separation into phases is absent and, consequently, nucleation at the critical point cannot occur. It was noted¹⁴ that the fifth assumption can follow from the second one.

Let us consider a fragment of the phase equilibrium diagram in the vicinity of the triple point *t* (Fig. 6). The vapour–crystal (*kt*) and vapour–liquid (*tm*) equilibrium lines are extended to the region of existence of the third equilibrium phases. The nucleation rate surface of liquid-droplet nuclei is pale-grey. The dark-grey surface corresponds to the nucleation rate of crystalline nuclei. The surfaces intersect in the line *et*. The intersection of the surfaces forms an ascending branch *ke* (and the dashed line is its extension to conditions for spinodal decomposition) corresponding to the nucleation rate of crystals. The nucleation rate of liquid-droplet nuclei is represented by the line *eh* (and its extension to zero rates). If a saturated vapour at the point *m* begins to be cooled at a constant pressure, a liquid-droplet aerosol can be prepared. At the temperature corresponding to the point *l* and below, the formation of crystalline nuclei starts. The nucleation rates of both phases increase as the temperature is decreased, but the nucleation rate of crystals increases faster. At the point *e*, the rates of formation of liquid-droplet and crystalline nuclei are equalised. It is easy to understand that if the phase state of nuclei is retained in the course of subsequent condensation growth, the sizes of aerosol particles are different due to the known nonequality of the accommodation coefficients of molecules on surfaces with different phase states. This conclusion was experimentally confirmed in the study.¹⁵

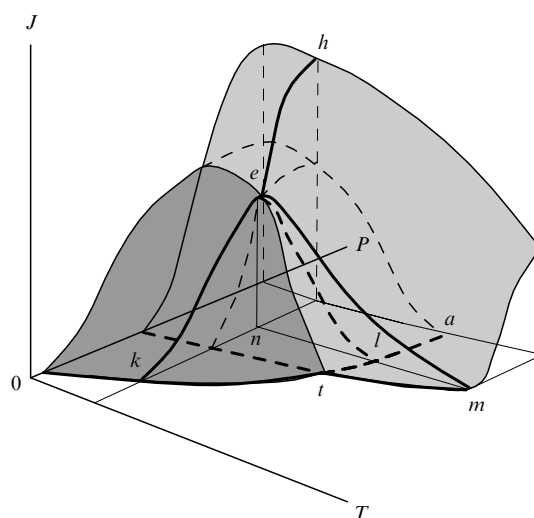


Figure 6. Nucleation rate surfaces for a one-component vapour.¹⁵

Surfaces of nucleation rates in superheated (or stretched) crystals, nucleation in a supercooled liquid and cavitation were constructed.¹⁴ It should be noted that the assumption of a non-zero nucleation rate in the zero temperature limit¹⁴ is, most likely, erroneous. Actually, the pressure vapour at absolute zero is also equal to zero and there is no question about nucleation in a vapour. Hence it follows that the nucleation rate in a vapour above the line of spinodal decomposition first increases as the temperature decreases from the critical one, then reaches a maximum and falls to zero in the zero temperature limit. Under conditions for spinodal decomposition, the nucleation rate is equal to the pre-exponential coefficient in the equation for the nucleation rate. In the case of a vapour, this coefficient increases from zero to a maximum and then again decreases to zero as the temperature decreases from the critical value to absolute zero. By contrast, in the case of nucleation in condensed phases, the pre-exponential coefficient, apparently, only increases with decreasing

temperature. However, this assumption needs further verification. Such a verification can be performed in the case of simultaneous homogeneous and heterogeneous nucleation, as was demonstrated using ion-induced nucleation as an example.³³³

Nucleation rate surfaces of binary vapours can be represented in the four-dimensional surface JTa_1a_2 , where J is the nucleation rate, T is the temperature and a_1 and a_2 are the activities of the vapours of the components. Let us consider the simplified PX diagram of a binary solution at the fixed temperature T , total pressure in the system P and composition x . In this case, the phase diagram is cigar-like in shape (lines mfn and $nrgm$ in Fig. 7).

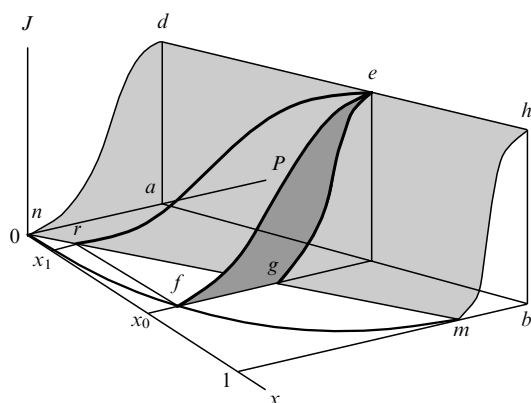


Figure 7. Nucleation rate surface (J) for ideal solutions (P is the total pressure, x is the composition of a binary solution).¹⁴

The nucleation rates of individual components are represented by the curves nd and mh . At the point of vapour equilibrium (n, m), the nucleation rates of the vapour are equal to zero. The nucleation rates of the components have maximum values above the spinodal decomposition points a and b . These maximum rates in a simplified form can be related by the line deh corresponding to maxima of the binary nucleation rate. The nucleation of a binary vapour with composition x_0 starts at the point f .

A condensed phase has the composition x_1 at the point r . Each point on the line nfm corresponds to a point on the line $nrgm$. The latter line, which is an equilibrium line between a liquid and two-phase states, is the trajectory of points of the zero nucleation rate and forms a surface boundary of the nucleation rates. The nucleation rate surface is contoured by $hednrgm$. Above the spinodal, the composition of a vapour is identical with those of condensed phases due to the absence of the barrier to transformation into the condensed phase. The line re describes the nucleation rate of a vapour (with the known composition of critical nuclei) in the course of an increase in the pressure from the point r to the point e at the constant nucleation temperature T and the initial composition of the vapour x_1 . The curve fe is a projection of the curve re onto the plane corresponding to the composition x_0 . No information on the composition of critical nuclei can be extracted from the curve fe .

In the case of an unknown composition of critical nuclei, a nucleation rate surface can be constructed if all experimental nucleation rates (analogous to the curve re) correspond to the initial composition of the vapour in the phase diagram (for example, the line fe for the composition x_0). In this case, the points of the zero rate of vapour nucleation are located on the lower line of the cigar-like diagram. The rate surface under consideration is presented in the JxP coordinates. Apparently, the mode of representation of binary nucleation rates of a vapour depends on whether or not the composition of critical nuclei is known. If the composition of critical nuclei is unknown, a nucleation rate surface for an ideal binary solution is contoured by $hednfm$ (see Fig. 7). In experiments, the composition of nuclei is usually unknown and the measured nucleation rate in a binary

system is assigned to its initial composition. Thereafter, the composition of nuclei of the condensate can be determined from the slopes of nucleation rate isotherms.^{324, 343}

The nucleation in a binary system with partial mutual solubility of the components was discussed in the study.³⁴⁴ Earlier, it was demonstrated⁶⁹ that in this case, two-channel nucleation takes place. In the publication,³⁴⁴ a new assumption was made according to which each channel is characterised by its own nucleation rate surface for ideal solutions. The authors of the cited study used the rule of summation of nucleation rates for both channels in the linear approximation analogous to the lever rule for solutions. The validity of assuming linear summation of nucleation rates calls for experimental verification. However, an essential advantage of this approach is that it substantiates the possibility of the presence of local maxima in a nucleation rate isotherm, which does not follow from the classical theory. This result can be illustrated by the experimental dependence of the nucleation rates on the activity of an alcohol vapour in n-pentanol–argon (Fig. 8) and n-pentanol–sulfur hexafluoride systems.³⁴⁴

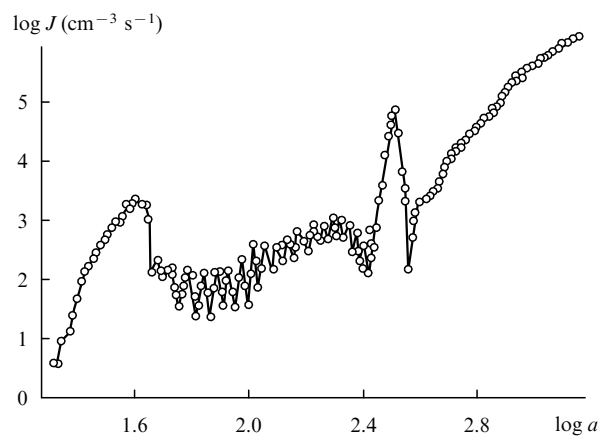


Figure 8. Nucleation rate in an n-pentanol–argon system vs. the activity of an n-pentanol vapour.³³⁸

The pressure in the system influences the course of nucleation. However, this fact has not been noted in early experiments performed by Wilson and other researchers. Examples of the pronounced effect of the pressure in the course of boiling water, ethanol, acetone and their solutions were given in the studies.^{345, 346} Noteworthy is the idea of bond percolation used by the authors of these studies. However, this idea was not confirmed experimentally and, hence, the assumption about the continuity threshold of unbroken intermolecular bonds in a liquid in the metastable region was made. The authors of the study³⁴⁷ and their colleagues^{233, 348–350} still attributed the pronounced effect of the total pressure on the nucleation rate in vapours of a number of chemical compounds to other factors by referring to corrections for non-ideality of a vapour, compressibility of a critical cluster and the Poynting effect. Undoubtedly, all these factors should be taken into account, but there is one more important factor as well. Thus, direct experiments demonstrated (see, for example, Ref. 73) that a gas and a vapour form a binary system in which phase transitions take place in critical nuclei due to the presence of a carrier gas.

VI. Nucleation in binary systems

The nucleation in a binary solution in which a chemical reaction proceeds (see, for example, Ref. 351) has distinguishing features. In this case, the phase diagram consists of the phase diagrams of two individual binary systems and a newly formed compound is considered as a limiting compound in each of these diagrams.

None of the available nucleation theories can predict nucleation rate surfaces resulting from interactions. Many problems remain to be solved among which is the problem of the rates of non-stoichiometric chemical reactions, which are determined by extension of the nucleation rate surface to the non-stoichiometric region. It is not inconceivable that in further studies, approaches of chemical kinetics will be combined with nucleation kinetics.

1. Phenomenological consideration of intermolecular interactions

A semiempirical approach to the construction of nucleation surfaces^{12–14} is based on the relationship between nucleation rates and phase diagrams. This relationship is evident in the case of stationary dynamic systems, which occur close to the equilibrium. However, a more careful examination should be carried out for systems existing far from equilibrium. For example, large flows of matter occur upon the formation of a cloud layer in the atmosphere or upon atmospheric precipitation. It is known that a strong dynamic response is characteristic of flow systems.¹⁸² This dynamic response is manifested in the transformation of the system to another dynamic mode (hydrodynamic or thermodynamic crisis, autowave mode). The effect of this type, which was studied first, is called the Benard (convective) instability. This effect is manifested in the appearance and rearrangement of convective cells in a liquid layer heated from below. Under conditions far from equilibrium, instabilities are responsible for the long-range order and, as a result, the system acts as an organic whole.¹⁸² Besides, in the case of a non-equilibrium first-order phase transition, a compound goes through a metastable state (supersaturated vapour, superheated or supercooled liquid). As a result, the metastable phase by itself becomes a flow system, which can produce a stationary flow of nuclei of a new phase at a given temperature, pressure and composition. The study³⁵² examined the evolution of dynamic phase diagrams of a binary system as the flow J (nucleation rate) increases on the assumption that the latter plays a dominant role compared to other types of flows (for example, a hydrodynamic flow). The deviations of the nucleating system from equilibrium are characterised by the flow of nuclei of a new phase. Hence, nucleation isorates ($J = \text{const}$) can be treated in the corresponding coordinates as dynamic phase diagrams.

Experimental data on nucleation rates were compared with empirical phase diagrams of binary systems using a water–propan-1-ol system with an azeotropic point as an example.³⁵³ Figure 9 shows static ($J = 0$ at $T = 298$ K) and dynamic ($J = 1 \text{ cm}^{-3} \text{ s}^{-1}$ at $T = 298$ K and $J = 10^7 \text{ cm}^{-3} \text{ s}^{-1}$ at $T = 260$ K) phase diagrams of a water–propan-1-ol system in the coordinates of the mole fraction of alcohol vs. the reduced pressure (the total pressure related to the pressure of the saturated

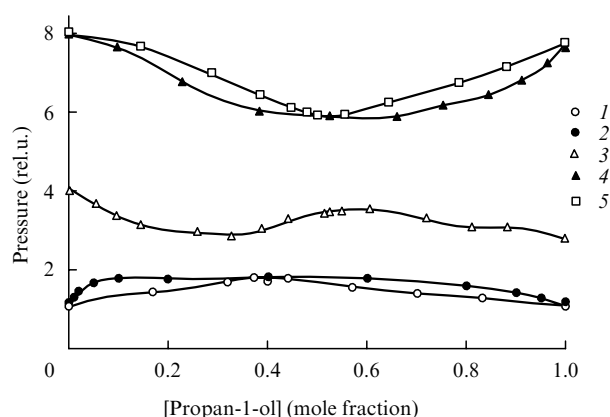


Figure 9. Phase diagrams of a water–propan-1-ol system at nucleation rates $J = 0$ [(1) vapour, (2) liquid]; $J = 1$ [(3) vapour] and $J = 10^7 \text{ cm}^{-3} \text{ s}^{-1}$ [(4) vapour, (5) liquid].³⁵³

propan-1-ol vapour in an ideal solution $P_{298} = 2700 \text{ Pa}$ at $T = 298 \text{ K}$ and $P_{260} = 125 \text{ Pa}$ at $T = 260 \text{ K}$). The line 5 for a liquid in the dynamic phase diagram is constructed based on the data on the molar composition of critical nuclei (see references cited in the study³⁵³).

In the case of large deviations from an ideal solution, dynamic phase diagrams are transformed as the nucleation rate increases. As can be seen from Fig. 9, this transformation is accompanied by a shift of the azeotropic point of a water–propan-1-ol system along the axis of composition. An analogous change from a convex diagram to a concave one was observed for a water–ethanol system.³³⁵ In Fig. 10, the spinodal is schematically represented by the line be . It was taken into account that the convexity of the diagrams changes for concavity as the nucleation rate increases and it was also considered that the lines for a vapour and a liquid should coincide under conditions of spinodal decomposition. The dynamic diagrams corresponding to $\log J = 0, 4, 7$ and $10 \text{ (cm}^{-3} \text{ s}^{-1})$ are schematically represented by the corresponding contours (the nucleation rate surface shown in grey colour passes through the vapour lines). The spinodal be has a concave shape, i.e., the vapour pressure of the mixture at the end of the line of azeotropic solutions is lower than the vapour pressures of the pure components. By contrast, the equilibrium diagram (ad) is convex (the pressure reaches the maximum values at the azeotropic point in the phase equilibrium diagram). Deviation of dynamic diagrams from the equilibrium diagram should primarily be observed upon enrichment of the mixture with water, which takes place in the experiment (see Fig. 9). A change in the shape of the spinodal curve can lead to another transformation of dynamic diagrams.

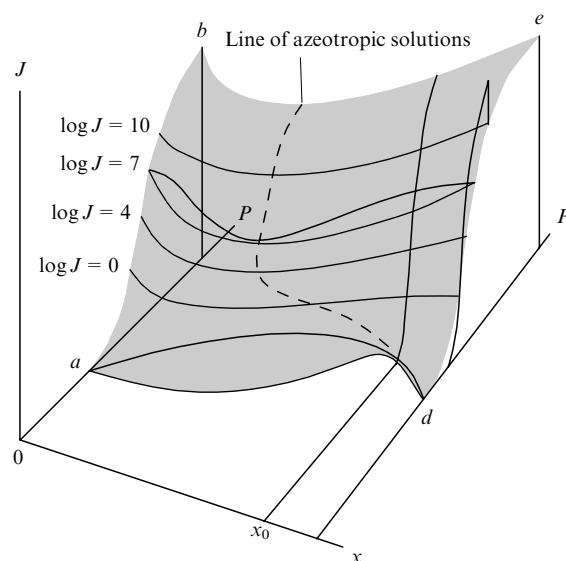


Figure 10. Schematic representation of the nucleation rate surface in a binary system constructed on the basis of experimental data for a water–ethanol system.

As a binary system moves away from the equilibrium, small contributions of binary interactions between the molecules can, on the contrary, appear to be prevailing. In such nonlinear systems, components lose their individuality (typical of an equilibrium state) and the mixture behaves as a whole, i.e., in the case of substantial deviations from equilibrium, intermolecular interactions are collective in character. A strengthening of intermolecular interactions, as applied to static phase diagrams of binary systems, is manifested in an increase in the negative deviation of the system from an ideal solution (the total vapour pressure is lower than the additive value). The evolution of the phase diagrams presented in Figs 9 and 10 is also accompanied by a decrease in the total

pressure as the system moves away from the equilibrium (as J increases). In other words, the changes in dynamic phase diagrams are analogous to the changes in usual phase diagrams as intermolecular interactions are strengthened.

In calculations of phase diagrams of a binary system within the framework of a single-liquid model (homogeneous liquid), the correction parameter k , which takes into account binary interactions and determines mutual attractions between molecules of different components, was entered into the equation of state (for example, into the van der Waals equation).³⁵³ Therefore, the nucleation isorates of a vapour can be interpreted as phase diagrams corresponding to the parameters of the binary interactions k . For a metastable state, the boundary of a stable homogeneity of a phase is determined by the condition of vanishing vapour tension ($\partial P/\partial V$) in an isotherm of state, *i.e.*, by a spinodal.

A choice of an algorithm for calculating a spinodal is governed by the condition for stability of a binary solution. As the system moves deep inside the metastable region, it retains the fixed entropy S , volume V and amount of matter at a constant internal energy $dU = 0$. Instability of relatively continuous changes in the parameters of state is initially manifested in the vanishing of the diffusion coefficient of stability

$$\left(\frac{\partial \Delta \mu}{\partial x}\right)_{P,T} = 0, \quad (43)$$

where x is the composition of the binary system. Then the necessary and sufficient conditions for stability of a binary solution are expressed by the inequality

$$\left(\frac{\partial \Delta \mu}{\partial x}\right)_{P,T} > 0 \quad (44)$$

or a system of inequalities

$$-\left(\frac{\partial P}{\partial V}\right)_{T,x} > 0, \quad (45)$$

$$\left(\frac{\partial T}{\partial S}\right)_{V,x} > 0. \quad (46)$$

In the van der Waals single-liquid model, a binary solution at fixed x is considered as an efficient one-component fluid obeying the equation of state in the above-mentioned variables

$$\pi = \frac{8\tau}{\varphi - b(x)/b_{11}} - \frac{27a(x)/a_{11}}{\varphi^2}, \quad (47)$$

where $\pi = P/P_{c1}$, $\tau = T/T_{c1}$ (P_{c1} and T_{c1} are the pressure and temperature, respectively, at the critical point of the low-temperature component 1); $\varphi = V/b_{11}$; the coefficients $a(x)$ and $b(x)$ depend on the concentration of the second component and are calculated by the equations

$$a(x) = (1-x)^2 a_{11} + 2(1-x)x a_{12} + x^2 a_{22}, \quad (48)$$

$$b(x) = (1-x)b_{11} + xb_{22}, \quad (49)$$

the constants a_{11} and a_{22} characterise the intensity of intermolecular attractions in the components 1 and 2, respectively; the constant a_{12} characterises the intensity of attractions between the molecules of different components; the parameters b_{11} and b_{22} are determined by the sizes of the molecules of the solution. According to the combination rule, the constant a_{12} can be written through the binary interaction parameter k^*

$$a_{12} = k^*(a_{11}a_{22})^{1/2}. \quad (50)$$

Taking into account Eqn (47), Eqn (46) is fulfilled. The condition (45) goes to zero at the spinodal line. Considering Eqn (47), we obtain the equation for the diffusion spinodal

$$\varphi^3 - \left[\varphi - \frac{b(x)}{b_{11}}\right]^2 \frac{a(x)}{a_{11}} \frac{27}{4\tau} = 0. \quad (51)$$

The constants in the equation of state can be determined using the critical parameters

$$a_{11} = \frac{27}{64} \frac{(RT_{c1})^2}{P_{c1}}; \quad a_{22} = \frac{27}{64} \frac{(RT_{c2})^2}{P_{c2}};$$

$$b_{11} = \frac{RT_{c1}}{8P_{c1}}; \quad b_{22} = \frac{RT_{c2}}{8P_{c2}}.$$

Figure 11 shows the calculated spinodal curves for a water – propan-1-ol system at 260 K and different values of the parameter k^* in the coordinates of the mole fraction of propan-1-ol *vs.* the reduced pressure (the total pressure related to the critical pressure of the alcohol). It can be seen^{352,353} that the asymmetry associated with the difference in the individual properties of the components decreases as the binary interaction is strengthened. At high k^* , the spinodal curve becomes symmetric with respect to an equimolar composition. This fact can be attributed to a loss of individuality of the components of the system as the latter moves away from equilibrium. Apparently, this situation is something common to the phenomenon mentioned in the review:³⁵⁴ ‘...a loss of individuality of a substance appears as the system approaches the critical conditions. The character of the properties is determined by the degree of approach to the critical conditions rather than by the individuality of substances and even rather than by the type of phase equilibrium’. As the system approaches the conditions for spinodal decomposition, the free energy of formation of critical nuclei decreases. The vanishing of this energy is the condition for spinodal decomposition. This superficially resembles a continuum of liquid – vapour phase transitions ending in the critical point. It should be noted that under normal conditions of vapour nucleation, vapour supersaturation is as great as a thousand units. This indicates that the density of a supersaturated vapour approaches the density of a condensate thus providing conditions for a phase change with a low enthalpy of transition. Here one can speak about a first-order phase transition similar to a second-order phase transition. Hence, there are certain grounds to assume that a substance can lose individuality as it approaches the spinodal curve.

Dynamic phase diagrams become similar to a spinodal curve as J increases. It is assumed that the parameter k^* in the equation of state for a metastable phase can be substantially larger than that allowable in the equation of state for an equilibrium phase. In other words, the equations of states for equilibrium and metastable phases can differ in the parameters determining intermolecular interactions in a binary system. For example, according to the above-considered calculations [see Eqns (43)–(51)], the pres-

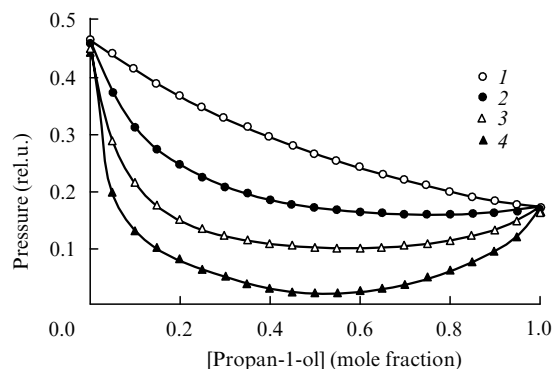


Figure 11. Spinodals of a water – propan-1-ol system at 260 K for various parameters of binary interactions. k^* : (1) 1, (2) 2, (3) 4, (4) 8.

sure in the spinodal corresponds to the binary interaction parameter $k^* = 5.65$.

Based on a spinodal curve for which the binary interaction parameter k^* is close to unity, the transformation of phase diagrams shown in Fig. 9 becomes impossible. Therefore, the behaviour of a binary system as it moves away from equilibrium is determined by the spinodal. It was assumed³⁵³ that the deviation of the system from linearity characterises a change in intermolecular interactions as the system moves away from equilibrium. Knowing the parameter k^* in a metastable state, one can determine the limiting values J thus finding the stability boundary of the state under consideration. As the system moves further away from equilibrium, it should go to another mode, which is, as a rule, accompanied by an organisation of a new structure.¹⁸²

2. Bimodal distribution of aerosols

The well-known effect of the bimodal distribution of an atmospheric aerosol remains to be adequately explained. Attempts to attribute this effect to fluctuations of the parameters of atmosphere with time and space seem to be artificial, because the time interval of averaging is generally equal to a few minutes. As a result, the conditions of growth of all heterogeneous nuclei are statistically equalised giving rise to a broad unimodal distribution. Actually, the use of time-averaged values cannot lead to a bimodal distribution because the nucleation time is several orders of magnitude smaller than a hundredth of a second, *i.e.*, the nucleation has time to proceed and nuclei have time to grow within one fluctuation cycle.

The bimodal distribution of aerosols can be reasonably explained assuming the existence of two independent surfaces (channels) of nucleation for the separate formation of crystals and liquid nuclei. Evidently, the accommodation coefficients of molecules on nuclei occurring in different phase states differ from each other. The difference in the growth rates of liquid and crystalline aerosol particles can lead to a bimodal distribution of particles in the atmosphere, where nucleation of a water vapour generally occurs in the vicinity of the triple point. A direct experiment on nucleation of glycerol in the vicinity of the triple point¹⁵ demonstrated that the presence of condensation nuclei is not required for the occurrence of the bimodal distribution of particles. It should be noted that in a real atmosphere, condensation nuclei undoubtedly make an additional contribution to the size distribution of particles.

The above-mentioned experiment¹⁵ is of fundamental importance for testing the semiempirical procedure for the construction of nucleation rate surfaces above phase equilibrium diagrams. The problem of the order of phase formation upon vapour nucleation below the triple point was easily solved. Crystalline and liquid-droplet nuclei appear simultaneously in ratios determined by the arrangement of the rate surfaces of formation of each phase relative to one another. Evidently, supercooled droplets can adopt a crystal or amorphous structure with certain probability. Apparently, the initial phase states of nuclei were retained in the study¹⁵ due to the use of a high-viscosity sample. Undoubtedly, such experiments give a clue to the separation of nucleation channels, which is of fundamental importance for the estimation of the agreement between theory and experiment. Actually, researchers had no possibilities to test the validity of a particular theory because theoretical results obtained in the one-channel approximation were generally compared with the characteristics corresponding in reality to two-channel nucleation.

3. Ion-induced nucleation

In the present review, the problem of heterogeneous nucleation is not discussed in detail. The detailed description of this process under conditions of a slowly changing supersaturation was given in the study.¹²⁰

Under conditions of ion-induced nucleation, the following rules are fulfilled.³⁵²

1. The energy of ion-induced vapour nucleation is always lower than the energy of homogeneous nucleation. Compared to homogeneous nucleation, lines (or in the case of a multicomponent system, a subspace) of ion-induced nucleation rates correspond to lower supersaturations (activities) of a vapour or, in the case of isobaric nucleation, to higher nucleation temperatures.

Let us note the well-known fact^{326, 327} that the lines of ion-induced nucleation rates coincide with the line of homogeneous nucleation rate when all ions pass into a condensed phase. The properties of a nucleating substance (for example, polarisability) can influence the relative intensity of heterogeneous nucleation of various vapours. This parameter depends on the differences in the vapour activity and temperature in the case of isothermal and isobaric nucleation, respectively.³³³

2. At a constant vapour supersaturation, the rate of heterogeneous isothermal (or isobaric) vapour nucleation is proportional to the concentration of ions. If the concentration of ions is nearly equal to or higher than the concentration of nucleating molecules, the heterogeneous nucleation rate reaches its upper limit. This limit determines the envelope curve (or a multidimensional surface), which corresponds to the limiting rate of ion-induced nucleation as a function of vapour activity. The lines of the highest and zero rates of heterogeneous nucleation are located on the surface of homogeneous nucleation rates.

3. Surfaces of homogeneous and heterogeneous vapour nucleation intersect at high temperatures in the line of spinodal decomposition.

Examples of the qualitative construction of nucleation rate surfaces describing phase transformations of various initial phases were given in the study.¹⁴

4. Experimental determination of conditions for spinodal decomposition

The experimental method for the determination of conditions for spinodal decomposition was developed in the study.³³³ The lines ct_p and mt_p in Fig. 12 correspond to vapour–liquid and vapour–solid equilibria. For simplicity, the spinodal line sc is considered to be common to the liquid and solid states. The isorates of homogeneous and heterogeneous nucleation of a liquid can be measured at moderate supersaturations. The extrapolation of both lines gives an intersection w belonging to the spinodal line for a liquid as follows from the third rule for ion-induced nucleation. An analogous extrapolation can be carried out also in the case of the crystalline state (point r in Fig. 12). The results of measurements of the supersaturation as a function of the nucleation temperature of *n*-butanol³⁵² are presented in Fig. 13. For homogeneous nucleation, the linear regression of the logarithm of the vapour pressure on the inverse temperature is described by the equation

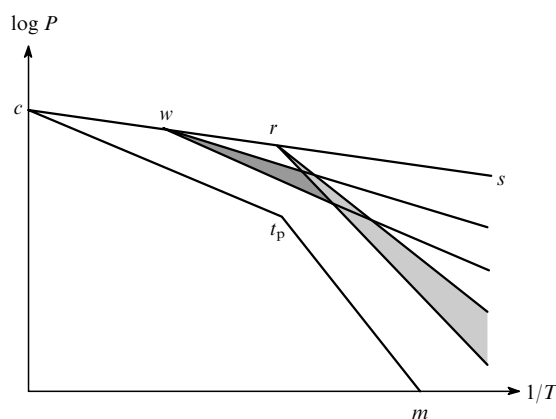


Figure 12. Schematic representation of vapour–liquid and vapour–solid equilibria for $\log P$ vs. $1/T$.³³³

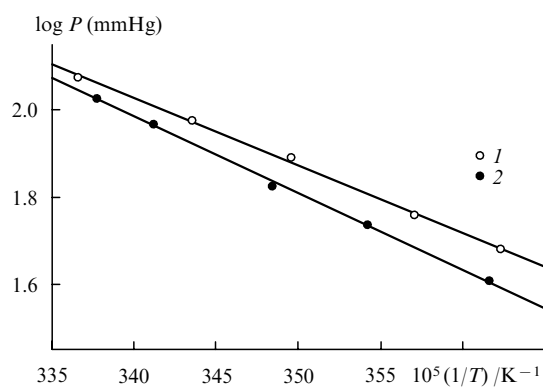


Figure 13. Experimental data on critical supersaturations of n-butanol for $\log P$ vs. $1/T$.³³³

(1) Homogeneous nucleation, (2) ion-induced nucleation.

$$\log P_{\text{hom}} = 7.4076 - \frac{1582}{T}.$$

For ion-induced nucleation, this regression is described by the equation

$$\log P_{\text{het}} = 8.0728 - \frac{1791}{T}.$$

The extrapolation allows one to determine the pressure (230 mmHg) and temperature (310 K) of spinodal decomposition. This pressure corresponds to a reasonable estimate of the vapour supersaturation in the spinodal ($\log S = 2.6$). In other words, studies of heterogeneous and homogeneous nucleation enable one to estimate experimentally the conditions for spinodal decomposition, which makes it possible to find the temperature dependence of the pre-exponential coefficient in the equation for the nucleation rate in the classical theory. Evidently, in the case of spinodal, the exponential multiplier becomes equal to unity and, hence, the only remaining multiplier is pre-exponential. Generally, this multiplier is considered to be constant. Taking into account that the nucleation rate at the critical point of a liquid–vapour system is equal to zero, it is easily understood that the pre-exponential coefficient increases from zero at the critical point to a maximum value and then again decreases and goes to zero at absolute zero of temperature.

The studies by Fuks[‡] and Sutugin³⁵⁵ have made an impact on the development of concepts of aerosol mechanics and the application of these concepts to the description of cluster growth.

VII. Use of nucleation in scientific studies and some technological processes

Nucleation is used in one way or another in many scientific studies and in a number of technological processes. This phenomenon is so widespread that researchers are often not aware that they deal with nucleation.

Aerosols are used for visualisation of particle motions, which occur upon nuclear decay, in a Wilson chamber. The latter is extensively employed for studying nucleation of supersaturated vapours. More than a half-century ago, Sinclair and La Mer designed a generator of monodispersed particles, which was

described, for example, in Ref. 356. In different laboratories throughout the world, researchers extensively used a particle condensation counter, which is based on the Sinclair–La Mer scheme. A lack of theoretical support for the principles of its action stimulated experimental and theoretical investigations. In the study,³⁵⁷ a theoretical model of the counter was proposed and the results of its tests at different pressures, nucleation temperatures and amounts of the gas to be analysed were reported. A condensation counter was used as a detector for capillary chromatography.³⁵⁸ Initially, the sensitivity has been 100 ng ml^{-1} , but then this limit was improved by two orders of magnitude.^{347, 359} Being an instrument for research, a condensation counter by itself was also the object of an individual study.³⁶⁰ The construction of a counter of aerosol particles is gradually improved. Thus, the schemes have already been developed,^{361, 362} which enable one to detect particles with sizes of 3 nm with an efficiency of almost 100%.

Nanoparticles are used for creating quantum points, luminescent materials, gas sensors, resistors, conducting and capacitive films, high-temperature superconductors, thermoelectric, optical, magnetic, laser materials, etc. Methods for the synthesis of such particles were surveyed in the study.³⁶³

The generation of nanoparticles in plasma holds promise. Powders formed by evaporation and condensation of various materials in a plasma were studied experimentally and their numerical simulation was carried out.³⁶⁴ The theoretical consideration of the processes occurring in an inductively coupled plasma made it possible to give recommendations on the construction of apparatus for the production of nanoparticles.³⁶⁵ In the investigation on simulation of nucleation and growth of iron particles in a plasma reactor, a parametric equation was derived for the description of a spectrum of sizes and number of the particles formed.³⁶⁶ These parameters depend substantially on the rate of cooling and the initial concentration of monomers. A mathematical model was proposed for the formation of metal powders and ceramics of high purity.^{367, 368} Experimental methods for the preparation and simple models of generation of metal clusters were surveyed in the review.³⁶⁹ An experimental apparatus for the generation of ultradispersed titanium oxide, which is used as a pigment, catalyst, for the construction of electronic devices, etc., was described in the study.³⁷⁰ It was noted that the nanoparticles thus formed have a high mechanical strength and low sintering temperatures.

High-temperature chemical reactors, in which materials are oxidised under an oxygen atmosphere and conditions are provided for the generation of ultradispersed particles, are characterised by high performance and relative simplicity. The scheme was elaborated for the production of ultradispersed powders (with particle sizes of $< 100 \text{ nm}$) of titanium oxide.³⁷¹ Experimental investigations of metal evaporation under the action of electrical pulses followed by the formation of ultradispersed metallic powders in a medium of various gases at different temperatures and pressures were carried out in Russia as early as the 1960s. The results of these studies were analysed in the review.³⁷² It was noted that the nucleation processes depend on the nature of the gas and the total pressure.

Advances in the new line of research, viz., nanochemistry, demonstrated that the classical equations of chemical kinetics are inapplicable to nanosized particles. The excess energy of surface atoms whose percentage with respect to internal atoms is high has a substantial effect on the temperature of phase transitions in nanoparticles. If their sizes are comparable, for example, to the radius of delocalisation of charge carriers, nonlinear optical and electrical phenomena take place. This fact gives rise to the development of new original methods for the preparation of nanoparticles.

It was proposed to prepare nanoparticles by metal evaporation in a static diffusion chamber under the action of pulse laser radiation.^{373–375} The desired compound is formed by the chemical reaction of heated metal atoms with a gas reagent (for example,

[‡] The monograph by N A Fuks 'The Mechanics of Aerosols' (Moscow: Academy of Sciences of the USSR, 1955), which the author wrote in Stalin's camps, is still extensively cited. The contribution of N A Fuks to the development of the science of aerosols was recognised by establishing the prize in his memory. This prize is awarded at International Conferences on Problems of Aerosols.

O₂, N₂, NH₃, *etc.*) in a medium of an inert gas (Ne or Ar) at a pressure of 1–0.01 Torr. The molecules thus formed and the unconsumed metal atoms deposit on the cold upper surface of a diffusion chamber. By varying the gas composition, temperature gradient and laser pulse power, one can control the chemical composition and size of nanoclusters.

The size of a nanocluster influences, for example, the gap width in semiconductors,³⁷⁶ which, in turn, has a strong effect on the rate of luminescence quenching. It was noted³⁷⁷ that the rate of luminescence quenching by oxygen molecules depends on the size of light-irradiated MoS₂ nanoparticles. Therefore, nanoparticles can influence redox processes, which is of importance for solving a number of practical problems. Examples of such a 'size' influence on the gap width, in particular, upon photoreduction of methyl viologen on nanoparticle surfaces of metal chalcogenides can be cited.^{378, 379} The use of nanoparticles in photocatalysis opens up considerable possibilities. Metals deposited onto nanoparticle surfaces can serve as catalysts. For instance, platinum deposited onto TiO₂ nanoparticles catalyses the liberation of hydrogen from water.³⁸⁰

The kinetics of formation of a metal-polymer material was studied.³⁸¹ Metal polymers are composite materials whose properties depend on the composition and size of dispersed particles distributed in a polymer matrix. The widely used methods for their preparation were surveyed in the publications.^{382, 383} The simplified scheme of the thermal synthesis involves three steps, *viz.*, decomposition of a metal-containing compound, the nucleus growth of a metal phase and the formation of a volatile compound, which is then removed from the reaction zone. Real processes occurring in the course of formation of a composite are much more complicated.

Industrial technologies are devised using numerical simulation of the kinetics of growth of metal clusters. The reaction space is divided into cubic cells in which only one nucleus can form. It is assumed that the appearance of a new phase results from homogeneous nucleation. The probability of nucleus formation is calculated within the framework of the classical theory.³⁸⁴ Nuclei grow due to diffusion of the substance from the bulk of the solution to the phase formed. It is believed that nuclei do not decompose and do not migrate due to high viscosity of polymer melts. Two models of the substance exchange between the adjacent cells were considered. In a model with stirring, a change in the concentration in one cell leads to instantaneous changes in the concentrations in other cells. In a model without stirring, the substance exchange between the adjacent cells takes place. In the latter case, the average particle size first increases with time and then remains virtually constant. The number of particles also sharply increases until the nucleation rate reaches a maximum after which it ceases to change. In a system with stirring, larger particles are formed, but their number is smaller than that observed in a system without stirring. The calculated size distributions of particles are in agreement with experimental values.³⁸⁵ If a reagent is added dropwise, a model with stirring is characterised by a polymodal distribution. In the absence of stirring, the modes overlap.

Nucleation processes are used for the preparation of metallic ultradispersed powders serving as catalysts. Studies of such catalysts contribute to the development of scientific fundamentals of catalysis and corresponding technologies. For example, the use of ultradispersed powders, which are prepared using an electrical explosion of conductors, instead of usual silver powders made it possible to extend substantially the temperature range of selective oxidation of ethanol to acetaldehyde.³⁸⁶ It appeared that ultradispersed metals are essentially non-equilibrium systems whose relaxation gives rise to particles of the same type exhibiting high catalytic activity.

Van der Waals interactions play a decisive role in the formation of such compounds.³⁸⁷ In the mid-1930s, Nikitin formulated the analogy rule: 'If two substances have similar van der Waals forces and their molecules are similar in size and shape, they

should form analogous compounds with a third substance, and the resulting compounds should exhibit similar stability and can form mixed crystals with each other'. Nikitin has forestalled one of the main concepts of supramolecular chemistry, *viz.*, spatial complementarity, and its decisive role in the formation of supramolecular compounds.

A radically new organisation of a chemical material at a higher level has been discovered and described.³⁸⁸ In this case, the compatibility of sizes and shapes of one type of molecule, the so-called guests, with the cavities of the framework consisting of molecules of another type, the so-called hosts (or a cavity of another larger host molecule), rather than their reactivities plays a decisive role in the formation of particular compounds from components. This principle of organisation of compounds allows one to combine coordinatively saturated molecules, which are not involved in chemical interactions with each other, into supramolecules or supramolecular crystalline phases, which are thermodynamically more stable than mixtures of the starting components. From the viewpoint of traditional chemistry, it is difficult to imagine that compounds of different chemical nature, such as Xe, SO₂, H₂S, HBr, CH₄, CO, HCOOH, *etc.*, can react in a similar way, for instance, with hydroquinone to form isostructural clathrate compounds. However, these compounds are analogous from the viewpoint of clathrate chemistry. At the same time, of two chemical analogues, *viz.*, CH₃OH and C₂H₅OH, only methanol forms a clathrate with hydroquinone because the ethanol molecule is too large to be located in the cavity of the hydroquinone framework.

The main concepts of clathrate chemistry stated by Powell³⁸⁸ stimulated studies in this field and gave impetus to a target search for supramolecular substances. A number of discoveries were made. Statistical thermodynamic studies of clathrates^{389, 390} provided an explanation why the initial components can be combined to form a thermodynamically stable phase in the case of the absence of chemical valence bonds between the molecules.

The French chemist Lehn has emphasised an important role of nonbonded interactions in the formation of such compounds.[§] He introduced a new concept 'supramolecular chemistry', which he defined as the 'chemistry beyond the molecule', the 'chemistry of molecular ensembles and intermolecular bonds'.^{391, 392}

The discovery of clathrate-forming metal complexes gave rise to the preparation of numerous new compounds and offered inexhaustible possibilities for the rapid and target construction or modification of host molecules. The discovery of supramolecular compounds made it possible to reveal yet another mechanism of nucleus formation of a new phase. This mechanism is thermodynamically favourable to an extent that it enables one to solve a complex problem of preparing high-purity gases (gaseous hydrates were recognised as a new class of impurities in high-purity gases and gas mixtures).³⁹³

In 1970, deposits of methane hydrates were discovered in Yakutiya,³⁹⁴ after which it was found that huge deposits of fossil methane are available in the world. Presumably, methane will be the main fuel in the future. However, safe conditions of its recovery is a limiting factor. This problem is directly associated with nucleation. Actually, the equilibrium of methane hydrate can be easily disturbed after drilling operations. Upon decompression, methane hydrate becomes unstable and decomposes to eliminate methane, which can give rise to a substantial volume of metastable water ice. Since the thermodynamic potential of the metastable state is higher than the corresponding potential of the stable state, relaxation can assume a character of explosion in the case of a large volume of ice, and the energy of such an explosion can be higher than the energy of a powerful hydrogen bomb.³⁹⁵ The frequencies of the 'boiling' of methane hydrates remain to be studied. The seemingly special problem of estimating the rates of

§ In 1987, J-M Lehn (France), C J Pedersen and D J Cram (USA) were awarded the Nobel Prize in Chemistry.

formation of gas bubbles in gas-hydrate systems becomes one of the key current problems. The possible schemes of experimental investigations of the frequencies of gas nucleation in metastable gas hydrates were analysed in the publication.³⁹⁵

Intercalation compounds of graphite and fullerene belong to an important class of clathrates.³⁹⁶ The specific chemical and physical properties of intercalation compounds offer considerable possibilities for their use in different fields among which heterogeneous catalysis and electrochemistry are of the most importance. These compounds are also used in analytical chemistry and pharmacology.

* * *

Theoretical methods for studying nucleation have some fundamental limitations. Hence, experimental investigations are of great importance, because they provide information, which cannot be obtained by theoretical methods. By analogy with classical mechanics, it can be stated that the classical stage of nucleation theory has come to an end. However, in the nucleation theory there are no analogues equivalent to quantum mechanics.

The present-day situation can be characterised as 'pre-revolutionary' when the stage was set for the development of a semi-empirical nucleation theory because all drawbacks of the theory become increasingly evident, nucleation models become increasingly complicated and theorists have high skills. However, a new key idea is required, whose appearance can be facilitated by an original experiment in combination with a critical review of the axiomatic concepts of the theory. One of the steps involves a semiempirical method for the construction of nucleation rate surfaces. Actually, this seemingly simple approach based on the use of phase equilibrium diagrams enables one to determine the topology of the nucleation rate surfaces in the zero limit. This is already sufficient for revision of certain approximations employed in experiments and particular axioms of the nucleation theory.

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Neural networks as a method for elucidating structure – property relationships for organic compounds

N M Halberstam, I I Baskin, V A Palyulin, N S Zefirov

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Abstract. The published data devoted to the use of the neural network approach in the simulation of structure – property relationships for organic compounds are reviewed. The basic principles of the neural network simulation are discussed along with the characteristic features of the neural network approach typical of the representation and classification of structural chemical data. Brief information on neural network models of spectral characteristics, reactivities, physicochemical properties and biological activities of organic compounds is presented. The bibliography includes 159 references.

I. Introduction

The use of computer technologies in virtually all branches of science has really acquired a mass character in the past decade. The wealth of experimental data accumulated by now makes it possible to focus specific attention on the methods for generalisation and mathematical processing of diverse parameters of known compounds aimed at the computer simulation and forecasting of properties of novel compounds that have not been synthesised nor investigated hitherto. This, in turn, opens up broad opportunities for the solution of one of the central tasks of chemical science, *viz.*, a purposeful search for novel compounds and materials with predetermined properties.

Artificial neural networks have become one of the most popular methods for the construction of various quantitative relationships. The methodology of artificial neural networks, which enables the construction of nonlinear models of any degree of complexity, has found wide application in a search for quantitative relationships between structures of organic compounds and their physicochemical properties (QSPR) or biological activities (QSAR).

Among the known architectures of neural networks used for elucidating structure – property relationships (hereinafter, the term ‘property’ relates to both physicochemical properties and biological activities of organic compounds), multilayered feedforward backpropagation neural networks come first in popularity. Their attractiveness is mostly due to the ability of such neural networks to generalise and approximate data with high accuracy and to the possibility of processing large arrays of disembodied data.

A search for neural network structure – property relationships may be reduced to sequential execution of the following operations: (1) description of structures of compounds under study by special numerical parameters (descriptors); (2) choice of an optimum set of descriptors; (3) classification of the whole set of experimental data into training and control samples; (4) selection of the most adequate type, architecture and the method for training of the neural network; (5) choice of statistic parameters for estimating the quality of training; (6) training of neural networks and estimation of training results; (7) the use of neural network models for forecasting the properties and activities of hitherto unknown compounds.

The first publications devoted to the application of neural networks (perceptrons) to the solution of various chemical problems appeared in the late 1980's.¹ The interest of chemists in the new method has begun to increase sweepingly since that time.

Neural networks, commonly referred to as artificial neural networks or computing neural networks, represent a simplified mathematical model for information processing by the human brain. However, the majority of existing architectures of neural networks cannot reproduce brain functions exactly and should be considered as a modification of parallel algorithms.^{2,3}

Owing to their ability for being trained, combining and generalising information, neural networks have been successfully used in chemistry, especially in those cases where the analytical types of relationships between the structures and properties of chemical compounds are unknown.⁴

II. Basic principles of neural network simulation

1. Description of architectures and methods for training of neural networks used for elucidating structure – property relationships

Neural networks consist, as a rule, of a set of relatively simple computing elements termed neurons; the latter are arranged in several layers and are linked to one another by numerous connections. The layers are usually subdivided into three groups, *viz.*, input, hidden and output (Fig. 1). Each connection between two neurons is defined by a real number termed connection

N M Halberstam, I I Baskin, V A Palyulin, N S Zefirov N D Zelinsky
Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky
prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28.
Tel. (7-095) 939 35 57. E-mail: n.halb.@g23.relcom.ru (N M Halberstam)
Department of Chemistry, M V Lomonosov Moscow State University,
Leninskie Gory, 119992 Moscow, Russian Federation.
Fax (7-095) 939 31 81. Tel. (7-095) 939 35 57.
E-mail: baskin@org.chem.msu.su (I I Baskin), vap@org.chem.msu.su
(V A Palyulin). Tel. (7-095) 939 16 20. E-mail: zefirov@org.chem.msu.su
(N S Zefirov)

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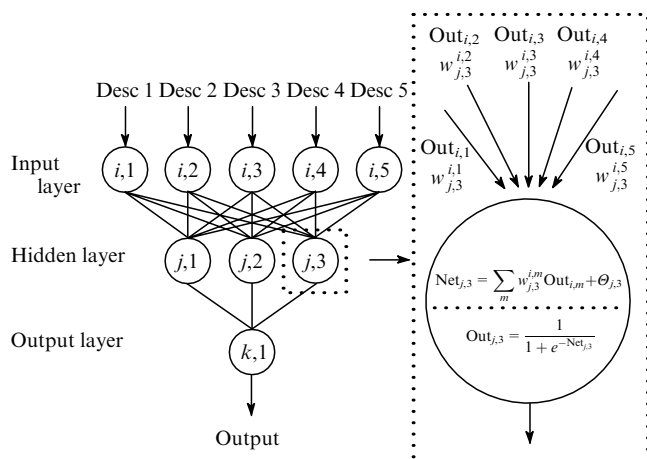


Figure 1. The structure of a feedforward neural network. The enlarged fragment depicts the main computational operations performed by the neuron with a sigmoidal transfer function. Desc is descriptor.

weight. The sum of connection weighting coefficients of interneuronal bonds determines the computational capabilities of neural networks; therefore, training of neural networks is reduced to the adjustment of their connection weighting coefficients.

The computations within each i th neuron of the n th layer are performed in two steps (see Fig. 1), *viz.*, computation of the net input signal Net_j by summation of all weighted input signals and computation of the output signal Out_j of this neuron on the basis of the transfer function:

$$Net_j = \sum_i w_{ij} Out_i + \theta_j,$$

$$Out_j = f(Net_j),$$

where Net_j is the net input signal of the neuron j pertaining to the layer n ; Out_i is the output signal of the neuron i pertaining to the layer $n-1$; w_{ij} is the weighting coefficient of the connection between the neurons i and j ; θ_j is the threshold value for the neuron j ; and Out_j is the output signal of the neuron j in the layer n .

The sigmoidal functions (1) are used most commonly as transfer functions, but threshold (2), linear (3), hyperbolic tangential (4) and some other functions can also be used.^{5,6}

$$Out_j = \frac{1}{1 + e^{-Net_j}}, \quad (1)$$

$$Out_j = \begin{cases} 0, & Net_j < 0 \\ 1, & Net_j \geq 0, \end{cases} \quad (2)$$

$$Out_j = k Net_j \quad (k = \text{const}), \quad (3)$$

$$Out_j = \frac{e^{Net_j} - e^{-Net_j}}{e^{Net_j} + e^{-Net_j}}. \quad (4)$$

The so-called bias pseudoneurons² with a constant output signal equal to 1 are usually added to each (except for the output layer) layer of a neural network instead of the threshold values θ .

Prior to training, all connection weights are initialised by random numbers. A correct choice of initialisation boundaries enables reduction of the training time and improvement of the quality of the neural network models derived.^{7,8} In some cases, where the training procedures (*i.e.*, the adjustment of connection weights) do not converge, the training is repeated using another set of parameters or a different mode of initialisation of connection weights.

The architecture of a neural network is determined by the connection topology between the neurons. Simulation of structure–property relationships usually employs multilayered neural networks the number of layers in which is determined by a specific architecture of the neural network.^{2,9} Each neuron pertaining to one layer has the same number of input connections with the preceding layer. The output signals of the last computing layer of the network represent computed output values of the whole network. When neural networks are used for forecasting the properties of chemical compounds, the values of output signals of the input neurons are set up with regard for the values of computed descriptors after normalisation (see below); the signals identified with the values of predicted properties (also, taking normalisation into account) are read from the output neurons.

a. Multilayered feedforward neural networks

The majority of publications devoted to the elucidation of structure–property relationships deal with multilayered feedforward neural networks. The main advantages of such networks include their ability to establish multiparametric nonlinear relationships with a high interpolation accuracy even in those cases where experimental data are not representative enough or contain noises.¹⁰

A characteristic feature of feedforward neural networks is a layer-by-layer transfer of signals from the input of the network to its output. Classical feedforward neural networks usually possess several hidden layers (Fig. 2a) or contain exclusively an input and an output layer (Fig. 2b).

The adjustment of weighting coefficients of the connections during training of multilayered feedforward neural networks is carried out sequentially starting from the output layer connections; therefore, the methodology of training of such networks has got the name of back propagation of errors.^{11,12} A brief description of the most popular procedures is given below.

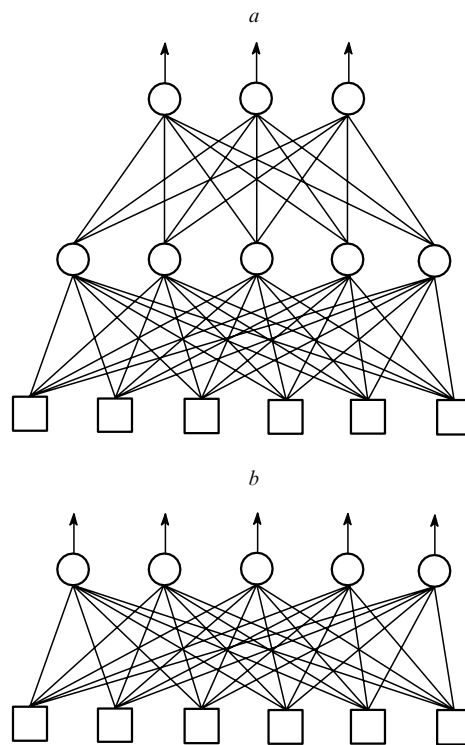


Figure 2. The classical feedforward neural networks with one hidden layer (a) and without any hidden layers (b).

b. A generalised delta rule

Training of each layer n out of N layers of a neural network is carried out in accordance with the Widrow–Hoff rule or the delta rule:^{13, 14}

$$\Delta w_{ij} = \eta \delta_j o_i,$$

where Δw_{ij} is the change in the weighting coefficient of the connection between the neurons i and j ; η is the empirical constant for the training rate; δ_j is the computational error for the neuron j pertaining to the layer n and o_i is the output signal of the neuron i pertaining to the layer $n - 1$.

In the case of a generalised delta rule, an additional parameter termed a ‘training momentum’ and calculated with consideration of changes in the weighting coefficients in the previous iteration is introduced in order to avoid oscillations which often take place where error surface is characterised by a very narrow valley region:^{13–15}

$$\Delta w_{ij}^{(k+1)} = \eta \delta_j o_i + \alpha \Delta w_{ij}^{(k)},$$

$$\delta_j = \begin{cases} f'(\text{Net}_j)(t_j - o_j), & n = N \\ f'(\text{Net}_j) \sum_m \delta_m w_{jm}, & n \neq N, \end{cases}$$

where t_j and o_j are the experimental and the calculated values of the property under investigation for the neuron j , respectively; α is the constant reflecting the influence of the training momentum and k is the iteration number.

c. The resilient propagation method (RPROP)

If the training is performed with the use of RPROP, the adjustment of connection weighting coefficients is performed exclusively on the basis of the data about the signs of partial derivatives of error functions of the neural network E usually defined as a sum of squared errors on the output neurons.^{16, 17} The changes in the connection weighting coefficients are calculated in the following way:

$$\Delta w_{ij}^{(t)} = \begin{cases} -\Delta_{ij}^{(t)}, & \text{if } \frac{\partial E^{(t)}}{\partial w_{ij}} > 0 \\ +\Delta_{ij}^{(t)}, & \text{if } \frac{\partial E^{(t)}}{\partial w_{ij}} < 0 \\ \frac{\partial E^{(t)}}{\partial w_{ij}} = 0, \end{cases}$$

$$\Delta_{ij}^{(t)} = \begin{cases} \eta^+ \cdot \Delta_{ij}^{(t-1)}, & \text{if } \frac{\partial E^{(t-1)}}{\partial w_{ij}} \cdot \frac{\partial E^{(t)}}{\partial w_{ij}} > 0 \\ \eta^- \cdot \Delta_{ij}^{(t-1)}, & \text{if } \frac{\partial E^{(t-1)}}{\partial w_{ij}} \cdot \frac{\partial E^{(t)}}{\partial w_{ij}} < 0 \\ \frac{\partial E^{(t-1)}}{\partial w_{ij}} \cdot \frac{\partial E^{(t)}}{\partial w_{ij}} = 0. \end{cases}$$

Here, $\frac{\partial E^{(t)}}{\partial w_{ij}}$ is the value of the partial derivative of the error

function of the neural network with respect to the connection weight w_{ij} in the i th iteration, η^+ and η^- are the empirical constants for the increase or decrease in the training rate and t is the iteration number.

d. Quasi-Newtonian training methods

This group of methods is based on the Newtonian principle of function fitting. A vector all the components of which are taken equal to the partial derivatives of the error function of the network with respect to all weighting coefficients is calculated for each iteration. The Broyden–Fletcher–Goldfarb–Shanno (BFGS) method is the most efficient in this group.^{14, 18}

2. Other neural network architectures

Neural networks having different architectures are successfully used for the simulation of structure–property relationships. A brief description of some of these architectures is given below.

Feedforward neural networks containing at least one hidden layer may possess additional direct connections linking the neurons of the input and output layers^{19–21} as well as recursive bonds between the output and the input of a neuron.^{21, 22}

Kvasnicka *et al.*^{23, 24} have proposed the use of a tree-shaped neural network for the solution of problems related to classification of compounds; the topology of such a network was the most close to the molecular structures under investigation. The values 0 or 1 were ascribed to the input neurons so as to obtain subgraphs isomorphous to the structures of the molecules. Later, a similar approach was realised in the computer programme ‘ChemNet’.²⁵

An interesting neural network procedure for the description of chemical compounds has been proposed, which allows elucidation of structure–property relationships without computation of descriptors for molecules as a whole using only atom and bond descriptors.^{26, 27} In this method, the presentation of structures is effected through the use of an additional neural network which consists of two principal elements, *viz.*, a sensorial area to which the basic structural information is fed and an ‘eye’ which transforms the data from the sensorial area into a signal invariant to the renumbering of the atoms in compounds under study. The structural information thus processed is fed to the input of ordinary feedforward neural networks in order to obtain structure–property relationships.

The Kohonen neural networks (see Refs 28–32) (Fig. 3a) widely employed in cluster analysis allow data mapping in such a way that similar vectors of input values are mapped onto neighbouring output neurons on the lattice.

Counterpropagation neural networks^{33, 34} utilise two different types of layers, *viz.*, a hidden Kohonen layer and an output Grossberg layer (Fig. 3b). The salient advantages of networks trained by counterpropagation include a relatively small (of the order of several hundreds) number of interactions required for the training of networks^{35, 36} and the possibility of finding a global minimum of the error function for any starting setup of the weighting coefficients.^{37, 38} One disadvantage is a weaker approximating capacity of such networks in comparison with other architectures.

A neural network with a linear transfer function for the output-layer neurons and hidden neurons which accomplish radial-basis nonlinear approximation is usually referred to as a radial-basis neural network. This is also used for elucidating structure–property relationships.^{39–41}

The functioning of Fuzzy ARTMAP (Fuzzy Adaptive Resonance Theory for Mapping) neural networks is based on clusterisation (categorisation) of training set vectors in accordance with the adaptive resonance theory (see Ref. 42 and References cited therein). In this method, categorisation of vectors is performed by comparing each successive vector to reference vectors describing previously established categories (clusters). If a successive vector ‘resembles’ a reference vector in terms of a definite proximity criterion, it is used for its adjustment. In the opposite case, a vector becomes a representative of a new data category and is memorised as a new reference vector. This procedure is implemented in a neural network consisting of a reference layer, which estimates the ‘similarity’ of the vectors, a recognising layer where each neuron describes its own data category (cluster) and several accessory elements. Such architectures have been termed ART-1 (categorisation of binary vectors) and ART-2 (categorisation of real number vectors). ARTMAP represents a modular neural network made up of two networks for categorisation of vectors of the ART type (in QSAR/QSPR studies, these vectors are linked to the vectors corresponding to descriptors and properties of organic compounds) and a comparison module responsible for memorisation of ‘associations’ between different categories of descriptors and properties.

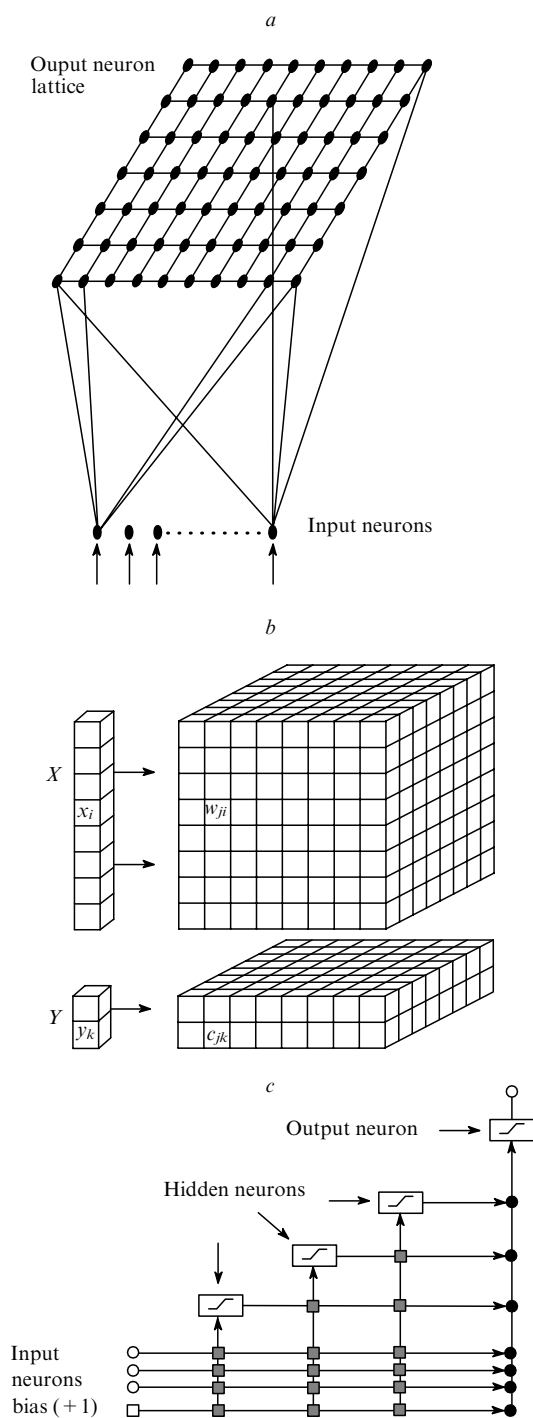


Figure 3. A schematic representation of architectures of some neural networks used for the simulation of structure–property relationships. (a) The Kohonen neural network, (b) back propagation neural network, (c) cascade-type neural network.

A neural network of functional links⁴³ is made up of two layers. The outputs of the neurons forming the input layer result from nonlinear transformations (e.g., squaring, taking a square root, a sinus, *etc.*) of the values of a descriptor; each neuron in the output layer corresponds to a predicted property. It is of note that this category represents a neural network simulation of a linear regression analysis based on the use of nonlinearly transformed descriptors and properties.

Sometimes, in the simulation of structure–property relationships several neural networks having different architectures are combined into a hierarchical system.^{21, 44}

Alongside neural networks with static architectures (which have to be selected prior to training) there are the so-called cascade networks (Fig. 3 c); their topology is formed during training.^{45–47} The training is begun with a neural network containing exclusively input and output neurons. If the error of the neural network exceeds the threshold value, one hidden neuron which accumulates signals from all input and previously added hidden neurons is added after each training cycle. It may therefore be assumed that each hidden neuron forms a separate layer. After addition of a successive hidden neuron, the weights of its connections are determined only once to enable maximisation of covariation of values of output signals with the error and do not change any further in the course of training. As far as the output neurons are concerned, the weights of their connections have to be adjusted every time in order to diminish the error function of the network.

III. Approaches to structural description of compounds

The first question arising in connection with the application of neural networks, especially in the solution of various chemical problems, is related to the choice of a method for the description of source data.

The combination of parameters fed to the input of a neural network is usually presented in the form of a vector. Therefore, a topological or a three-dimensional molecular structure has to be described as a unidimensional array without considerable losses of significant information. The following conditions should be met:³⁶

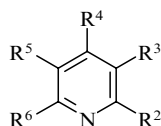
- (1) the quantity and the type of descriptors are the same for all the structures to be described;
- (2) there is a correspondence between each descriptor and a particular component in a parameter vector;
- (3) different parameter vectors correspond to different molecules.

As a rule, neural network simulation of structure–property relationships utilises a set of numeric values (descriptors)⁴⁸ for the description of structures of chemical compounds containing all relevant information. According to the type of information, all descriptors are subdivided into fragmental,⁴⁹ topological,^{50, 51} quantum-chemical⁵² and physicochemical. All of them demand additional computation prior to construction of neural network models. Moreover, one should have a clear idea about the nature of a relationship in order to select an appropriate group and a type of descriptors for each concrete case.

In the majority of studies devoted to neural network simulation of structure–property relationships, descriptors are computed with the aid of various software packages, e.g., ADAPT.^{53–55} This usually results in an excessive set of descriptors; the most significant ones are selected for further analysis using various procedures. Sometimes, it is rather difficult to explain the physical sense of the descriptors selected and to establish their relationship to the property under investigation.

The first attempts to use a well-known procedure for the presentation of chemical structures as modified connectivity matrices with charges on nuclei of the corresponding atoms on their diagonals and formal bond orders as non-diagonal elements were undertaken by Elrod *et al.*⁵⁶ It was proposed to form input vectors for neural networks by combining the diagonals of the connectivity matrices with subdiagonal elements taken row-by-row. These authors recommended using two connectivity matrices (one for reactants and one for reaction products) for the description of chemical reactions.⁵⁷ Evidently, the use of this approach is confined to compounds containing a small number of atoms due to a great number of elements in the connectivity matrix. In addition, such a presentation of structures is not invariant with respect to the renumbering of atoms.

The classical approach to the construction of quantitative structure–property relationships is used for the description of a series of structural analogues using substituent constants, *e.g.*, Hammett σ constants, Taft's E_s constants, lipophilic constants π , parameters L , B_1 , B_2 (STERIMOL), *etc.* However, if structures contain topologically equivalent substitution positions, the use of these parameters is not quite correct. For example, the pyridine molecule contains two pairs of topologically equivalent positions of substituents, *viz.*, the α -position for R^2 and R^6 and the β -position for R^3 and R^5 . As a consequence, the same compound will be represented by different sets of descriptors based on the use of different parameters of substituents, which may result in ambiguous prognosis.



This problem may be overcome through the introduction into the source set of copies of compounds with different arrangements of substituents in topologically equivalent positions,⁵⁸ possessing the same activities as the starting compound. Such an enlargement of the source sample makes prognosis independent in cases of ambiguous assignment of substituents to topologically equivalent positions.

An interesting method has been proposed which enables one to reduce the number of input parameters of neural networks without any loss of significant information.⁵⁹ This approach is based on the computation of the principal components⁶⁰ which represent linear combinations of original descriptors. The values thus obtained are further used as the input parameters of neural networks.

1. Normalisation of input parameters of neural networks

Almost all publications devoted to the use of neural networks for the solution of various chemical problems describe normalisation of input data. As a rule, input parameters are normalised in such a way that their values lie in the range between 0 and 1 or are characterised by unit variance.

2. Selection of the most significant descriptors

Of no less importance is the selection, among all computed parameters, of only those parameters which make a significant contribution to the property under study. Such a selection can be made in advance or in the course of training of neural networks.

Preliminary selection of parameters is performed using independent methods, *e.g.*, stepwise multiple regression analysis,^{61, 62} or neural network algorithms.⁶³ In the latter case, the type of neural network used for the selection of descriptors does not usually coincide with the type of main neural network used for the construction of the model.

A neural network utilising a 'genetic' training algorithm can serve as an example.^{64–66} The 'genetic' algorithm represents a stochastic optimisation procedure based on evolutionary principles. Its operation ensures the selection of a description with the most significant parameters from the whole set of object descriptions over the course of several generations. The significance of parameters, *i.e.*, the success of genetic combinations, is defined by a criterion function computed by a neural network as a residual error for the property under investigation. Diverse methods for the production of a new generation within the framework of a 'genetic' algorithm have been described. Approximation of the genetic function⁶⁷ and evolutionary programming⁶⁸ are the most popular.

Brinn *et al.*⁶⁹ have recommended using the so-called evolutionary approximation for the rejection of insignificant descriptors. Some descriptors randomly selected from a multitude of computed descriptors are fed to the input of a neural network after which the root-mean-square error is computed at the output of the

network. Then, one of the input neurons is excluded from the neural network and the new root-mean-square error is recalculated. This procedure is repeated for all neurons. The descriptors are scored according to the magnitude of the change in the error at the output of the neural network. The neurons are then removed from the neural network starting from the least significant descriptors until the change in the error at the output of the network becomes significant. After replacement of discarded descriptors by new ones taken from the set of computed descriptors, the calculations are repeated.

In the course of training of neural networks, less significant descriptors can be discarded using the so-called pruning algorithms. Their main function consists of simplification of neural network architectures by discarding the connections with less significant weighting coefficients. If all the connections of input neurons are insignificant, these neurons are discarded.^{70, 71} Pruning procedures can be classified into two groups,⁷² *viz.*, sensitivity methods based on computation of significance or sensitivity of all connections followed by elimination of the connections with the least sensitivity, and 'penalty component methods' based on the introduction of the so-called penalty functions which reduce weighting coefficients to zero values in the course of training.

Tetko *et al.*⁷³ have provided a detailed description of five methods designed for the computation of connection sensitivities. A method for the selection of the most significant descriptors based on the calculation of sensitivities of connections and the contribution of each descriptor to the total error of the neural network has been developed.^{74, 75}

A reconstructive method based on the forgetting principle, *i.e.*, a sequential decrease in the absolute values of all weighting coefficients, has been developed.⁷⁶ Reiteration of training–forgetting cycles enables enhancement of significant or weakening of less significant connections.

The degeneration algorithm of weighting coefficients is yet another example of a procedure based on penalty functions.^{13, 20} In each training step, the values of calculated weighting coefficients of the connections diminish by a fraction of their previous values as a result of which insignificant weighting coefficients decrease to 0 in the course of training.

3. Choice of an optimum training set

The design of training samples is yet another problem related to the application of neural networks in chemistry. Chemical compounds constituting a training set should be evenly distributed along the whole range of possible values of input parameters.

The majority of published data deal with random division of the whole array of compounds under investigation into training and control sets, but only some of them provide a description of special procedures for the selection of an optimum training set. The use of Kohonen neural networks has been described in Refs 35, 77, 78; a neural network based on the theory of adaptive resonance (ART 2-A, see above) and intended for preliminary classification of the whole set of experimental data has been described.⁷⁹ The choice of a correct size of training set is yet another critical factor.

4. Optimisation of the number of hidden neurons

The number of adjustable parameters (weighting coefficients) of neural networks is determined by the number of hidden neurons. If the number of hidden neurons is too large and the number of adjustable parameters is comparable with the number of structures in the training set, the neural networks will try to 'memorise' the training set (the over-determination effect). Neural networks with an insignificant number of hidden neurons are unable to utilise the whole array of input information for generalisation and classification.^{80, 81}

The expediency of the introduction of a special parameter r for the estimation of an optimum number of hidden neurons has been demonstrated.^{82–84}

$$r = \frac{N}{P},$$

where N is the number of molecules in the training set and P is the total number of connections in the neural network.

The optimum values of this parameter lie in the range $1.8 < r < 2.2$. The number of hidden neurons thus calculated enables the construction of neural networks manifesting the best forecasting ability.⁸⁰

5. Effect of 'overtraining' of neural networks

The overdetermination of a model (see above) leads to the so-called 'overtraining' of neural networks.^{85–87}

The training of neural networks includes two phases, *viz.*, generalisation and memorisation of information. The first phase is characterised by a decrease in the mean computational error of the property under study for compounds in both training and control sets. However, in the next phase, memorisation, the error calculated for the control set increases in parallel with a constantly decreasing error of the training set. As a consequence, completely trained neural networks can reliably forecast the properties of only those compounds which are included in the training set; for other compounds, the quality of forecasting is much worse. This effect is especially pronounced when the first phase of neural network training is either short-lasting or absent. 'Overtraining' can be avoided by reducing the number of adjustable parameters of a neural network model either actual (by decreasing the number of input parameters of the neural network) or effective⁸⁶ (by 'regularisation', *e.g.*, Bayesian regularisation^{88,89}).

Early termination of training of neural networks at the moment of phase changes is yet another popular procedure. In the majority of publications, the forecasting ability of neural networks was estimated using the same control set as that used in previous studies for establishing the starting point for 'overtraining'. However, in this case the error can be underestimated (see Ref. 90).

6. Analysis of activities of hidden neurons

An analysis of results obtained with a three-layered neural network used for the simulation of structure–property relationships has shown that hidden neurons can be used for cluster analysis of starting compounds.

Kvasnicka *et al.*⁹¹ have carried out a recurrent cluster analysis aimed at classification of functional groups. Each functional group was represented as an output vector of hidden neurons which was normalised for all compounds under investigation using standard statistical methods.

An analysis of activities of hidden neurons of a three-layered associative neural network aimed at classification of data from the training set was used for the determination of the content of eight fatty acids in samples of olive oil produced in nine different regions of Italy.³¹ The use of this approach has made it possible to obtain a more precise, in comparison with the Kohonen neural network, classification of samples with respect to oil-producing regions.

7. Analysis of derived neural network relationships

The need for reliable interpretation of derived models consistent with the data available from the corresponding branches of chemistry, physics or biology is an extremely important aspect which determines the application of virtually all statistical methods including neural networks to the construction of structure–property models in chemistry (particularly those based on the use of physicochemical and quantum-chemical descriptors). Very often, it is this interpretation that represents the most weighty argument in favour of the validity of the constructed model. The impossibility of establishing clear-cut relationships between the properties under study and the input parameters of neural networks, *viz.*, the presentation of a neural network as a 'black box',

is still the main argument against the application of neural networks to the solution of various chemical problems.

The majority of papers do not provide any interpretation of neural network models; however, the possibility of analysis of neural network relationships has been demonstrated^{92,93} as well as that of estimation of contributions of input parameters to neural network models in neural networks with one output neuron based on analytical formulas for the calculation of partial derivatives of neural network functions.^{94–96} It was recommended to supplement a standard sigmoidal transfer function with a parameter b which reflects the degree of mixing of linear and nonlinear functions.

$$\text{Out}_j = \frac{\beta}{(1 + e^{-\alpha \text{Net}_j})} + (1 - b)\text{Net}_j,$$

where Out_j is the output signal of the neuron j ; Net_j is the net input signal of the neuron j ; α and β are the coefficients.

The use of specially computed statistical parameters which characterise the function of a trained neural network has been proposed.⁹⁷ These parameters allow interpretation of neural network models by conventional methods similar to those used for the interpretation of linear regression models. Indeed, the significance of one or another parameter of a linear regression equation is determined by the value and sign of the corresponding numerical coefficient which, in turn, is equal to the value of a partial derivative of the regression function with respect to this particular parameter. The coefficients are calculated on the whole set of experimental data in the course of regression analysis. A similar interpretation of neural network models demands computation of partial derivatives of properties under study on all examples in succession from the training set for all descriptors. This approach enables computation of a set of statistical functions which allows estimation of the contribution of all original descriptors to the derived neural network models.

8. Choice of a function for estimating computational errors

The derived neural network models are usually estimated on the basis of standard statistical functions by calculation of, *e.g.*, root-mean-square errors,^{61,98} correlation coefficients,^{36,99} recognition coefficients,^{43,100} *etc.*

The forecasting ability of neural network models is often estimated using a cross-validation procedure (see, *e.g.*, Refs 35, 82, 101).

9. Comparison of a neural network algorithm with standard statistical methods used for information processing

In many cases, conclusions on the adequacy of the use of neural network simulation are drawn by comparing models obtained using neural network algorithms with the models obtained by other methods.

Thus the results of neural network classification of compounds are compared with the results of the hierarchical cluster analysis, analysis of the main components,³² the results of PLS (Partial Least Squares) in the framework of CoMFA (Comparative Molecular Field Analysis),⁹ chemical expert systems,⁵⁶ *etc.*

Neural network models of structure–property relationships are most frequently compared with equations obtained by the multiple linear regression method.^{77,102,103} Most authors conclude that the use of neural network methods ensures the best results in both the description of structure–property relationships and forecasting properties of novel compounds. However, a conclusion¹⁰⁴ about a poor forecasting ability of neural networks in comparison with multiple linear regression can be explained by an incorrect choice of parameters for a neural network model.

Some papers^{95,105} point to a relationship between neural network simulation and multiple regression analysis. It was shown that the results obtained with neural networks containing one hidden layer and utilising a linear transfer function for all

Table 1. Characteristics of neural network models obtained in the simulation of relationships structure–spectral properties and structure–retention index in chromatography.

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^b			
IR spectra	monosubstituted benzenes	185	topological	32–(10 × 10)–128	A	for different compounds	$R = 0.42–0.94$	99
	aliphatic compounds containing 4–100 carbon atoms	200	calculated IR spectra (PM3)	254–(from 76 to 650)–1	B	decrement of errors of the PM3 method for different compounds (from 10% to ~1.25%)	—	108
¹³ C NMR spectra	acyclic alkanes	21	fragmental	12–2–4–6–2–1	C	calculated values of chemical shifts are close to experimental values	—	24
	monosubstituted benzenes	20	topological	11–6–4	D	satisfactory classification and forecasting of chemical shifts	—	22
	the same	20	the same	11–6–4	E	the same	—	22
	heterogeneous set	40 000	fragmental	360–(5, 10 or 20)–1	D	averaged results of training of 3 neural networks	$MD_t = 1.79$, $SD_t = 2.10$, $R_t = 0.979$; $MD_p = 1.75$, $SD_p = 1.97$, $R_p = 0.981$ (ppm)	109
	pyranoses and pyranosides	55	topological, electronic, geometrical	11–5–1	D	—	$RMS_t = 1.03$, $RMS_{cv} = 0.766$, $RMS_p = 1.11$ (ppm)	110
	furanoses and furanosides	56	the same	8–5–1	D	—	$RMS_t = 1.58$, $RMS_{cv} = 0.995$, $RMS_p = 0.898$ (ppm)	110
	ribonucleosides	17	quantum-chemical	4–2–1	D	—	$RMS_t = 0.69$, $RMS_{cv} = 0.47$, $RMS_p = 0.39$ (ppm)	111
	acyclic alkenes	130	topological	12–4–1	D	four networks with different transfer functions	$SD_t = 0.59–0.63$, $SD_p = 0.89–1.07$ (ppm)	112
	amino acids	123	physicochemical	hierarchical networks: 52–4–3, 39–4–3	F	—	$C_t = 77\%$ for $^{13}C_\alpha$ $C_t = 75.3\%$ for $^1H_\alpha$ $C_t = 78.3\%$ for ^1HN	44
Retention indices in gas chromatography	alkanes, alkenes, alcohols, esters, ketones	216	types of bonds	29–2–1	D	—	$RMS_t = 14.7$, $RMS_p = 23.6$	102
Retention indices in reversed-phase chromatography	steroids	85	quantum-chemical	11–3–1	D	—	$SD_p = 0.08$, $SD_{cv} = 0.09$	113

Table 1 (continued).

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^b			
Kovats indices	substituted phenols	43	molar refraction, dipole moment	2–3–6–1	A	—	$RMS_p = 1.1$ for the support SE-30 $RMS_p = 2.1$ for the support OV-225 $RMS_p = 0.8$ for the support NGA	37
Retention indices in thin-layer chromatography	substituted benzoic acids	22	quantum-chemical	7–4–1	D	—	$R = 0.973$	103

Note. Here and in Tables 2–4, the architectures of neural networks are described by the number of neurons for each neural network layer starting from the input neuron and ending with the output neuron.

^a The parameters for assessing neural network training results: R is the correlation coefficient; MD is the mean deviation; RE is the relative error; SD is the standard deviation; RMS , MSE and S are the root-mean-square errors; C is the recognition coefficient; SE is the standard error; MAE , AAE are the mean absolute errors; RSD is the relative standard deviation; ME is the mean forecasting error; ADD is the standard absolute deviation; RV is the residual variation and SSO is the sum of squared differences between the calculated and experimental values. The letterings for the subscript indices are as follows: t is the training set; p and v are the control sets; o designates ‘for all compounds’ and cv is the cross-validation.

^b A is the back propagation neural network; B is the feedforward neural network; C is the neural network reproducing the topology of molecules under study; D is the feedforward neural network trained according to the delta rule; E is the recurrent neural network; F is the feedforward neural network trained by the resilient propagation method; G is the Kohonen neural network; H is the wavelet neural network; I is the feedforward neural network trained by the Broyden–Fletcher–Goldfarb–Shanno method; J is the radical-basic neural network; K is the fuzzy ARTMAP neural network; L is the feedforward neural network with additional direct bonds between input and output layer neurons trained by the delta rule; M is the feedforward neural network with additional direct bonds between input and output layer neurons trained by the Broyden–Fletcher–Goldfarb–Shanno method; N is the feedforward neural network trained by the scaled conjugated gradient method; O is the feedforward neural network trained with the help of Bayesian regularisation; P is the Kohonen nonlinear distribution neural network; Q is the feedforward functional links neural network.

Table 2. Characteristics of neural network models obtained in the simulation of structure–reactivity relationships of organic compounds.

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Cleavage of the C–C bond between the α - and β -atoms relative to the carbonyl group	carbonyl compounds	32	fragmental	8–(9 × 9)	G	clear-cut separation of the starting array of compounds into four clusters according to bond cleavage type	—	28
Heterolytic bond cleavage	aliphatic compounds	29	physicochemical	7–(11 × 11)	G	correct classification of reactions according to bond cleavage type for both the training and control sets	—	2
	the same	29	"	7–3–1	D			
Ratio of isomers upon electrophilic substitution	monosubstituted benzenes	45	quantum-chemical	6–10–2	D	—	$RMS_t = 5.2\%$, $RMS_p = 19.8\%$	2, 56
	the same	45	tables of bonds of substituents	25–5–2	D	—	$RMS_t = 0.3\%$, $RMS_p = 12.1\%$	2, 56
Yield of <i>m</i> -isomers upon nitration	"	31	fragmental	9–4–4–1	D	good correlation with experimental data for the training set; for the control set the result is at 'semiquantitative level'	—	23
	"	31	"	9–5–5–1	I			
	"	31	"	9–6–6–1	I			
The Markownikoff addition of hydrogen halides	alkenes	25	connectivity matrix	36–8–8–28	D	correct recognition of the addition site for the training and control sets	—	57
Direct and retro Diels–Alder reactions	cycloalkenes	36	the same	120–36–36–105	D	correct classification into forward and retro reactions and identification of the main product of the forward reaction for training and control sets	—	57
Elimination of hydrogen halides according to the Zaitsev rule	alkenes	83	"	66–24–24–55	D	correct identification of the main reaction product for the training and control sets	—	57
Constants of complex formation with α -cyclodextrin	substituted benzenes	24	physicochemical	3–3–3–3–1	D	—	$R = 0.97$, $SD_t = 0.22$ (ln K_a)	114
Constants of complex formation with β -cyclodextrin	mono- and 1,4-disubstituted benzenes	40	"	6–6–1	H	—	$R = 0.992$, $SD_t = 0.089$ (ln K_a)	115
Heats of formation of aromatic salts	dihydropyridines and related heterocyclic compounds	71		22–4–1	D	—	$R = 0.92$, $SD_t = 0.298$, $SD_p = 1.80$ kcal mol ^{–1}	116

Table 2 (continued).

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Addition rate constants of the methyl radical	unsaturated compounds of various types	191	quantum-chemical	6–4–1	D	—	$RMS_t = 0.381$, $RMS_p = 0.496$	53
	the same	191	"	7–3–1	D	—	$RMS_t = 0.424$, $RMS_p = 0.409$ ($\log k$)	53
Reaction with tetrazolium blue, composition of a multicomponent mixture	cortisone and hydrocortisone mixtures	40	"	6–4–2	D	—	$SE_t = 3.47\%$, $SE_p = 4.12\%$ for cortisone; $SE_t = 5.12\%$, $SE_p = 5.25\%$ for hydrocortisone	117

^a Designations as in Table 1.

Table 3. Characteristics of neural network models obtained in the simulation of structure – physicochemical property relationships of organic compounds.

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a		
Boiling temperature	alkyl halides C ₁ –C ₄	171	topological	7–14–1	D	$R = 0.995$	118
	acyclic ethers, peroxides, acetals and their sulfur analogues	185	fragmental	20–5–1	D	$R = 0.998$, $SE_t = 2.9$ °C, $SE_p = 5.1$ °C	82
	the same	185	topological	3–20–1	J	$R = 0.990$, $SE_t = 4.9$ °C, $SE_p = 5.9$ °C	39
	tetrahydrofurans, thiophenes, furans, pyrans	299	topological and electronic	16–3–1	D	$RMS_{cv} = 8.49$ °C	119
	pyridines	291	the same	7–3–1	D	$RMS_{cv} = 15.8$ °C	119
	heterogeneous set	298	electrotopological	19–5–1	D	$R = 0.9975$, $MAE_t = 3.86$ °C, $MAE_p = 4.57$ °C	120
	fluoro-substituted ethanes and propanes	31	topological	8–6–1	D	$MAE_t = 4.7$ °C	121
	alkenes	82	"	5–5–1	D	$RSD_t = 4.88\%$, $RSD_{cv} = 3.5\%$	122
	alkanes	140	topological and physicochemical	7–4–1	D	$AAE_t = 1.65$ °C, $AAE_p = 1.73$ °C, $AAE_o = 1.54$ °C	42
	"	140	the same	7–4–1	K	$AAE_t = 0.81$ °C, $AAE_p = 1.30$ °C	42
	alkenes	144	"	7–10–1	D	$AAE_t = 6.79$ °C, $AAE_p = 6.45$ °C, $AAE_o = 4.42$ °C	42
	"	144	"	7–10–1	K	$AAE_t = 0.73$ °C, $AAE_o = 0.95$ °C	42
	alkanes, alkenes and alkynes	327	"	7–9–1	D	$AAE_t = 6.09$ °C, $AAE_p = 4.68$ °C, $AAE_o = 4.85$ °C	42
	the same	327	"	7–9–1	K	$AAE_t = 1.15$ °C, $AAE_o = 1.35$ °C	42
	heterogeneous set	298	topological, electronic and mixed	8–3–1	I	$RMS_t = 7.75$ °C, $RMS_{cv} = 7.17$ °C, $RMS_p = 8.69$ °C	123
	the same	400	topological	26–36–2	J	$AAE_t = 11$ °C, $AAE_p = 14$ °C	40
	hydrocarbons	134	"	7–8–6	D	$ME_p = 1.19\%$	101
	heterogeneous set	421	the presence of functional groups	36–3–4	L	$ADD_p = 2.9\%$	19
Critical temperature	the same	165	electrotopological	19–4–1	D	$R = 0.9965$, $MAE_t = 4.39$ °C, $MAE_p = 5.59$ °C	120
	fluoro-substituted ethanes and propanes	38	topological and boiling temperature	9–4–1	D	$MAE_t = 5.9$ °C	121
	heterogeneous set	421	the presence of functional groups	36–3–4	L	$ADD_p = 3.1\%$	19
	alkanes	69	topological	12–5–6	D	$R = 0.994$, $S_t = 3.80$, $S_v = 3.94$	124
	"	69	fragmental	14–6–6	D	$R = 0.995$, $S_t = 3.37$, $S_v = 3.58$	124
Self-ignition temperature	acyclic hydrocarbons with low self-ignition temperature	47	topological and quantum-chemical	5–3–1	I	$RMS_t = 8.77$ °C, $RMS_{cv} = 6.88$ °C, $RMS_p = 5.11$ °C	125
	acyclic hydrocarbons with high self-ignition temperature	51	the same	6–2–1	I	$RMS_t = 18.5$ °C, $RMS_{cv} = 17.0$ °C, $RMS_p = 15.7$ °C	125

Table 3 (continued).

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a		
Self-ignition temperature	nitrogen-containing organic compounds	40	topological and quantum-chemical	6–2–1	I	$RMS_t = 34.9\text{ }^{\circ}\text{C}$, $RMS_{cv} = 23.6\text{ }^{\circ}\text{C}$, $RMS_p = 28.2\text{ }^{\circ}\text{C}$	125
	organic compounds containing oxygen or sulfur atoms	132	the same	7–5–1	I	$RMS_t = 30.8\text{ }^{\circ}\text{C}$, $RMS_{cv} = 29.7\text{ }^{\circ}\text{C}$, $RMS_p = 32.5\text{ }^{\circ}\text{C}$	125
Ignition temperature	heterogeneous set	400	topological	26–36–2	J	$AAE_t = 10\text{ }^{\circ}\text{C}$, $AAE_p = 12\text{ }^{\circ}\text{C}$	40
Heat of evaporation	fluoro-substituted ethanes and propanes	38	"	8–4–1	D	$MAE_t = 1.1\text{ kJ mol}^{-1}$	121
	alkanes	69	"	12–5–6	D	$R = 0.994$, $S_t = 0.44$, $S_v = 0.51$	124
	"	69	fragmental	14–6–6	D	$R = 0.996$, $S_t = 0.44$, $S_v = 0.56$	124
Thermal capacity	hydrocarbons	134	topological	7–8–6	D	$ME_p = 0.87\%$	101
Density	"	134	"	7–8–6	D	$ME_p = 0.60\%$	101
	fluoro-substituted ethanes and propanes	38	"	8–4–1	D	$MAE_t = 0.03\text{ g cm}^{-3}$	121
	alkenes	82	"	5–5–1	D	$RSD_t = 0.43\%$, $RSD_{cv} = 0.4\%$	122
Refraction index	hydrocarbons	134	"	7–8–6	D	$ME_p = 0.19\%$	101
	alkenes	82	"	5–5–1	D	$RSD_t = 0.13\%$, $RSD_{cv} = 0.14\%$	122
The Gibbs energy Enthalpy	hydrocarbons	134	"	7–8–6	D	$ME_p = 1.36\%$	101
	"	134	"	7–8–6	D	$ME_p = 1.42\%$	101
Critical volume	heterogeneous set	421	the presence of functional groups	36–3–4	L	$ADD_p = 3.4\%$	19
Acentric factor	the same	421	the same	36–3–4	L	$ADD_p = 9.1\%$	19
Molar volume	alkanes	69	topological	12–5–6	D	$R = 0.999$, $S_t = 0.84$, $S_v = 0.89$	124
	"	69	fragmental	14–6–6	D	$R = 0.999$, $S_t = 0.88$, $S_v = 1.10$	124
Molar refraction	"	69	topological	12–5–6	D	$R = 1.000$, $S_t = 0.15$, $S_v = 0.18$	124
	"	69	fragmental	14–6–6	D	$R = 0.999$, $S_t = 0.20$, $S_v = 0.18$	124
Critical pressure	"	69	topological	12–5–6	D	$R = 0.984$, $S_t = 0.46$, $S_v = 0.39$	124
	"	69	fragmental	14–6–6	D	$R = 0.986$, $S_t = 0.44$, $S_v = 0.23$	124
	heterogeneous set	421	boiling temperature, critical temperature, critical volume	3–3–1	L	$ADD_p = 6.4\%$	19
Surface tension	alkanes	69	topological	12–5–6	D	$R = 0.996$, $S_t = 0.18$, $S_v = 0.28$	124
	"	69	fragmental	14–6–6	D	$R = 0.996$, $S_t = 0.17$, $S_v = 0.17$	124

Table 3 (continued).

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a		
Saturated vapour pressure [log VP (Pa)]	compounds with heteroatoms	420	topological	8–3–1	I	$RMS_t = 0.26$, $RMS_p = 0.37$, $RMS_{cv} = 0.29$	54
	the same	420	"	10–4–1	I	$RMS_t = 0.19$, $RMS_p = 0.33$, $RMS_{cv} = 0.24$	54
	hydrocarbons and halogenohydrocarbons	352	topological, geometrical and electronic	7–3–1	I	$RMS_t = 0.163$, $RMS_{cv} = 0.163$, $RMS_p = 0.209$	126
Viscosity [log M (mPa s)]	heterogeneous set	361	experimental physico-chemical values	9–3–1	D	$R = 0.958$, $RMS_t = 0.118$, $RMS_p = 0.161$	127
Solubility in water [log S (mol litre ⁻¹)]	the same	350	quantum-chemical	17–18–1	D	$SD_t = 0.23$, $SD_p = 0.43$	128
	"	332	topological, electronic and geometrical	9–6–1	I	$RMS_t = 0.394$, $RMS_{cv} = 0.358$, $RMS_p = 0.343$	129
	heterogeneous set of drugs	211	electrotopological and topological	23–5–1	D	$R_t^2 = 0.90$, $SE_t = 0.46$, $R_p^2 = 0.86$, $SE_p = 0.53$	130
	heterogeneous set	136	topological, electronic, geometrical and mixed	9–3–1	I	$RMS_t = 0.145$, $RMS_{cv} = 0.151$, $RMS_p = 0.166$	131
Solubility in carbon dioxide in a supercritical state [log S (mol litre ⁻¹)]	the same	58	topological and quantum-chemical	7–2–1	I	$RMS_t = 0.65$, $RMS_{cv} = 0.68$, $RMS_p = 0.64$	132
Activity coefficient at infinite dilution (log γ^∞)	"	325	the same	12–6–1	I	$RMS_t = 0.472$, $RMS_{cv} = 0.538$, $RMS_p = 0.484$	133
Lipophilicity (log P) ^b	"	250	quantum-chemical	8–5–1	D	$R = 0.923$, $SE_p = 0.379$	134
	"	250	"	13–6–1	D	$R = 0.952$, $SE_p = 0.300$	134
	"	1870	molecular weight and electrotopological	39–5–1	D	$R_t^2 = 0.90$, $RMS_t = 0.46$, $R_p^2 = 0.94$, $RMS_p = 0.4$	135
	"	323	quantum-chemical	6–7–1	I	$SE_p = 0.30$	136
	"	323	"	11–3–1	D	$SD_t = 0.31$, $SD_p = 0.29$, $SD_{cv} = 0.32$	113
	compounds with heteroatoms	7719	topologo-physicochemical	35–32–1	D	$R_t = 0.97$, $RMS_t = 0.37$, $R_p = 0.98$, $RMS_p = 0.39$	137
Phase-transition temperature (°C)	nematic liquid-crystalline compounds	17383	fragmental	205–100–1	D	$SD_t = 3.8$, $SD_p = 16.4$	138, 139
	the same	6304	"	205–10–1	D	$SD_p = 18.8$	138, 139
Solvatochromic polarity – polarisability index	heterogeneous set	333	topological, electrostatic, quantum-chemical, structural	16–7–1	D	$R^2 = 0.980$	77
Molar adsorption (log ϵ)	asymmetric phosphobisazo derivatives	43	topological	4–4–3–1	I	$RMS_t = 0.05669$, $RMS_p = 0.09621$	61

Table 3 (continued).

The property that is simulated	Compounds under study	Number of compounds	Descriptors	Architecture of neural networks		Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a		
Impact sensitivity ($\log H_{50\%}$) ^c	nitro compounds	204	topological, quantum-chemical	11–2–1	D	$R = 0.941$, $SE_p = 0.154$	62
	"	204	the same	13–2–1	D	$R = 0.937$, $SE_p = 0.159$	62
	"	204	"	13–3–1	D	$R = 0.95$, $SE_p = 0.13$	140
Position of the long-wave absorption band	symmetrical cyanine dyes	398	quantum-chemical, indicators of the presence of substituents	8–10–1	D	$R_s = 0.9928$, $S_t = 10.6$ nm, $S_v = 7.0$ nm	141
Interatomic distances	compounds containing two heteroatoms	2615	geometrical	78–8–1	D	$C_t = 80\%$, $C_p = 80\%$ for remote atoms; $C_t = 66\%$ for adjacent atoms	100
Odour	aliphatic alcohols	99	topological	6–3–1	D	$C_t = 100\%$, $C_p = 85\%$	142
Total energy of π -electrons	unsubstituted polycyclic hydrocarbons	265	"	3–3–1	D	$SD_t = 0.06$, $SD_{cv} = 0.27$	143
Inductive and resonance constants of substituents	monovalent functional groups ^d	37	"	14–8–2	D	—	144

^a Designations as in Table 1.

^b $\log P$ is the common logarithm of the distribution coefficient in the n-octanol–water system.

^c $H_{50\%}$ is the height for which the explosion occurs with 50% probability.

^d For compounds under study, the result of neural network training is a correct classification of substituents and a good estimation of the values of substituent constants for both training and control sets.

Table 4. Some characteristics of neural network models obtained in the simulation of structure–biological activity relationships of organic compounds.

The property that is simulated	Number of compounds	Compounds under study	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Affinity to transport proteins (globulins)	31	corticosteroids and testosterone	physicochemical	32–(10 × 10)	G	clear-cut separation of steroids into three clusters (strong, medium and weak affinity)	—	99
		the same	map of atomic coordinates	9–(7 × 7)	G	separation of steroids into two clusters (strong and weak affinity)	—	29
		"	map of atomic coordinates and charges	9–(7 × 7)	G	clear-cut separation according to the type of receptors for training and control sets	—	30
Affinity to estrogen receptors	22	disubstituted hexestrol derivatives	topological and physicochemical	2–6–1	D	—	$RMS_t = 0.09131$ ($\log RBA$) ^b	145
	16	hexestrol ethers	topological	1–4–2–1	D	—	$RMS_t = 0.018219$ ($\log RBA$)	145
	16	deoxyhexestrols	"	1–4–2–1	D	—	$RMS_t = 0.018219$ ($\log RBA$)	145
Affinity to progesterone receptors	55	androst-4-en-3-one derivatives	physicochemical	6–2–1	M	—	$R = 0.96$, $RMS_t = 0.30$, $RMS_p = 1.32$ ($\log IC_{50}$) ^c	20
Affinity to benzodiazepine receptors GABA _A	57	1,4-benzodiazepin-3-ones	"	10–3–1	N	—	$R_t = 0.954$, $SD_t = 0.007$, $R_{cv} = 0.901$ ($\log IC_{50}$)	146
				6–2–1	N	—	$SD_{cv} = 0.009$, $R_{cv} = 0.938$	146
Inhibition of reverse transcriptase of the human immunodeficiency virus	44	derivatives of AZT ^d , TIBO ^e and related compounds	topological	4–3–2	D	—	$C_t = 100\%$, $C_p = 86\%$	74, 75
	107	1-[(2-hydroxyethoxy)-methyl]-6-(phenylthio)-thymine derivatives	quantum-chemical	6–6–1	D	—	$MSE_t = 0.073$, $MSE_p = 0.372$ ($\log 1/C$) ^f	147
Inhibition of protein tyrosine kinase p56 ^{lck}	105	substituted flavonoids	physicochemical constants of substituents	6–(10 × 10)–1	A	—	$R^2 = 0.92$, $SD_p = 0.55$ ($\log 1/IC_{50}$)	35
			quantum-chemical	3–(10 × 10)–1	A	—	$R^2 = 0.96$, $SD_p = 0.40$ ($\log 1/IC_{50}$)	35
Inhibition of 5-lipoxygenase <i>in vitro</i>	68	arylhydroxamic acids	physicochemical	1–4–1	D	—	$RMS_t = 0.09043$ ($\log 1/K$) ^g	145
Inhibition of dihydrofolate reductase	157	3,4-diamino-6,6-dimethyl-5-phenyldihydrotriazines	"	6–4–1	D	—	$R = 0.922$, $SD_t = 0.374$ ($\log IC_{50}$)	80

Table 4 (continued).

The property that is simulated	Number of compounds	Compounds under study	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Inhibition of dihydro-folate reductase	61	symmetrical 1-aryl-4,6-diamino-2,2-dimethyl-1,2-dihydrotriazines	physicochemical	3–1–1	M	—	$R = 0.87$, $SD_t = 0.27$	20
	68	2,4-diamino-(5 <i>R</i>)-benzyl-pyrimidines	"	4–7–1	D	—	$R = 0.97$, $RV_t = 0.0126$, $RV_p = 0.323$	83
Inhibition of acyl-cholesterol- <i>O</i> -acyl transferase	157	aminosulfonyl-, hydroxy-sulfonyl- and (2,6-diisopropylphenoxy)carbonates, aminosulfonyl- and hydroxysulfonylureas	topological, geometrical and electronic	8–3–1	I	—	$RMS_t = 0.226$, $RMS_{cv} = 0.208$, $RMS_p = 0.242$ (log IC_{50})	55
Inhibition of [³ H]diazepam binding	245	benzodiazepines	topological	50–4–1	O	—	$R^2 = 0.63$, $SE_p = 0.14$ (log IC_{50})	88, 89
Antifungal activity	103	(3 <i>R</i>)-1-(3,5-dichlorophenyl)-pyrrolidine-2,5-diones	physicochemical parameters of substituents	5–(5 × 5)	O	clear-cut separation of starting compounds into groups	—	78
Anthelmintic activity	31	2-hydroxyphenylamides	physicochemical	3–3–1	D	—	$R = 0.919$, $RMS_t = 0.322$	64
		"	"	53–(8 × 8)	G	clear-cut separation into groups possessing different activities	—	32
Hypotensive activity	24	(3 <i>R</i>)-phenylthiopropyl-substituted heterocycles	"	6–3–1	D	—	$SD_{cv} = 11.6\%$	148
	29	arylacryloylpiperazines	"	7–14–4	D	—	$C_t = 19/21$, $C_p = 6/8$	149
Anticonvulsant activity	60	benzodiazepine derivatives	"	14–15–57–1	A	—	$RMS_t = 0.16$	38
			"	14–28–1	D	—	$SD_t = 0.33$	10, 38
			"	5–6–1	D	—	$R = 0.887$	2, 43
			"	5–1	Q	—	$R = 0.876$, $RMS_t = 0.369$	43
Antitumour activity (minimum effective dose for multiple injections)	39	2,5-bis(1-aziridinyl)- <i>p</i> -benzoquinones	"	6–7–37–1	A	—	$RMS_t = 0.08$	38
			"	12–13–37–1	A	—	$RMS_t = 0.06$	38
			"	7–12–1	D	—	$RMS_t = 0.21$	2, 10, 38
			"	13–26–1	D	—	$RMS_t = 0.21$	10, 38
Antitumour activity (minimum effective dose for single injection)	39		"	6–7–37–1	A	—	$RMS_t = 0.04$	38
			"	12–13–37–1	A	—	$RMS_t = 0.20$	38
			"	7–12–1	D	—	$RMS_t = 0.25$	2, 10, 38
			"	13–26–1	D	—	$RMS_t = 0.24$	2, 10, 38
Antitumour activity (optimum dose for multiple injections)	39		"	6–7–37–1	A	—	$RMS_t = 0.02$	38
			"	12–13–37–1	A	—	$RMS_t = 0.05$	38
			"	7–12–1	D	—	$RMS_t = 0.19$	2, 10, 38

Table 4 (continued).

The property that is simulated	Number of compounds	Compounds under study	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Antitumour activity (optimum dose for multiple injections)	39		physicochemical	13–26–1	D	—	$RMS_t = 0.18$	2, 10, 38
			"	4–13–1	D	—	$R = 0.960$	43
			"	4–1	Q	—	$R = 0.951, RMS_t = 0.169$	43
Antitumour activity (optimum dose for single injection)	39		"	6–7–37–1	A	—	$RMS_t = 0.08$	38
			"	12–13–37–1	A	—	$RMS_t = 0.05$	38
			"	7–12–1	D	—	$RMS_t = 0.20$	2, 10, 38
			"	13–26–1	D	—	$RMS_t = 0.17$	2, 10, 38
Inhibition of methotrexate-sensitive tumour cells	61	3-substituted triazines	"	3–3–1	M	—	$R = 0.86, SD_t = 0.25$	20
Inhibition of methotrexate-resistant tumour cells	62		"	3–1	M	—	$R = 0.58, SD_t = 0.53$	20
Mechanisms of anti-tumour activity	141	drugs	activities with respect to different tumour cells	60–7–6	D	—	$C_p = 129/141$	150
Toxicity	91	benzothiazolium salts	fragmental	30–2–1	D	—	$SSO_t = 0.017, SSO_p = 0.850$	151
Anticarcinogenic activity	16	carboquinones	physicochemical	7–12–5	D	—	$C_t = 100\%, C_p = 3/5$	84, 94, 149
				7–4–5	D	—	$C_t = 100\%, C_p = 3/5$	84
Carcinogenic activity	45	mono- and polysubstituted benzenes	topological	90–100–100–1	A	—	$R_t = 0.95, R_p = 0.70$	36
			topological and quantum-chemical	90–100–100–1	A	—	$R_t = 0.98, R_p = 0.72$	36
			quantum-chemical	90–100–100–1	A	—	$R_t = 1.00, R_p = 0.63$	36
	11	polycyclic aromatic hydrocarbons	¹³ C NMR spectra	10–3–1	D	clear-cut separation into active and inactive compounds	—	76
	81	aromatic compounds with nitrogen-containing substituents	quantum-chemical	6–12–2	D	—	$C_t = 84.6\%, C_p \approx 80\%$	152
Mutagenic activity	104		topological, physico-chemical and quantum-chemical	12–4–1	D	—	$R_{cv}^2 = 0.691, MSE_{cv} = 0.0416$ [log ($MW \cdot 1000/ID_{50}$)] ^{h,i}	153
	197	aromatic and hetero-aromatic compounds	physicochemical	2–4–2–1	D	—	$RMS_t = 0.14331 (\log TA_{98})^j$	145
			"	4–8–4–1	D	—	$RMS_t = 0.11515, RMS_p = 0.1216$	145
			"	4–4–1	D	—	$R_t = 0.919, SD_t = 0.789, R_p = 0.853, SD_p = 1.049 (\log TA_{98})$	154

Table 4 (continued).

The property that is simulated	Number of compounds	Compounds under study	Descriptors	Architecture of neural networks		Training results	Statistical characteristics of neural network training ^a	Ref.
				number of neurons	type of neural network ^a			
Mutagenic activity	488	heterogeneous set	fragmental	100–10–2	D	good separation into clusters according to size and activity	—	69, 155
	54	heterocyclic analogues of pyrene and phenanthrene, fluorenes, biphenyls	energy of LUMO, lipophilicity, presence of a nitro group in the <i>p</i> -position	3–2–1	D	—	$R = 0.87$, $S_t = 1.03$, $S_v = 1.47$ ($\ln N_{\text{his}^+}$) ^k	156
Inhibition of intracellular ion exchange Na^+/H^+	113	benzoylguanidine derivatives	topological, geometrical, electronic and combined	5–4–1	D	—	$R_t^2 = 0.812$, $RMS_t = 0.278$, $R_p^2 = 0.697$, $RMS_p = 0.362$ (log IC_{50})	157
Hallucinogenic activity	64	phenylalkylamines	fragmental	15–(33 × 33)	G	clear-cut separation of compounds into clusters according to activity	—	28
	35	"	constants of substituents, indicators of the presence of substituents	7–2–1	D	—	$R = 0.932$, $S_t = 0.55$, $S_v = 0.47$ ($\ln MU$) ^{l,m}	58
							$R = 0.820$, $S_t = 0.89$, $S_v = 0.54$ ($\ln MU$) ⁿ	58
Blocking of Ca^{2+} channels	46	1,4-dihydropyridines	constants of substituents	5–2–1	D	—	$R = 0.832$, $S_t = 0.79$, $S_v = 0.71$ (log $1/EC_{50}$) ^{m,o}	58
					D	—	$R = 0.870$, $S_t = 0.70$, $S_v = 1.59$ (log $1/EC_{50}$) ⁿ	58
Adsorption by human gastric mucosa	86	drugs	quantum-chemical and topological	6–4–1	D	—	$RMS_t = 9.4\%$, $RMS_{cv} = 19.7\%$, $RMS_p = 16.0\%$	158
Antibacterial activity ^p $MIC \leq 0.05$ $MIC \leq 0.10$ $MIC \leq 0.20$	111	fluoroquinolones	topological	62–2–1	D	—		
							$C_t = 100\%$, $C_p = 93.88\%$	159
							$C_t = 97.28\%$, $C_p = 82.36\%$	
							$C_t = 99.53\%$, $C_p = 87.99\%$	

^a Designations as in Table 1; ^b RBA is the affinity for the receptor; ^c IC_{50} is the concentration causing 50% inhibition; ^d AZT is azidothymidine; ^e TIBO is 4,5,6,7-tetrahydroimidazo[4,5,1-*j,k*][1,4]benzodiazepin-2(1*H*)-one; ^f C is the concentration of a compound causing a certain biological response; ^g K is the inhibition constant; ^h MW is the molecular weight; ⁱ ID_{50} is the dose causing 50% inhibition; ^j TA_{98} is the number of revertants in the Ames test TA_{98} ; ^k N_{his^+} is the number of revertants in the Ames test TA_{1538} ; ^l MU are the muscarine units; ^m the initial set of compounds was supplemented with topologically equivalent structures; ⁿ without multiplication of the initial set of compounds; ^o EC_{50} is the effective concentration; ^p MIC is the minimum inhibiting concentration /mg ml^{−1}.

neurons are identical with the results obtained by multiple linear regression analysis.

If the neurons of the hidden layer of a three-layered neural network are described by a nonlinear (most commonly, sigmoidal) transfer function and the neuron of the output layer is described by a linear function, the resulting neural network (termed MR neural network) will function similarly to a nonlinear multiple regression.^{96, 106, 107}

IV. The use of neural network algorithms for elucidating structure–property relationships

The neural network approach can successfully be employed for elucidating both qualitative and quantitative structure–property relationships. Some brief information about the use of neural network models for the simulation of spectral characteristics, reactivities, physicochemical properties and biological activities of organic compounds is given in Tables 1–4.

The information contained in the IR^{99, 108} and NMR spectra^{22, 24, 44, 109–112} as well as chromatographic retention indices^{37, 102, 103, 113} is closely related to the structures of organic molecules. In the studies cited in Table 1, the neural network algorithm for processing of such information was successfully used for the solution of miscellaneous practical problems related to the search for relationships between molecular structures and spectral properties, classification and forecasting of structural data and refinement of molecular structures on the basis of spectral information.

In one pioneering study, neural network methods were used for the classification of reactions of organic compounds, viz., according to the cleaved bond type,^{2, 28} regiochemistry of the addition reaction,⁵⁷ isomer ratios,^{2, 23, 56} main reaction products,⁵⁷ etc. (Table 2). In these studies, connectivity matrices of organic compounds were used as input information for neural network models, since they do not require additional calculations at the preceding steps. Neural network methods can be used for quantitative estimation of reactivities of organic compounds and simulation of complex kinetic processes in the course of chemical transformations.

The publications devoted to the analysis of various physicochemical properties of chemical compounds using neural networks are rather numerous; the most popular characteristics of organic compounds include boiling temperature^{19, 39, 40, 42, 82, 101, 118–123} (predominantly with the use of topological indices), density,^{101, 121, 122} solubility in water,^{128–131} lipophilicity^{134–137}, etc. (Table 3).

Today, simulation of biological activities of organic compounds presents considerable practical interest: the overwhelming majority of publications devoted to the use of artificial neural networks for elucidating structure–property relationships are related to this particular area (Table 4).³¹ Some publications describe the results of successful quantitative neural network simulation of affinities of organic compounds to various receptors^{20, 145, 146} and transport proteins,^{29, 30, 99} simulation of inhibition constants of enzymes,^{20, 35, 55, 74, 75, 80, 83, 145, 147} antitumour,^{20, 38, 43, 105, 150} carcinogenic,^{36, 76, 152, 153} mutagenic^{69, 145, 154–156} and antibacterial activities,¹⁵⁹ etc.

* * *

Artificial neural networks represent a potent comprehensive computational tool for the solution of miscellaneous problems related to processing of chemical information, particularly classification and simulation of disembodied experimental data. The number of publications on the subject is increasing annually, which testifies to the unrelenting interest of chemists in the simulation of structure–property relationships using artificial neural networks.

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Erratum

to the article by M V Basilevsky, M V Vener

‘Theoretical investigations of proton and hydrogen atom transfer in the condensed phase’

published in *Russian Chemical Reviews* **72** 1 – 33 (2003)

The following text should be inserted at the end of Section III.1.b, page 17.

The HAT reactions in the H + H system and its isotope analogues make an exception. There are no high curvature regions on the canonical reaction path (RP) curves for these reactions and it is just this condition that is required in order to construct a curvilinear coordinate system using a RP curve as a frame. The variational TS theory in its conventional formulation is applicable to for such systems. Their computations proved to be successful even at low temperature.^{1–4} On the other hand, special effort is needed for extending the variational approach to the HAT between heavy atomic or molecular fragments (the systems considered in Section II.3.b with a large curvature of the RP in the vicinity of the TS region). Here a significant modification of the theory is required that includes a search of tunneling trajectories avoiding the RP.^{5–7}

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Self-organisation processes in the chemistry of materials

Yu D Tretyakov

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Abstract. The review concerns conservative and dissipative self-organisation phenomena in those physicochemical systems, whose evolution involves formation of diverse chemically complex products, including functional ceramics, supramolecular compounds, and nanocomposites as well as fractal, template and epitaxial structures. It is demonstrated that the use of nonlinear dynamics approaches facilitates organisation of the reaction zone during the synthesis of materials under nonequilibrium conditions in an optimum manner and that biomimetism and biomineralisation processes open up new prospects for materials design. The bibliography includes 308 references.

I. Introduction

Design of advanced functional and structural materials is a critically important research field.¹ Attempts at employing basic research methods in materials design have long been undertaken. It is sufficient to remind readers of an approach proposed by the author of this review nearly two decades ago; this strategy was then successfully applied to the chemistry of magnetic dielectrics and semiconductors as well as materials with ionic and electronic conduction.^{2,3} However, modern chemistry of materials is still characterised by the predominance of intuitive approaches and experimental screening techniques that underlie the combinatorial chemistry (the development of this research field is associated with the development of fast screening techniques).^{4–6}

Methods for the design of advanced materials can be conventionally divided into two groups:

— techniques involving variation of the composition of the precursor system and

— methods involving variation of processes (including synthesis) and conditions for subsequent treatment (*e.g.*, heat treatment).

Often, the role of the temporal evolution of a system during the preparation of a certain material becomes so important that one should use the *TTT* (Temperature–Time–Transition) diagrams.^{7,8} In particular, this approach has proved itself in determining the nature of changes in the critical temperature (T_c) of the neodymium/barium cuprates that are characterised by very low rate of cation ordering.

While on the subject of a material's structure, one should keep in mind different levels of structural organisation of matter, from the structure of a unit cell to the polycrystalline structure exhibiting specific defects including domain boundaries, pores and cracks (Fig. 1). At the same time, interrelations between different levels of structural organisation of a material should also not be overlooked, though this does not imply the possibility of controlling the situation. The diversity of manifestations of synergism as an effect of co-operative behaviour of certain elements (such elements exhibit a chaotic behaviour at the microlevel) of a complex system is often analysed in the framework of the nonlinear dynamics paradigm.^{9–12}

II. Nonlinear behaviour of physicochemical systems during the preparation of materials

Considering the chemical complexity of a precursor system, one should take into account the nonlinear character of the physical response. The nature of this nonlinearity is not known with certainty; it is determined by both thermodynamic and kinetic factors.^{2,3,13,14} Methods for improving the properties of a material by successively complicating its chemical composition and structure are not necessarily efficient. This can be exemplified by the dependence of the superconducting transition temperature (critical temperature) of cuprates belonging to the $\text{HgBa}_2\text{Ca}_{n-1}.\text{Cu}_n\text{O}_{2n+2+x}$ homologous series on the number of CuO_2 layers (Fig. 2).¹⁵

When preparing homogenous chemically complex products, the best precursor systems are either true or colloidal solutions, melts or gaseous mixtures with the highest possible (ideally, atomic or molecular) degree of mixing of the material-

Yu D Tretyakov Department of Chemistry and Department of Materials Science, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax (7-095) 939 09 98. Tel. (7-095) 939 20 74. E-mail: yudt@inorg.chem.msu.ru

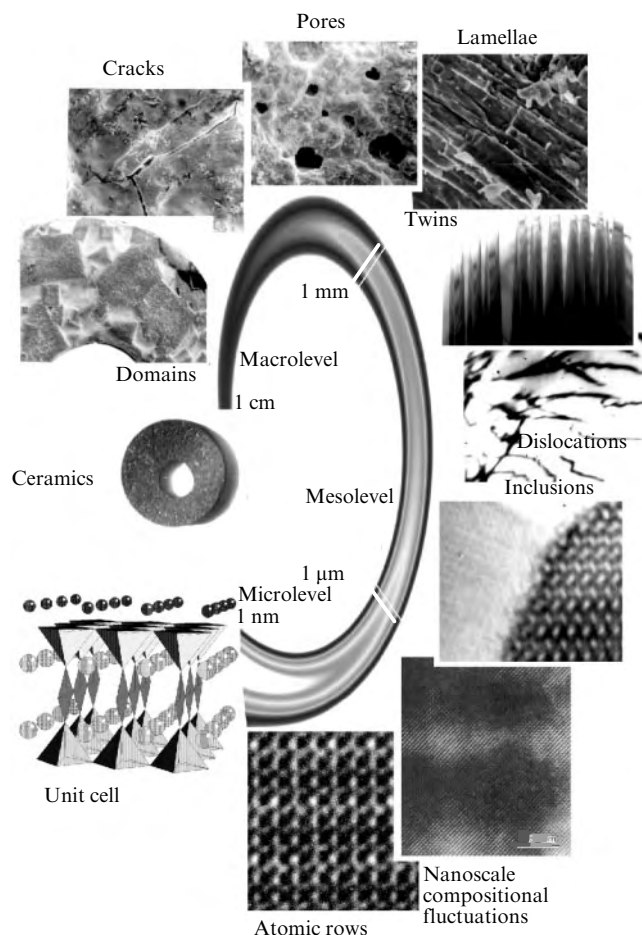


Figure 1. Structural levels of a material (bulk ceramics).

Macroscopic level (10^{-3} – 10^{-2} m): pores, cracks, domains, ceramics; mesoscopic level (10^{-6} – 10^{-3} m): inclusions, dislocations, twins, lamellae; microscopic level (10^{-10} – 10^{-6} m): the unit cell, atomic rows, nanoscale compositional fluctuations. Ceramics is the visual appearance of a sample of the high-temperature superconductor $\text{R}\text{Ba}_2\text{Cu}_3\text{O}_x$; domains are macroscopic pseudo-single-crystal regions of the superconductor; cracks are macroscopic cracks developed as a result of thermal shock; pores are channels formed as a result of exchange of the superconductor matrix with oxygen from the gaseous atmosphere during the melting–crystallisation process; lamellae are intergrown plate-like crystallites; twins are defects formed as a result of oxidation of the superconductor; dislocations are a network of dislocations; inclusions are associated with boundaries between the particle of the normal phase (Y_2BaCuO_5) and the superconducting matrix; nanoscale compositional fluctuations are microscopic inhomogeneities of the chemical composition of the superconductor; atomic rows are the rows of atoms constituting the unit cell of the crystal along a specified direction; and the unit cell is a fragment of the crystal structure.

forming components. However, even in these cases there are basic obstacles associated with the incongruence of virtually all multi-component systems (different compositions of the coexisting phases).^{16,17} Hence one should carry out thorough studies of phase equilibria and use equilibrium or quasi-equilibrium processes. The field of application of such processes is of crucial importance but limited to the growth of perfect single crystals from solutions and melts¹⁸ and the preparation of thin films by the chemical vapour deposition technique.¹⁹

Another approach, which seems to be the simplest one, involves the use of individual oxides or salts of oxygen-containing acids as precursors. Mixtures of these compounds are transformed into the target product as a result of solid-phase reactions.¹³ For

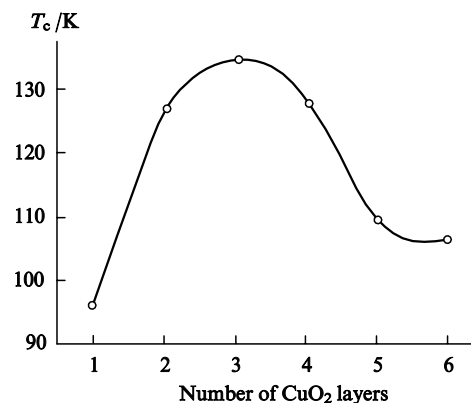
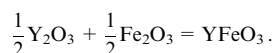


Figure 2. Superconducting transition temperatures (critical temperatures) of cuprates $\text{HgBa}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{2n+2+x}$ plotted vs. the number of CuO_2 layers.¹⁵

instance, magnetic ceramics based on yttrium orthoferrite are synthesised by the reaction



The small driving force of this and similar reactions ($-\Delta G_{1273\text{K}}^\circ \approx 20$ – 30 kJ mol^{−1}) and low solid-phase diffusion coefficients ($D < 10^{-12}$ cm² s^{−1}) preclude preparation of single-phase chemically complex oxides and the more so highly homogeneous products. Diffusion limitations are usually eliminated by using intermediate grinding levels (degrees of mixing) or by increasing the reaction temperature; however, both methods give rise to some additional difficulties. These are uncontrollable contamination of the product with particles of the abraded container in the former case and evaporation of the most readily volatile oxide components (*e.g.*, ZnO and alkali metal hydroxides), dissociation of readily reducible oxides (CuO , Fe_2O_3) and formation of non-stoichiometric (first of all, with respect to oxygen) complex phases of uncontrollable composition in the latter case.²⁰

The driving forces of solid-phase processes can be not only the chemical potential gradient, as in the case of the reaction of yttrium orthoferrite formation

$$\Delta G^\circ = \Delta \mu^\circ = \frac{1}{2} \Delta \mu_{\text{Y}_2\text{O}_3} + \frac{1}{2} \Delta \mu_{\text{Fe}_2\text{O}_3}$$

but also the temperature and pressure gradients (for oxides, the gradient of the partial pressure of oxygen is most often used), as well as the mechanical strain (in compaction and sintering of ceramic powders) or electrochemical potential gradients (in solid-phase galvanic cells). Often, these forces exhibit synergistic effects. For instance, intense sonication of heterophase systems gives rise to cavitation due to the simultaneous appearance of very large temperature and pressure gradients and mechanical strain.²¹

Nonequilibrium processes can occur in both isolated (or closed) and open systems, which differ from one another in character of response to external conditions and in evolution pattern. For any system, the total change in entropy can be written as the sum

$$dS = d_e S + d_i S,$$

where $d_e S$ is the entropy change due to exchange with the environment and $d_i S$ is the entropy change within the system under study (for the nonequilibrium state, this term is always positive).

For an isolated system (no exchange of matter and energy with the environment), one has $d_e S = 0$ and $dS = d_i S > 0$. Hence, the spontaneity of a process in the isolated system is governed by the trend towards an increase in the system's entropy, which reaches

its maximum value in the equilibrium state. In other words, the evolution of an isolated system causes the disappearance of the reasons that gave rise to the evolution.

Irreversible processes in isolated systems include mixing, interdiffusion (in the case of, *e.g.*, diffusion welding) and poisoning of ultrapure substances. Strictly speaking, perfectly isolated systems are a kind of idealisation, so we can deal with a certain extent of approximation in such systems.

If isolated systems can exchange energy with the environment (no mass transfer), the spontaneity of processes in such systems is governed by the trend towards a decrease in the Gibbs free energy

$$\Delta G = \Delta H - T\Delta S < 0.$$

For this relationship to hold, the entropy contribution, $T\Delta S$, must be larger than the enthalpy term ΔH . This means that raising the temperature of any isolated system from 0 K causes thermodynamically unavoidable defect formation processes involving different types of disordering^{22,23} and the appearance of non-stoichiometry in binary and more complex crystals with mainly ionic bonding.²⁴ Here, the source of the increase in entropy is of no concern: it can be the free surface, dislocations or point defects. Depending on particular experimental conditions, the growing crystal acquires those defects that provide a maximum increase in entropy at the lowest energy expenditure.

For instance, hematite $\alpha\text{-Fe}_2\text{O}_3$ dissociates to give a black substance, magnetite ($\text{Fe}_3\text{O}_{4+x}$), on heating to 1300 °C in air. This transformation is due to a substantial increase in entropy owing to structural (cation vacancies) and electronic disorder intrinsic in magnetite. However, the undesired dissociation can be inhibited by adding titania to hematite. The lattice of the iron titanate (or titanium ferrite) thus obtained can be so easily disordered on heating (in this case, ΔG decreases) that dissociation becomes thermodynamically unfavourable.

Being guided by their intuition, materials scientists have long employed the method of chemical and structural complication of materials in order to improve their chemical stability and mechanical strength. Based on the aforesaid, it becomes understandable why sintering of highly pure polycrystalline alumina does not result in transparent ceramics irrespective of the duration of heating. The reason is that internal pores, intercrystallite boundaries and dislocations are a source of the disorder, which provides a minimum value of the Gibbs free energy. However, transparent yttria-based ceramics were prepared by doping Y_2O_3 with zirconia and thus producing heterovalent defects (the sources of increased entropy). Doping causes formation of a structure with high concentration of point defects (the source of additional disordering).¹⁴

Taking into account the systems' trend towards a minimum Gibbs free energy and using the equivalence principle of entropy sources, it is an easy matter to understand why a perfect single crystal is thermodynamically unstable and spontaneously tends to acquire defects (formation of dislocations, adsorption of impurity atoms from the environment) on heating provided that no defect structure relevant to the operating characteristics of the material was designed artificially. Clearly, the higher the quality of a single crystal, the more pronounced its ability to spontaneously develop dislocations, form domain structures and adsorb impurity atoms.

Based on the above-mentioned considerations, one can explain such seemingly paradoxical phenomena as an increase in the rates of solid-phase reactions in the presence of a chemically inert component or a decrease in the very small thermal expansion coefficient of quartz upon doping with titania.

An abnormally large jumpwise increase in entropy is observed in some salts and salt-like systems due to a polymorphous transformation giving rise to high ionic conductivity. Noteworthy is that the entropy jump accompanying the solid-phase transformation is comparable with and sometimes greater than the change in entropy upon melting of the crystal. For instance, the transformation of Li_2SO_4 into the highly conducting α -modification at 850 K is accompanied by a jumpwise increase in entropy

$\Delta S = 31.9 \text{ J (mol K)}^{-1}$ [*cf.* $\Delta S = 6.7 \text{ J (mol K)}^{-1}$ for melting of Li_2SO_4 at 1130 K]. The substantial increase in entropy is associated with disordering of one sublattice in the crystal structure, which goes to the 'quasi-liquid' state.²⁵

Table 1 lists the changes in entropy upon polymorphous transformations and melting of some binary crystals that are used as solid electrolytes or electronic-ionic conductors.

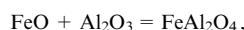
Table 1. Change in entropy upon polymorphous transformations and melting of some crystals.

Crystal	T_{tr}/K	$\Delta S_{\text{tr}}/\text{J (mol K)}^{-1}$	T_{m}/K	$\Delta S_{\text{m}}/\text{J (mol K)}^{-1}$
AgI	419	14.5	830	11.3
Ag_2S	452	9.3	1115	12.6
BaCl_2	1193	14.4	1233	13.3
LuF_3	1230	20.4	1457	20.8
YF_3	1350	24.0	1428	19.6

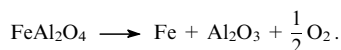
Chemically complex crystals (*e.g.*, ferrites, aluminates, manganites and cuprates) having two or more cation sublattices often exhibit the so-called antistructural disorder on heating. In binary crystals this is possible if the atoms of the constituent elements have similar characteristics (Cu-Sn bronzes). The existence of antistructural disorder in superconducting cuprates was proved taking $\text{Nd}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_7$ ('123' phase) as an example. In this compound, mutual substitution in the Nd and Ba positions can occur despite different stable oxidation states of these elements.^{26,27}

III. Conservative and dissipative self-organisation

As the temperature of an equilibrium or near equilibrium isolated system decreases, some ordering processes called conservative self-organisation²⁸ occur spontaneously. Though the term 'conservative self-organisation' was introduced in connection with the development of supramolecular inorganic chemistry, it has a much broader sense and covers many physical phenomena, such as melt or solution crystallisation, re-crystallisation upon sintering in polycrystalline systems, martensite transformations, spinodal decomposition and formation of magnetic or ferroelectric domains on cooling of the corresponding materials. Conservative self-organisation can also occur during the solid-phase interaction between, *e.g.*, wüstite and corundum in the reaction



which is accompanied by a large decrease in entropy, $\Delta S = -17 \text{ J (mol K)}^{-1}$. However, this reaction is irreversible, since iron aluminate dissociates at high temperatures by the reaction



Supramolecular chemistry has two terms, static self-assembly²⁸ and strict self-assembly,²⁹ for the ordering processes in isolated systems, which proceed towards minimisation of the Gibbs free energy. Such processes undoubtedly include ion hydration, complexation, clustering and formation of molecular crystals through the van der Waals forces.^{28–32}

A classical example of static self-assembly in biology is provided by the self-assembly of a DNA double helix. The change in the Gibbs free energy for this process is illustrated in Fig. 3. Other examples of static self-assembly of supramolecular structures can be found in the literature.^{33–42}

The open systems can exchange matter and energy with the environment. In essence, they provide a case for persistently nonequilibrium systems. The evolution of open systems can be characterised in terms of entropy production (dS_i/dt) and entropy

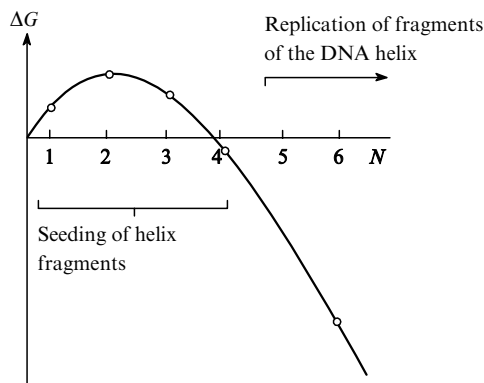


Figure 3. Change in the Gibbs free energy during self-assembly of a DNA double helix.

flow (dS_e/dt). If the negative entropy flow (entropy release) towards the environment exceeds the entropy production in the system, the total change in the entropy of the open system is negative

$$\frac{dS}{dt} = \frac{dS_e}{dt} + \frac{dS_i}{dt} < 0$$

or, which is the same, the negative entropy (negentropy) of the system increases. As the negentropy exceeds a certain critical value, the formation of new structures (dissipative structures after Nikolis and Prigogine⁴³) in the system becomes possible. Dissipative structures are formed due to co-operative interactions between microscopic building blocks in a strongly nonequilibrium macrosystem. The ability of the macrosystem to form various structures is sometimes characterised by exergy (the maximum work, which can be produced by the system on the pathway towards the equilibrium state).⁴⁴

Spontaneous formation and evolution of complex ordered structures in the open systems is called self-organisation while the theory of self-organisation is called synergetics. Having its origin in cybernetics, nonlinear optics and nonequilibrium thermodynamics, synergetics has a strong impact upon the development of modern physics, chemistry, biology, earth sciences, economics, as well as social and political sciences. Synergetics has its own specific lexicon, which includes such concepts as bifurcation, critical state, dissipative structures, feedback, autocatalysis, hysteresis, attractors, scaling, topochemical memory and stochastic and deterministic chaos. Of course, our interest in both synergetics and self-organisation phenomena is limited to their utility in designing advanced materials and technologies.[†]

Currently, several thousands of communications concerning the use of self-organisation models in solving materials science and technological problems are available. Most of them have been reported during the last five or six years. But admittedly, the equilibrium thermodynamics methodology is still at the frontiers of materials science, especially when one deals with problems concerning high-temperature processes, though most of them occur in strongly nonequilibrium open systems rather than isolated ones. Of course, linear, or additive, thinking is more customary; however, the future may undoubtedly lie with nonlinear models and systems including those used in the field of materials science.⁴⁵

The evolution of an open system can be illustrated by the dependence of the generalised flux I (mass, heat, *etc.*) on the

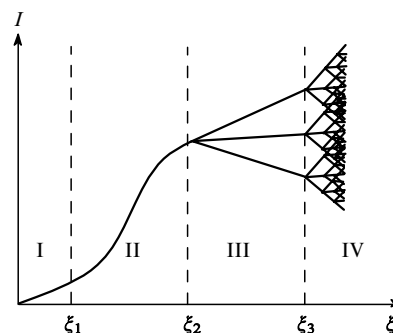


Figure 4. Generalised flux, I , as function of the driving force, ξ , of a process (for details, see text).

driving force of the process ξ (Fig. 4). The excess Gibbs free energy can act as the driving force in a chemical system. At $\xi = 0$, the system is in the equilibrium state. At small deviations from the equilibrium state (region I), the flux is a linear function of the driving force and the system behaves deterministically, which can be described by the Onsager reciprocal relation. In region II, the $I = f(\xi)$ dependence becomes nonlinear, while transition to region III at a certain critical value $\xi = \xi_2$ is associated with a bifurcation (appearance of several possible pathways of the system's evolution instead of one stable evolution pattern of the process). Here, the system chooses the evolution route by itself but the choice is fluctuation driven.⁴⁶ Going to region IV means the appearance of the so-called deterministic or turbulent chaos, which is characterised by an extremely complex structure and is fundamentally different from the stochastic chaos characterising the system in the equilibrium state.

It is possible to formulate at least three necessary (but not always sufficient) conditions for self-organisation in the open systems, resulting in dissipative structures:

- a deviation from the equilibrium state must exceed a certain critical value (*i.e.*, the system must be in the bifurcation region);
- the system's volume must be large enough and, in particular, be larger than a certain critical volume in which a necessary number of undamped fluctuations occur; the interaction between these fluctuations creates ordering in the system; and
- the presence of a positive feedback.

At small deviations from the equilibrium state, the system is on the so-called thermodynamic branch of its evolution pathway and its behaviour is a combination of many independent random events. Assuming that such behaviour can be characterised by a certain 'statistically averaged' parameter $\bar{X}_0$ (Fig. 5a), one gets that, in accord with the law of large numbers, for a sufficiently large system the deviations from the average value $\bar{X}_0$ are small and normally distributed with the probability distribution $P(X)$. In this sense the behaviour of the system can be treated as deterministic.

As the driving force increases due to the nonlinear behaviour of the system, any possible fluctuations are not damped and, hence, become equiprobable. Therefore, the $P(X)$ distribution near the bifurcation point becomes flattened (Fig. 5b). A feature of this state of the system is that any fluctuation can manifest itself on the macroscopic scale, *i.e.*, extend to a rather large volume and be undamped for an infinitely long time. At a critical point corresponding to sudden predominance of a certain fluctuation, a minor increase in the driving force of the process is sufficient for the system to make the ultimate choice of a new thermodynamic branch between several alternative branches. Thus, after passing the bifurcation point the distribution $P(X)$ becomes multimodal (Fig. 5c), while the choice of the new average value X (new

[†] To this end, the author of this review initiated the foundation of the Laboratory of Chemical Synergetics at the N S Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, in 1994.

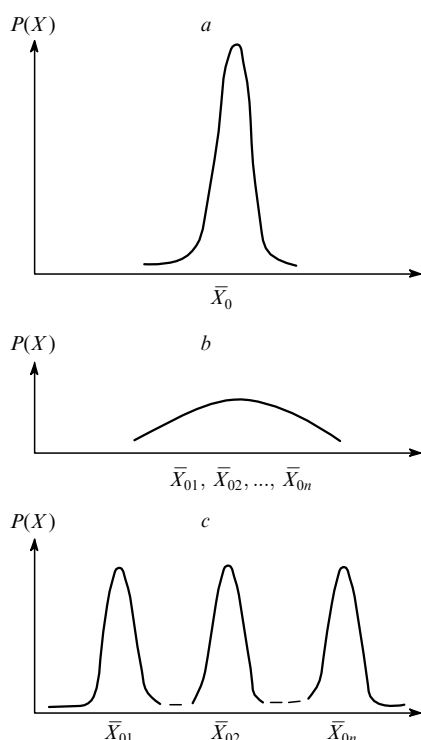


Figure 5. Probability distribution, $P(X)$, at different deviations of the system from the equilibrium state (for details, see text).

thermodynamic branch) from several possible values ($\bar{X}_{01}, \bar{X}_{02}, \dots, \bar{X}_{0n}$) occurs stochastically.

In real systems, such a behaviour can be due to the fact that local nonlinear processes (e.g., an autocatalytic reaction in a small volume or formation of a new solid phase with an ordered crystal lattice) in these systems coexist with the transport (diffusion) processes responsible for different types of exchange between adjacent local volume elements. Were chemical processes to occur in the adjacent local volume elements, they will tend to make the system less spatially homogeneous, while the diffusion processes act in the opposite direction, towards a maximum spatial homogeneity of the system. Clearly, uncorrelated behaviour of the local volume elements (hindered diffusion or no diffusion) results in a random set of combinations of local states. In the case of infinitely fast diffusion (zero response time of the cells) fluctuations are instantaneously damped and disappear. Both limiting cases do not give rise to spatial ordering.

At the same time, both diffusion and local chemical interactions are those essentially nonlinear processes, which are responsible for nonlinear behaviour of the entire system. At a large deviation from the equilibrium state, it can happen that these processes (different in their nature) will have similar characteristic times τ_d and τ_r . In this case both the frequency of chemical fluctuations, $\sim 1/\tau_r$, and the probability of their extension to the adjacent volume elements (relaxation within a given volume element), $\sim 1/\tau_d$, are high.

Thus, under particular conditions the complex systems can go to a certain 'critical state' in which the entire system behaves in a concerted way and chooses a new evolution pathway stochastically.

There is a variety of dissipative structures, e.g.,

- spatially nonuniform structures;
- temporal periodic structures (self-sustained oscillations);
- spatio-temporal periodic structures (waves);
- coexistence of several stationary states (bi- and tristability);
- structures with scaling properties (spatial self-similarity — fractals); and
- chaotic dynamic structures.

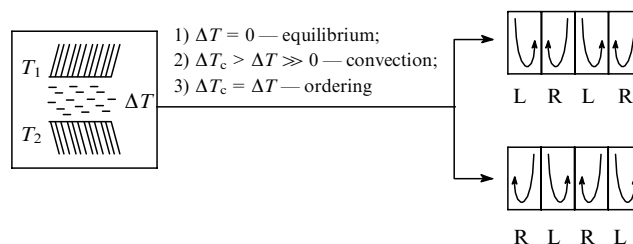
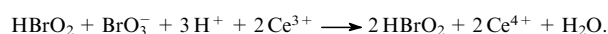


Figure 6. Formation of Benard cells on increasing the temperature gradient.

Dissipative self-organisation can be exemplified by the formation of Benard cells (Fig. 6). As the temperature gradient ($\Delta T = T_2 - T_1$) between horizontal walls of a vessel containing a liquid increases and reaches a critical value corresponding to the bifurcation point, ΔT_c , the type of heat transfer process is changed from convection (chaotic molecular motion similar to Brownian motion) to correlated molecular motion in microscopic fluid cells. The molecular motion occurs in a concerted way by clockwise (R) or counterclockwise (L) rotation. Formation of one of the two dissipative structures shown in the right part of Fig. 6 occurs as a random event as a result of the system's choice. A further increase in ΔT causes destruction of the cell structure and the appearance of turbulent chaos.

This example shows that diffusion, viscous flow and heat transfer, which disorder simple linear systems, can be 'architects of ordering' in nonlinear systems. Numerous examples of dissipative self-organisation in various open systems have been considered in monographs.^{47–49} Pioneering observations of self-organisation in physicochemical systems date back to 1828. At that time, Fechner discovered spontaneous oscillations of the electrochemical potential of iron in nitric acid as a result of alternating passivation and depassivation processes (Lillie wires).⁵⁰ The best example of self-organisation in homogeneous chemical systems is undoubtedly provided by the Belousov–Zhabotinsky redox reaction, i.e., oxidation of citric (or malonic) acid by potassium bromate in the presence of cerium(III) sulfate.^{51,52} This is a very complicated reaction, though visually it appears as a simple oscillating process involving a change in the colour of a solution. According to calculations, changes in the rate constants for the reaction stages by infinitesimal fractions of per cent can cause radical changes in the character of the process at the microlevel. However, under any conditions the most important is the self-oscillation stage, which can be tentatively described by the following equation:



Interestingly, pure temporal structures (self-sustained oscillations) can undergo transformation into spatio-temporal ones after some time.

It was Ostwald who contributed largely to the understanding of the energetics of oscillating chemical reactions.^{53–55} He generalised extensive experimental information accumulated by the early 20th century, including the data on famous Liesegang rings, dissolution of chromium in acids with oscillating character of H_2 liberation and on periodic decomposition of H_2O_2 on a mercury surface. Some monographs^{56–58} provide a rich source of information on recent studies of oscillating reactions. Returning to the problems of materials science, it should be noted that such important properties as the plasticity and yield of materials cannot be adequately described in the framework of the equilibrium methodology. Fracture of a mechanically loaded material is always preceded by ordering of planar defects and formation of dislocations in the region to be fractured. For instance, applying a periodic load to a metal rod causes formation of dislocation packets, which are ordered in some way.⁵⁹

Mechanical fracture of a material can be treated as a consequence of a critical transition (bifurcation) from the elastic

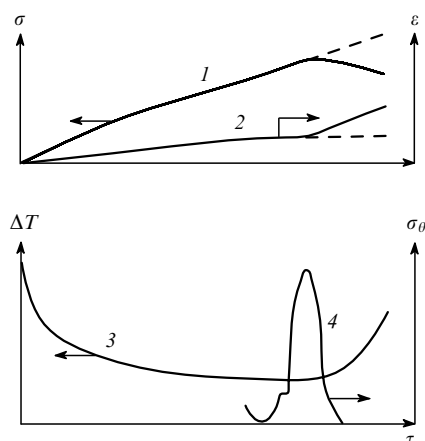


Figure 7. Strain (1), stress (2), temperature (3) and acoustic radiating capacity (4) of a mechanically loaded sample as functions of time.

deformation to the plastic deformation regime under the action of a rather heavy external load acting as the driving force of the process. Figure 7 presents the plots of the strain, stress, temperature and acoustic radiating capacity of a mechanically loaded sample constructed vs. time. Extrema or singularities in all the plots correspond to the critical point σ_0 . It should be noted that the maximum value of the acoustic radiating capacity at the critical point corresponds to ordering of defects in the sample. Moving the bifurcation point towards the heavy load region favours improvement of a material's strength. For instance, it was found that the doping of metals with zirconia causes a shift of the point corresponding to transition from elastic to plastic deformation due to the fact that ZrO_2 experiences a structural phase transition accompanied by heat release under load.⁶⁰

Of considerable interest are chemical vapour deposition (CVD) processes under strongly nonequilibrium conditions. Figure 8 presents micrographs of ordered structures formed using the CVD technique at high gas flow rates.⁶¹

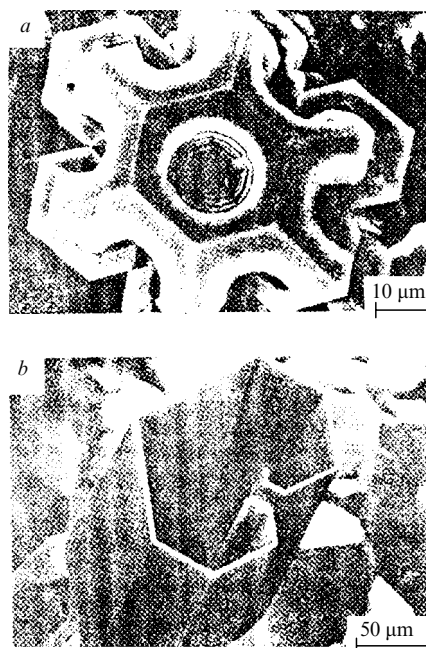


Figure 8. Micrographs of ordered structures formed using the CVD technique at high gas flow rates. Crystals: Cr_3Si (a) and CrB_2 (b).

Self-organisation processes also include a class of phenomena accompanying shock-compression induced crystallisation of metastable solid phases. Researchers at the I M Frantsevich Institute of Materials Science (National Academy of Sciences of Ukraine, Kiev) elaborated some methods for creation of strongly nonequilibrium conditions during the formation and quenching of metastable phases.⁶² Crystallisation in the presence of strong temperature and pressure gradients allowed the obtention of crystalline modifications with lower entropy compared to the samples synthesised under nearly equilibrium conditions.

Solid-phase crystallisation of graphite-like boron nitride $(\text{BN})_g$ under supercritical regime of energy supply causes formation of a new modification, wurtzite-like boron nitride $(\text{BN})_{w-II}$.^{63, 64} The entropy of the newly prepared compound is lower than that of $(\text{BN})_{w-I}$,⁶⁵ which is formed at lower energy supply rates.

Nonequilibrium crystallisation of diamond from the concentrated vapour phase and plasma is accompanied by unusual phenomena. Synthesis at 4500 °C gives a fine-crystalline cubic modification of diamond (X-ray phase analysis data), which is nearly free from microscopic distortions. Carrying out crystallisation at 4300 °C (this temperature corresponds to the triple point in the phase diagram) leads to a crystalline diamond-like phase containing a large number of microdistortions.⁶⁶ Hence, synthesis under strongly nonequilibrium conditions permits a structure with less defects to be obtained.

Most likely, formation of 'whiskers' (needle-shaped single-crystals of superconducting bismuth-containing cuprates with $T_c = 100$ K), which grow on slow cooling of the starting amorphous phase $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$ in an air stream (Fig. 9)⁶⁷ is also governed by self-organisation.



Figure 9. Whiskers of bismuth-containing superconducting cuprates formed on slow cooling of the starting amorphous phase $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_x$.

IV. Optimum organisation of reaction zone during synthesis of materials

In all stages of its evolution from precursor to the end product, any system exists under thermodynamically nonequilibrium conditions and can be described by some bifurcation pattern with one

or several bifurcation points corresponding to the intermediate phase transformations. It is convenient to consider the evolution of such a system using a model of deterministic chaos.^{68,69} This model implies that

- the evolution of a system makes its behaviour increasingly less predictable (*i.e.*, irreproducible);
- the higher the chemical or structural complexity of the system, the shorter the time necessary for transition to the region of indeterministic behaviour; and
- the longer the duration of the process, the more severe the requirements on the initial state of the system (*i.e.*, precursor).

To organise the reaction zone in an optimum manner, one should take into account the following.

1. The higher the complexity of the system, the more indeterministic its behaviour and less reproducible the initial state of the precursor. In this case 'complexity' means not only the chemical and phase compositions but also precursor's reactivity, which is determined by the chemical and heat treatment aspects of its prehistory ('topochemical memory' effect⁷⁰). In this connection the best precursors are provided by compounds with a molecular type of bonding,⁷¹ coordination compounds,⁷² solid solutions of double salts (shoenites or alms which are used in, *e.g.*, the synthesis of ferrites⁷³) and salt-like products of cryochemical synthesis.⁷⁴

2. The extent to which transformations from precursors to target products deviate from the equilibrium state is in essence the driving force of solid-phase interactions. It affects not only the reaction rates but also their mechanisms and can have both positive and negative effects on the formation of the target product. In particular, the highest homologue in the Bi–Pb–Sr–Ca–Cu–O system, $(\text{Bi,Pb})_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+\delta}$, is usually prepared from Bi_2O_3 , CuO , PbCO_3 , SrCO_3 and CaCO_3 (a mechanical mixture of these precursors is used). If such a mixture is heated in a gaseous atmosphere at a reduced total pressure, the lead, strontium and calcium oxides are formed under strongly non-equilibrium conditions. Being highly reactive, these oxides readily react with bismuth and copper oxides, thus forming a number of intermediate products simultaneously. Transformation of the products into the highest homologue, $\text{Bi}_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+\delta}$ ('2223' phase) is a very complicated task and is usually completed only after heating over a period of several days.⁷⁵ Decomposition of carbonates at a standard pressure (1 atm) occurs much more slowly, and it is possible to inhibit formation of some intermediates, though in this case low diffusion mobility of cations hampers the formation of the end product ('2223' phase) during reasonably short time intervals. A possible way out is to use efficient methods of activation of the reaction mixture including ultrafine grinding,⁷⁶ sonication^{77,78} or microwave irradiation.^{79–81}

3. Duration of the evolution from precursors to end product. The shorter the evolution, the more easily the deterministic behaviour of the system can be provided and a product with reproducible properties can be obtained. The question arises as to how to shorten the duration of the process taking into account that operation at elevated temperatures leads to bifurcation and to formation of such intermediate products whose crystallisation precludes shortening of the duration of the synthesis. In this case, the use of other methods for activation of the reaction mixture (and, especially, their combination) seems to be more efficient than heating. However, only an empirical approach, *e.g.*, combinatorial chemistry,⁸² provides the best way to optimise conditions for treatment of the system.

The efficiency of ultrafast synergistic effects can be clearly exemplified by sintering of ultradispersed ceramic powders of oxide–oxide composites $\text{Al}_2\text{O}_3\text{--Y}_3\text{Al}_5\text{O}_{12}$ using a press that furnished an increase in pressure on passing pulsed electric current (up to 2000 A) with millisecond-range pulse durations. Sintering was completed after several minutes, resulting in ceramics with rather high density and very narrow crystallite size distribution centred at the size typical of the precursor powder.⁸³

4. Bifurcation transformations, which occur during the evolution of a system and manifest themselves as formation of intermediate decomposition products in the reaction zone, should be eliminated, whenever possible. This is all the more important in those cases where such products are formed as readily crystallisable phases characterised by low diffusion mobility of components. This is possible if the phase diagram allows decomposition of the system into some components, which then interact to give the target product. 'Linear' synthesis of superconducting cuprates from copper-free precursors and copper oxide provides a good example of the efficiency of this technique. It was found that the phases $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ and $\text{Bi}_{1.7}\text{Pb}_{0.4}\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+x}$ can be efficiently prepared using mechanical mixtures of CuO with $\text{Bi}_2\text{Sr}_2\text{CaO}_6$ (Fig. 10) and $\text{Bi}_{1.7}\text{Pb}_{0.4}\text{Sr}_2\text{Ca}_2\text{O}_{7.35}$, respectively.^{75,84}

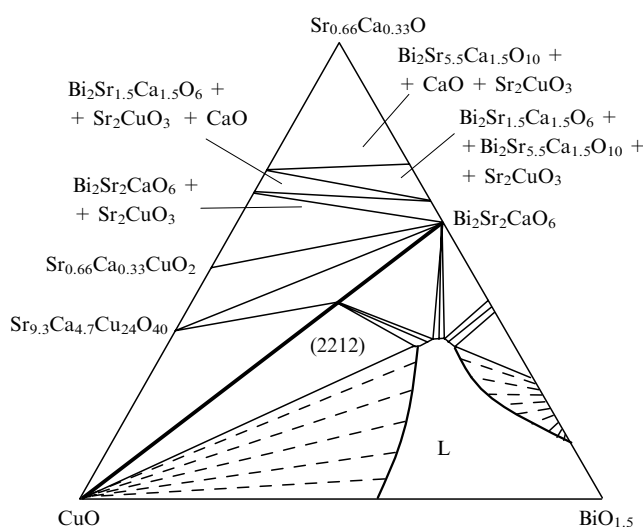


Figure 10. Decomposition of quasi-ternary system $\text{CuO--BiO}_{1.5}\text{--Sr}_{0.66}\text{Ca}_{0.33}\text{O}$ along the $\text{CuO--Sr}_2\text{CaBi}_2\text{O}_6$ direction.⁷⁵

In principle, the reaction zone can be organised in such a way that both the precursor and intermediate reaction products lying on the pathway of the figurative point of the system during its evolution are X-ray amorphous and, hence, the formation of a crystalline end product is the first bifurcation. Particular methods for practical implementation of such a process depend on the target oxide products or materials (both of them are chemically complex systems) and, in particular, on the differences between the thermodynamic parameters of the constituent oxides. If these differences are rather large (the most often case), amorphisation of the precursor and intermediate decomposition products is achieved by quenching oxide melts (*e.g.*, preparation of whiskers⁸⁵) or by freezing of aqueous salt solutions of the material-forming elements (sulfates, nitrates, acetates) followed by thermal decomposition under optimum conditions.⁷⁴

5. Deterministic evolution of a system can be organised using templates (including seeds) in the form of perfect crystals of the oxide product (bulk ceramics) or under conditions that provide epitaxial film growth (substrate with optimally matched structural parameters). An example of a perfect substrate for the growth of perfect high-temperature superconducting films is provided by NdGdO_3 single crystals whose parameters are close to those of films, including the thermal expansion coefficients.

An original method for preparation of homogeneous microporous SiO_2 , TiO_2 and ZrO_2 ceramics has been reported.⁸⁶ The technique involves an oil-in-water emulsion and is based on the use of the interface between monodispersed oil droplets and the water phase as a template (Fig. 11).

6. Intense suppression of chaos by interaction based on a feedback requires thorough knowledge of chaotic behaviour of

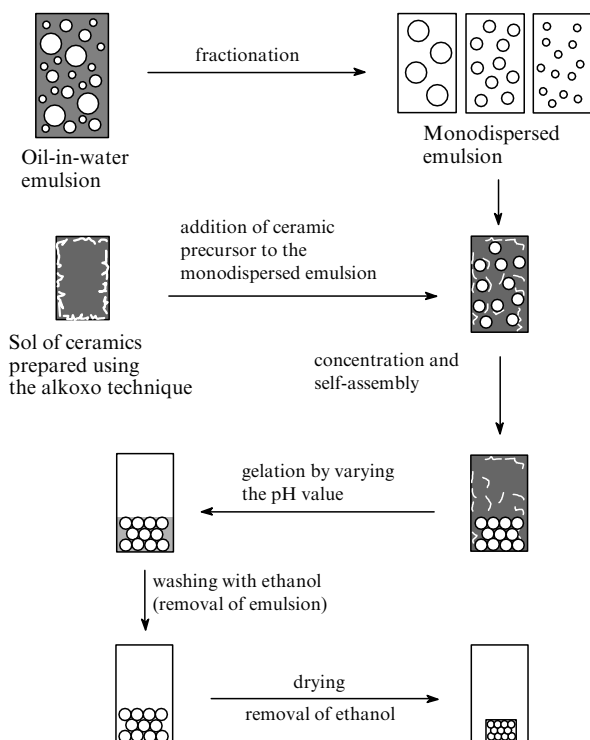


Figure 11. Scheme of formation of homogeneous microporous SiO_2 , TiO_2 or ZrO_2 ceramics involving an oil-in-water emulsion and based on the use of the interface between monodispersed oil droplets and the water phase as a template.

the system. This method for control of chaos involves both computer simulation and experimental studies of topochemical reactions proceeding in the kinetic, diffusion or mixed regimes.

Controlled suppression of chaos can be achieved using different methods including directed chemical complication of the system. This can be exemplified by the effect of rare-earth element (REE) ions, which partially replace yttrium in the superconducting cuprate $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$, upon melt crystallisation of this compound.⁸⁷ For instance, doping with Yb^{3+} ions results in the formation of giant ribbed crystals of the BaCuO_2 phase, which cover nearly the whole surface of the sample. Doping with Eu^{3+} ions causes the formation of rather large square-shaped surface crystallites, while Nd^{3+} -doped samples are comprised of small plate-like crystallites of the $(\text{R},\text{Y})\text{Ba}_2\text{Cu}_3\text{O}_{7-x}$ phase, which form a fine-grained ceramic structure. Finally, studies of both blank samples and samples doped with Ho^{3+} ions revealed the presence of two types of crystallite, viz., 'cubic' crystallites of the superconducting phase and 'pyramidal' barium cuprate crystallites.

As can be seen in Fig. 12, doping with Nd^{3+} , Eu^{3+} and Gd^{3+} should favour retention of homogeneity of the system and formation of high-temperature superconducting material with strongly coupled grains. This is due to the fact that the crystallisation centres of the superconducting phase are formed in the 'stable' crystallisation branch of $(\text{R},\text{Y})\text{Ba}_2\text{Cu}_3\text{O}_{7-x}$ solid solutions (line 2), which is characterised by higher temperatures than the crystallisation temperature of $\text{R}_x\text{Ba}_{1-x}\text{CuO}_{2+x}$ (line 4).

No crystallisation centres of the '123' phase occur upon doping of the system with Yb^{3+} ions. As a result, barium cuprate is formed in the 'unstable' crystallisation branch of solid solutions (line 3) in the melt region of the system, which precedes crystallisation of the superconducting phase.

In the case of intermediate 'unstable' crystallisation of $(\text{Y},\text{Ho})\text{Ba}_2\text{Cu}_3\text{O}_{7-x}$ the process becomes very sensitive to particular experimental conditions.

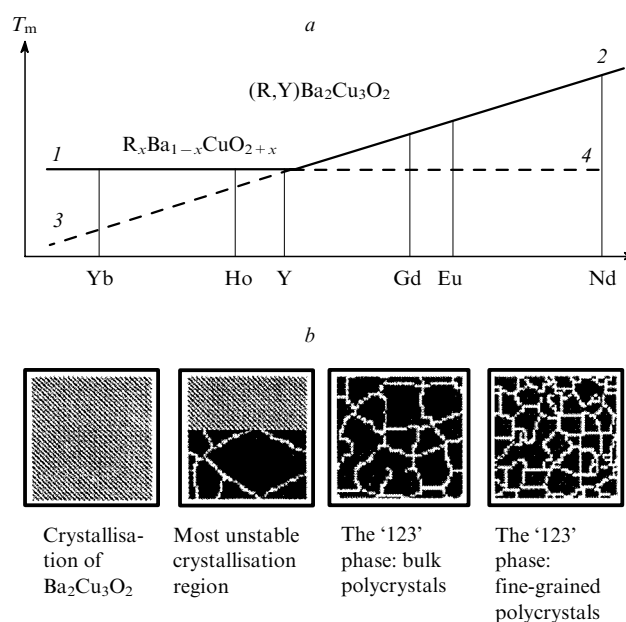


Figure 12. Crystallisation model of REE-doped yttrium-containing cuprates.

(a) Crystallisation temperatures of the ' $\text{R}_x\text{Ba}_{1-x}\text{CuO}_{2+x}$ ' and $(\text{R},\text{Y})\text{Ba}_2\text{Cu}_3\text{O}_2$ phases doped with different REE at constant dopant concentrations ($V_{\text{REE}}/V_{\text{Y}} = 0.1$): stable crystallisation branch of barium cuprate [$T_{\text{cr}(011)} \approx \text{const}$] (1), stable crystallisation branch of yttrium-barium cuprate [$T_{\text{cr}(123)} \neq \text{const}$] (2), unstable crystallisation branch of yttrium-barium cuprate [$T_{\text{cr}(011)} > T_{\text{cr}(123)}$] (3) and unstable crystallisation branch of barium cuprate [$T_{\text{cr}(011)} < T_{\text{cr}(123)}$] (4); (b) results of computer simulation of crystal morphology corresponding to real experiments.

This model was substantiated by the results of computer simulation of crystallisation. It was established that

- under certain critical conditions, local interactions in the complex system are responsible for the appearance of new interrelations determining transformation of the evolution pattern of the entire system into a self-organisation regime;

- depending on the initial state of a peritectic melt, its solidification can occur in different manners, thus causing the appearance of different crystallisation regions. Each of them corresponds to a specific morphology of polycrystalline finished material (target product). The most important condition for preparation of high-temperature superconducting materials with high current densities is to provide stable crystallisation of the superconducting phase by stabilising the nucleation process;

- preparation of high-temperature superconducting materials in the region of stable crystallisation of the superconducting phase requires the formation of a rather large number of seeds; if the seed lifetimes are longer than the mutual seed 'adjustment' time, the one and only process in the system is 'front-side' crystallisation followed by the formation of a material comprised of strongly coupled crystallites.

Based on the aforesaid, we can state that the nonlinear character of the evolution of processes in the open physicochemical systems complicates preparation of many chemically complex products and materials with reproducible compositions, structure and properties. This problem can be to some extent solved⁸⁸ by organising the reaction zone in an optimum manner. This includes:

- the use of highly homogeneous (better, molecularly bonded) precursors (alkoxides) or complex compounds in the form of solutions, melts, or vapours;

- treatment of precursors to provide preparation of X-ray amorphous intermediate states and formation of target crystalline products at lowest possible temperatures due to synergistic effects

of different forces (low pressure, intense grinding, sonication and microwave irradiation); and

— template synthesis or directed chemical complication of the system to ensure the preferred formation of the product with a prescribed structure.

V. Onset and suppression of chaos in metal corrosion processes

A number of communications concerning the conditions for onset and suppression of chaos in metal corrosion processes have been reported.^{89–91} Figure 13 presents a scheme of corrosion of metal M in an aqueous solution. The process is accompanied by the formation of two products, a metal hydroxide and a metal oxide. Let S_{OH} and S_O be the fractions of the metal surface covered by the hydroxide film and oxide film, respectively, and c_M be the concentration of metal ions in the solution. Then, the state of the system at any instant of time can be characterised by the position of the point in a three-dimensional phase space, *i.e.*, in the $S_{OH}-S_O-c_M$ coordinate system.

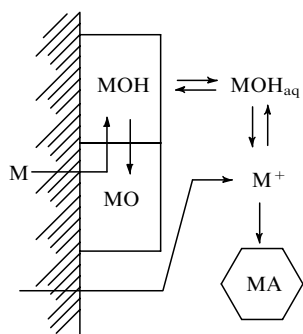


Figure 13. Corrosion scheme of metal M in aqueous solutions. Oxide film (MO), hydroxide film (MOH), dissolved hydroxide (MOH_{aq}), metal ions (M^+) and salt (MA).

The rate of change in each parameter can be calculated by solving the corresponding kinetic equations and plotting the trajectory of the motion of the figurative point based on the results obtained. Figure 14 presents a projection of this trajectory on the S_O-S_{OH} plane. As can be seen, after some time the trajectory represents an attractor of a rather complex shape. The question arises as to how to distinguish between the deterministic chaos and the pure stochastic process (the so-called stochastic chaos) based on experimental results. For instance, corrosion studies allow one to measure the corrosion current I at different time instants. The $I(t)$ plot (Fig. 15) is typical of random processes. Construction of the phase trajectory using these data requires the use of the return map method. The essence of the method is as follows: an appropriate time interval, τ , is chosen, corresponding to repetition of the height of corrosion current peaks, and then the phase trajectory is constructed in the $I(t)-I(t+\tau)$ coordinates. The shape of this trajectory (Fig. 16) indicates that the corrosion process is in some way deterministic. Though at first glance the corrosion current changes randomly during the process, the trajectory of the system in the correctly chosen phase space is a strange attractor. To inhibit corrosion, one should find certain conditions corresponding to degeneration of the system's attractor into a point. The results of suppression of the corrosion process using the return map technique are demonstrated in Fig. 17. The initial $S_O(t)$ dependence is shown in the left part, while the $S_O(t)$ plot after applying the suppressing signal

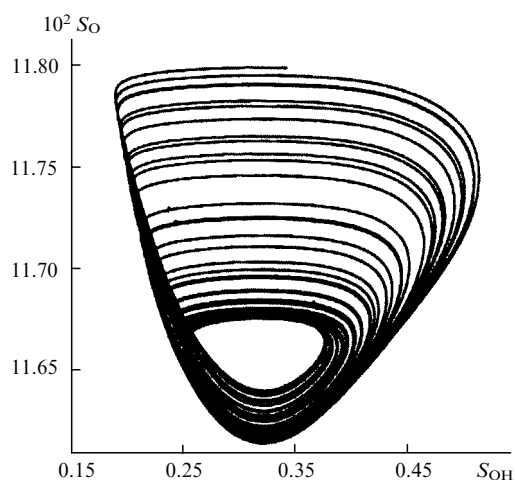


Figure 14. Phase trajectory of corrosion process (projection of the trajectory on the S_O-S_{OH} plane).

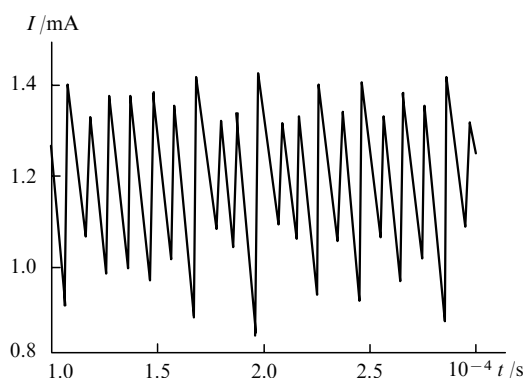


Figure 15. Experimental dependence of corrosion current, I , on time t .

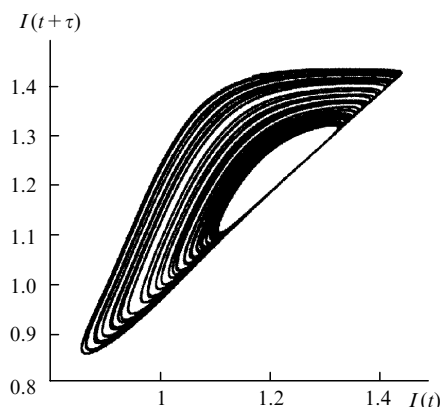


Figure 16. Attractor reconstructed from the experimental dependence $I(t)$ using the return map method (for details, see text).

(specially chosen voltage pulse) is presented in the central part; switching off the suppressing signal causes re-appearance of chaotic oscillations in the system (right part of Fig. 17), indicating that corrosion continues. By regularly applying such voltage pulses it is possible to achieve complete inhibition of corrosion.

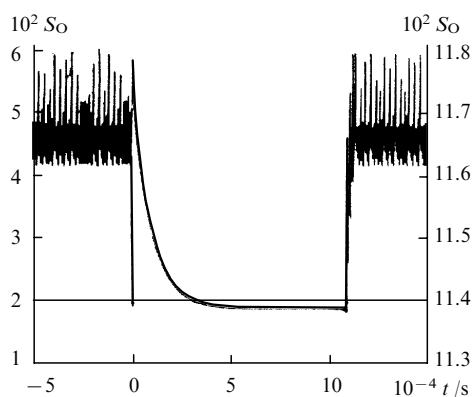


Figure 17. Suppression of chaotic oscillations during metal corrosion using special voltage pulses (for details, see text).

VI. Application of deterministic chaos models to poorly reproducible physicochemical processes

Chemistry of materials often deals with poorly reproducible solid-phase or heterophase processes. For instance, a yield of 25% is considered good in large-scale production of single crystals of many functional materials (ferrites, piezoelectrics). In the case of single crystals the (potentially) changeable (variable) parameters are the size, shape, composition, dislocation structure and some other, despite a high accuracy of control of the synthesis conditions. Some other examples of poorly reproducible processes can be found in the literature.^{91–93}

Traditionally, the dynamics of chaotic systems have been studied using time-series analysis, which involves observation of changes in a certain experimentally measured parameter. This approach allows determination of the type of system's behaviour (*e.g.*, chaotic one) and obtaining valuable information on the system's dynamics. However, specific features of solid-phase systems sometimes preclude measurements of characteristic dependences of their parameters on time (*e.g.*, for growth of single crystals). At the same time, it's quite an easy matter to obtain statistical data on the results of repeated experiments carried out under identical (within the limits of experimental error) conditions.

A procedure for determining fundamental characteristics of a chaotic system from statistical data obtained by repeated reproduction of experiments has been elaborated.⁹⁴ It was assumed that poor reproducibility of experimental results obtained under identical conditions is due to high sensitivity of the system's dynamics to minor changes in the starting parameters. The initial conditions for different experiments can be set to some finite accuracy, which is determined by the accuracy of the equipment used in the experiments. However, if the system under study behaves chaotically, small, experimentally undetectable, differences can have a strong effect on the overall result.

The model chaotic system was described by a differential equation of Duffing's oscillator⁹⁵

$$\frac{d^2x}{dt^2} + 0.05 \frac{dx}{dt} + x^3 = 7.5 \cos t,$$

which has a set of three phase variables, namely, the coordinate x , velocity dx/dt and time t .

Numerical integration of this equation was carried out by the fourth-order Runge–Kutta method. Randomly chosen initial conditions $x_0 = x$ ($t = 0$) were normally or uniformly distributed with different dispersions. All numerical experiments were carried out with the same initial velocities, namely, $dx/dt = 0$ at $t = 0$. Calculations were terminated after a rather long time

($t \geq 470$ arbitrary units) to ensure that the system's trajectory is the strange attractor.

Numerical experiments showed that the distribution of the end points obtained by integration at different initial conditions reflects only the attractor's structure and is independent of the distribution of initial conditions.

More detailed information was obtained by analysing the distributions of two (or more) independent parameters of the system. Fig. 18 *a* presents a correlation between the final values of the variables $\{x, dx/dt\}$ obtained after completion of calculations. In real experiments, the measured parameters can be functions of one or several phase variables. As can be seen, the final values obtained at $t = 470$ are distributed over the Poincaré cross-section of the strange attractor. The visual appearance of this cross-section is independent of the type and dispersion of initial conditions. It should be noted that exactly the same Poincaré cross-section can be obtained by applying a conventional time-series analysis procedure to the $\{x, dx/dt\}$ pair at times $470 + 2\pi n$, where $n = 1, 2, 3$ (Fig. 18 *b*).

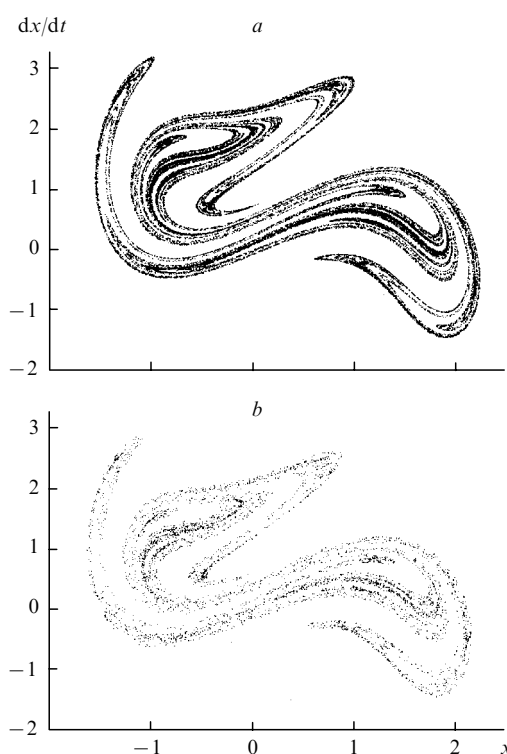


Figure 18. Poincaré cross-sections of Duffing's attractor, obtained from reproducibility experiments ($t = 470$, 30 000 points) (*a*) and using conventional time-series analysis ($t_n = 470 + 2\pi n$, 15 000 points) (*b*).

This approach can also be employed in reconstructing the attractor of the system under study. This requires knowledge of the number of dynamic variables. In the case of the Duffing oscillator, the third phase variable is the time t (see above). To reconstruct the attractor, a total of thirty-one Poincaré cross-sections were obtained at different times $t = 470 + 2\pi n/30$; the cross-section at $n = 0$ was equivalent to that obtained at $n = 30$. Each Poincaré cross-section contained a set of 2000 points obtained by numerical integration of Duffing's equation at normally distributed initial conditions. The three-dimensional image of the strange attractor is shown in Fig. 19. In the general case, reconstruction of the attractor of a poorly reproducible system requires that (i) as many parameters of the process under study as possible be measured to be deliberately larger than the number of phase variables; (ii) independent variables be chosen and (iii) a correlation between the independent variables be

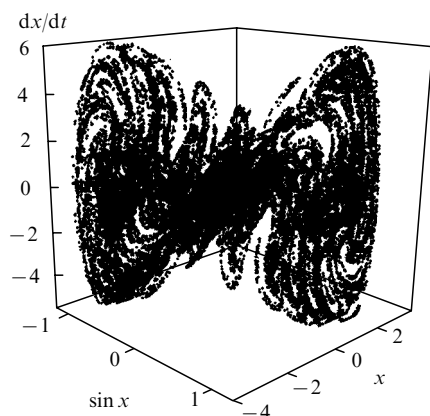


Figure 19. Three-dimensional image of the strange attractor of Duffing's oscillator in the $x - \sin x - dx/dt$ coordinates.

plotted. By virtue of the fact that the fundamental phase variables for the system are usually unknown, the shape of the reconstructed attractor can be distorted. This is also a standard situation for conventional reconstruction of an attractor using time-series analysis.

Thus, even by measuring a single parameter of the system one can say whether or not the poor reproducibility is due to chaos in the system. In this case, it is possible to determine fundamental characteristics of the chaotic system, such as the fractal dimension of the Poincaré cross-section, D_P , and then calculate the fractal dimension of the strange attractor (usually, this parameter equals $D_P + 1$). The possibility of using the reproducibility data for determining other dynamic properties of chaotic systems (*e.g.*, Lyapunov indices,⁹⁶ K-entropy,⁹⁷ *etc.*) is still to be clarified.

Yet another important problem concerns the number of experimental points necessary to obtain correct results. From the aforesaid it follows that even a thousand experimental points can appear to be insufficient. This is a serious impediment, since carrying out, *e.g.*, a thousand of syntheses of single crystals is usually impracticable. However, a way to obtain more than a single point in one experiment should be pointed out. In particular, each experiment on melt growth of superconducting cuprates gives nearly a hundred single crystals with (usually) different parameters (size, composition, *etc.*). Another method for solving this problem involves analysis of statistical data on quality control in large-scale productions. This is of considerable value for these productions, since an intimate relationship between poor reproducibility and chaos makes possible significant improvements in reproducibility of the characteristics of end products by suppression of chaos using known methods.^{98,99}

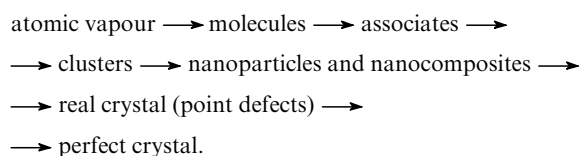
The examples considered above do not exhaust the list of materials science problems that can be solved using nonlinear dynamics approaches. In particular, such problems include studies of phase boundaries as self-organising systems. The phase boundary was treated¹⁰⁰ as an open nonequilibrium system comprising a number of interacting subsystems. A feature of the system is nonlinear interactions between subsystems and the presence of feedbacks. An example of a self-organisation related phase boundary is provided by the semiconductor/electrolyte interface. This interface comprises the ionic electrolyte layer adjacent to the semiconductor surface, the region of 'alien' surface phases, the region with the changed or broken crystal structure of the semiconductor and the space charge region, which retains the crystal structure of the bulk semiconductor but has different electronic characteristics. Specific properties of such a surface are determined by the processes occurring within all the above-mentioned regions and by their interactions. A salient feature, which serves as a prerequisite for self-organisation, is that the interface is formed as a result of nonlinear interaction between the

electronic subsystem of the semiconductor and the ionic subsystem of the electrolyte. Most often, the polarisation of semiconductors and adsorption of molecules on their surfaces are accompanied by phase transitions, which cause a jumpwise change in the charge of the interface. Sometimes these processes are accompanied by irreversible change in the charge, which is characteristic of the surface of the semiconductors with low density of surface states. This makes possible, *e.g.*, exclusion of pinning of the Fermi level on the GaAs and GaP surfaces and extension of the range of the surface potential values, which can be practically implemented in designing and fabricating metal–insulator–semiconductor transistors.

Of considerable interest are systematic studies on the nonlinear processes accompanying the first-order phase transitions on the surface of solids and on the growth of thin films from multicomponent vapour carried out by Kukushkin and Osipov.^{101,102} These researchers analysed various models for the vapour-phase and melt-solution growth of multicomponent films and proposed efficient methods of control of these processes.

VII. Self-assembly of supramolecular compounds

The evolution of a physicochemical system from atomic vapour to a solid depends on the system's composition. If the system comprises atoms of the same element, the evolution begins with formation of covalently bonded diatomic molecules followed by larger associates, clusters and nanoparticles that are often stabilised in inert matrices in the form of nanocomposites. The assembly is completed with the formation of a covalent (diamond), molecular (iodine) or metal (alkali and alkali-earth metals) crystals as the end product. At any non-zero temperature (in K), the crystal has to some extent a disordered structure, which contains, in the simplest case, point defects (vacancies or atoms occupying the interstitial sites). Thus, the evolution resulting in an elementary crystal as the end product can be represented by the following scheme:



In a more chemically complex system the interactions of different-type atoms cause the formation of molecules bonded through covalent or mixed ionic–covalent interactions. In the latter case the bond ionicity increases as the difference in electronegativity between the constituent elements increases. The next stage of the interaction involves formation of the so-called non-covalently bonded supramolecular ensembles and supramolecular materials. Usually, the formation of supermolecules is assumed to be driven by the system's tendency towards a minimum of the Gibbs free energy (the enthalpy of formation of supermolecules from individual molecules or molecules and ions contributes predominantly in this case). In spite of extensive literature on supramolecular chemistry, from academic monographs (see, *e.g.*, Refs 103–105) to recent publications in scientific journals (see, *e.g.*, Refs 106–110), the nature of the self-organisation of supermolecules and supramolecular crystals has been poorly studied. This uncertainty also covers the terminology of supramolecular chemistry.¹¹¹ First of all, the case in point is the so-called self-assembly and self-organisation processes, which are sometimes (but not always) treated as different. The term self-assembly can be used in a broader sense. It relates to all types of spontaneous binding of components through both covalent and noncovalent forces. According to Lehn,¹⁰³ self-organisation

(1) involves the interactions between systems, which can experience spontaneous ordering in space and/or time;

(2) involves spatial (structural) and temporal (dynamic) order in both the equilibrium and nonequilibrium dissipative structures;

(3) concerns only the noncovalent, supramolecular level of structural organisation; and

(4) results in the formation of polymolecular ensembles due to specific acts of molecular recognition of components.

The higher the extent of spatial organisation of fragments, the more substantiated the reasons for their treatment as self-organised (molecular layers, membranes, micelles, colloids, liquid crystals, molecular crystals). Thus, self-organisation extends to the interactions between fragments and the integration of these interactions, which are responsible for the collective behaviour of the system, as is observed during, *e.g.*, phase transitions or creation of spatial and temporal waves).

The interrelation between conservative and dissipative self-organisation during the evolution of physicochemical systems involving formation of supermolecules has not been studied as yet. We believe that such an evolution is possible due to a complex combination of these factors based on chance and necessity, respectively. According to Müller *et al.*,²⁸ conservative self-

organisation processes play a crucial role in the formation of supermolecules. On the other hand, Lehn pointed out that 'the inclusion of dissipative nonequilibrium processes, like those present in the living world, constitutes a major goal and challenge for supramolecular chemistry'.³¹ An important role in the formation of supermolecules is played by prehistory, or the topochemical memory, as well as the template effect of the central ion or molecule towards other fragments of supermolecules formed. Self-assembly of supermolecules can be employed to prepare advanced functional materials.¹¹²

Let us consider the self-assembly of comb-like supermolecules *via* formation of primary and secondary structures as an example.¹¹³ The simplest case is a flexible polymer having free binding sites along its main chain (component A in Fig. 20). Usually, the main chain is polar, while non-polar side groups can be connected by complementary bonds, thus leading to comb-like supermolecules, which then self-organise. The side chains are bonded to the main polymer chain by hydrogen or coordination bonds.¹¹⁴ Ionic

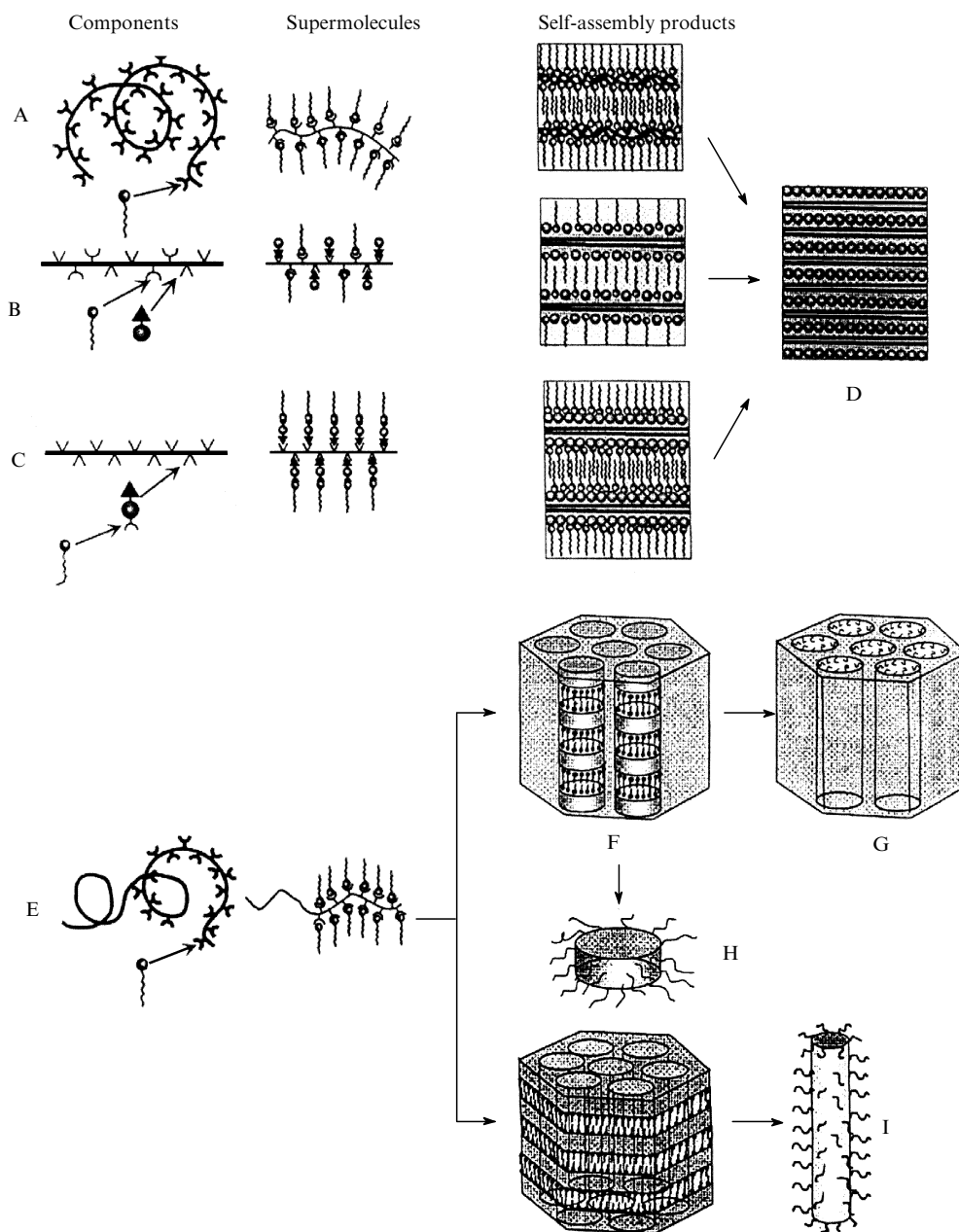


Figure 20. Self-assembly of comb-like supermolecules involving primary and secondary polymer structures (for details, see text).¹¹³

interactions in polyelectrolyte–surfactant complexes were also used to form comb-like supermolecules.¹¹⁵ The resulting self-organised multidomain structures can be transformed into single-domain ones.¹¹⁶ The properties of the latter group of structures can be tuned by varying the nature of the side chains. For instance, partial fluorination of the side chains reduces the surface energy and the friction coefficient of the material.¹¹⁷

If the main chain consists of the double helix of DNA, self-organisation can be achieved by ionically bonding liposomes or cationic surfactants to the anionic phosphate sites.^{118,119} This allows for materials design possessing unusual biochemical properties. For instance, colour centres can be intercalated into the DNA helices, thus suppressing their aggregation. Such structures can be used as templates for photonic applications.¹¹⁹ The main polymer chain can have two sorts of binding sites to which fragments of different nature can be bonded (component B in Fig. 20).

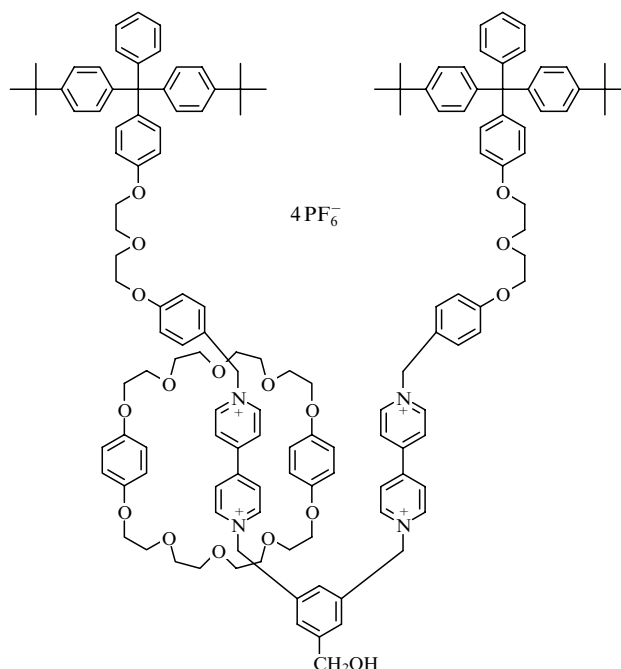
The side chains can also have different functional groups. For example, in addition to the side chains required for self-organisation, the system can contain acid groups that act as dopants for the conjugated polymer (*e.g.*, polyaniline), which leads to electronic conductivity.¹²⁰ An additional degree of freedom is introduced when polyaniline is first doped with, *e.g.*, camphorsulfonic acid and subsequently connected to hexylresorcinol molecules (component C in Fig. 20) through two H-bonds.¹²¹ The alkyl chains of the hexylresorcinol molecules act as plasticisers, thus making the infusible polymer thermoplastic. Camphorsulfonic acid doped polyaniline chains confined within nanoscale cylinders improve the material's conductivity. This technique also allows modification of rigid-rod polymers similar to polypyridine, which consists of *para*-linked heteroatomic rings. The optical properties of such polymers can be controlled by doping them with camphorsulfonic acid. Subsequent bonding to alkylresorcinol leads to comb-like supermolecules, which self-organise into lamellae in such a way that the material becomes fluid even without solvents.¹²² Such an unusual fluid contains rigid polymer 'rods' and allows processing towards monodomains with aligned 'rods.'

Finally, the plasticising alkylresorcinol molecules can be removed by evaporation *in vacuo*, thus interlocking the chains in solid stable polymer films (product D in Fig. 20). As a result, polarisation-induced luminescence is achieved.¹²² It is also possible to combine different self-organisation and recognition mechanisms within the same polymeric material. For instance, block copolymeric self-organisation fragments of lengths 100 to 200 Å can be combined with amphiphilic self-organisation fragments of length 10 to 60 Å (component E in Fig. 20).^{114,123} After selective doping of one block, the material's conductivity can be changed by using a sequence of phase transitions.¹¹⁴ Three-dimensional conductivity can be achieved by ordering the local structure.¹²⁴ There is a vast variety of phases,¹²³ such as lamellae-within-cylinders (product F in Fig. 20), which, by analogy with the product D, also permit selective cleavage of the constituent fragments that form the supermolecules. For instance, starting from polystyrene-*b*-poly(4-vinylpyridine), in which pentadecylphenol is hydrogen bonded, one can obtain a structure in which the glassy polystyrene matrix contains cylindrical pores with poly(4-vinylpyridine) 'brushes' on the walls (product G in Fig. 20).¹²⁵ By choosing different block copolymers and amphiphiles it is possible to tune the thickness of the pore walls. In principle, the shape of 'nanobrushes' can be controlled by selecting appropriate polymer and solvent. For instance, Saito¹²⁶ cross-linked the poly(4-vinylpyridine) slices using an original method for preparation of nanoscale colloidal disks (product H in Fig. 20). Other shapes of nanoparticles can also be obtained, *e.g.*, polymer 'rods' (product I in Fig. 20).¹²⁷

Complex self-organised supermolecules open up prospects for targeted variation (tuning) of many physical parameters. The possibility of using such molecules in design of advanced biomaterials is particularly attractive, which was successfully dem-

onstrated taking DNA and self-organising fungal proteins as examples.¹²⁸

Rotaxane molecules that are active in redox processes were used to create 'molecular switches', which can act as logical gates.¹²⁹ The rotaxane molecule consists of a dumb-bell chain and a macrocycle mechanically strung on the dumb-bell.



The dumb-bell fragments of the molecule comprise charged bipyridine moieties while the macrocycle consists of crown-ether chains. The molecules of rotaxane are formed as a monolayer and located between the metal and metal oxide electrodes. Passage of electric current causes oxidation of the rotaxane molecules and induces conformational changes, which lead to an increase in the resistance. In fact, the rotaxane molecules behave as a molecular switch. Switching on (oxidation of rotaxane) is a reversible process, while the resistance difference between the on and off states is readily detectable (resistance changes by a factor of 15 to 30).

VIII. Self-organisation in nanosystems

A decrease in the particle size in a dispersed system down to the nanometre scale is accompanied by changes in the bulk properties of the system, including the crystal lattice parameters (sometimes, also the lattice type), melting temperature, electric and heat conductivity, *etc.* This changes the character of interparticle interaction, thus providing a way to various nanostructures possessing unique optical, magnetic, catalytic properties and reactivity.^{130,131} The closer the particle size to the atomic scale, the more pronounced these changes and effects.¹³²

Nanoparticles are divided into two types. The first group comprises nanoclusters or nanocrystals, which consist of at most a thousand atoms, have ordered structure and are of size 1 to 5 nm. The second group comprises nanoparticles consisting of 10^3 to 10^6 atoms having diameters from 5 to 100 nm.¹³³ However, this classification is correct only for isotropic (spherical) particles. Whiskers and plate-like particles can comprise a much larger number of atoms and their linear dimensions (one or even two) can much exceed the threshold value, but the properties of these objects remain typical of matter in the nanocrystalline state. Based on the ratios of linear dimensions, nanoparticles can be treated as one-, two- or three-dimensional (1D-, 2D- and 3D-nanoparticles, respectively).¹³⁴ If a nanoparticle has a complex shape and structure, the linear dimension of the structural element rather than the entire particle is taken as the characteristic size. Such

particles are usually called nanostructures; their linear dimensions can be much larger than 100 nm. Depending on the predominant type of the anisotropy of structural elements, nanostructures are also divided into one-, two- or three-dimensional ones.

The most important feature of nanosystems is manifestation of quantum size effects. From the classical standpoint, as the particle size in the system decreases, the specific surface area of the particles increases. The effect of the particle size on the thermodynamic properties of the system is included by introducing an additional term, γds (γ is the size-independent surface tension coefficient and s is the surface area), into the expression for the free energy. According to Thompson's equation, a decrease in the particle size is accompanied by an increase in the equilibrium vapour pressure and solubility and by changes in the temperatures of melting and other phase transitions. At the same time, a number of extensive parameters of the system, related to surface processes (e.g., adsorption and catalysis), are proportional to the specific surface area. The role of the specific surface area of nanoparticles becomes much more important as their sizes approach the atomic scale. This is due to a considerable increase in the number of surface atoms.

On the other hand, many properties of materials (including magnetic, optical and electrical properties) are due to co-operative interactions in solids that are not retained on going from the bulk material to nanoparticles. In this case the properties of materials cannot be rationalised solely by an increase in the specific surface area and the number of surface atoms without considering quantum size effects. This can be exemplified by the formation of quantum dots in those cases where the sizes of the semiconductor particles are comparable with the de Broglie wavelength of the electron, by a change in the width of the band gap due to localisation of excitons and by transition of ferromagnetic materials to the superparamagnetic state. Sometimes the size effect manifests itself as a dramatic enhancement or reduction of catalytic activity (or reactivity) per metal atom with a decrease in the particle size. This effect is usually most pronounced for nanoclusters.

The magnetic, electrical and optical properties of matter also significantly change as the particle size decreases from 5–10 nm downward.^{135, 136} The properties of nanoclusters depend non-monotonically on the cluster size (i.e., the number of atoms).¹³⁶

Unique properties of nanoclusters are likely due to the limited number of constituent atoms. In most cases the cluster core is formed following the close packing principle. The number of atoms in a regular dodecahedral core is given by the expression

$$N = \frac{10n^3 + 15n^2 + 11n + 3}{3},$$

where n is the number of shells surrounding the central atom. Thus, the smallest close-packed cluster core comprises a total of thirteen atoms (a central atom and twelve atoms of the first outer shell). As a result, one gets a set of 'magic' numbers $N = 13, 55, 147, 309, 561, 923, 1415, 2057, 2869, \text{etc.}$, which correspond to the most stable cluster cores.^{136, 137} A tendency towards formation of cores containing 'magic' numbers of atoms can be followed taking metal clusters as examples. A number of gold, rhodium, platinum and palladium compounds were synthesised, containing from thirteen {e.g., $[\text{Au}_{13}(\text{diphos})_6](\text{NO}_3)_4$; diphos is $\text{PPh}_2\text{CH}_2\text{PPh}_2$ } to a total of 2057 metal atoms [e.g., $\text{Pd}_{2057}(\text{phen})_{840-1600}$].¹³⁸ It should be noted that clusters comprising non-'magic' numbers of atoms are also formed. The existence of more energetically favourable 'magic' clusters provides an explanation for non-monotonic dependence of the properties of nanoclusters on their sizes.¹³⁹ On going from nanoclusters to nanoparticles this effect becomes less pronounced. Detailed studies of gold and palladium clusters revealed that their conductivities, heat capacities and magnetic susceptibilities are significantly different from the corresponding properties of bulk metals.¹⁴⁰ It was established that, unlike the orbitals of metal atoms in bulk samples, those of the

metal atoms of the cluster core are not delocalised and form discrete energy levels that differ from molecular orbitals. On going from a bulk metal to nanoclusters and then to molecules and single atoms the metallic band structure (conduction band formed by delocalised s- and d-electrons) turns into discrete energy levels formed by localised electrons in cluster and then into molecular and atomic orbitals. The appearance of discrete electronic energy levels in clusters causes single-electron transitions that are characteristic of single atoms.

Very interesting quantum size effects were observed in studies of the magnetic susceptibility and heat capacity of nanoclusters.¹⁴¹ It was shown that the magnetic susceptibilities of both the Pd_{2057} cluster and a bulk palladium sample are temperature independent (the absolute value of a cluster's susceptibility is much lower than that of the bulk sample). With inclusion of magnetic effects this means that the Pd_{2057} cluster is a Pauli paramagnetic and similar to the bulk metal. A decrease in the cluster size down to Pd_{1415} causes an increase in the low-temperature magnetic susceptibility, which is in good agreement with the results of quantum-mechanical calculations and is associated with a decrease in the density of states near the Fermi level. At the same time, increasing the cluster size leads to an increase in the specific magnetic susceptibility, which reaches a value typical of bulk metal at a particle size of nearly 30 nm. Nanoclusters exhibit a quadratic (or more complex) temperature dependence of the heat conductivity (cf. a linear dependence for bulk material and larger nanoparticles). The quadratic temperature dependence of the heat conductivity is typical of amorphous solids; in the case of nanosystems it is associated with tunnelling effects.

We have considered only a few examples of specific properties of small nanoparticles. Due to the small number of atoms these properties can be reasonably described using quantum-mechanical approaches. However, many fundamental properties of matter in the nanocrystalline state are different from the properties of bulk materials over a rather wide range of particle sizes (up to hundreds of nanometres).¹⁴² In this case one can use both statistical and thermodynamic methods that allow for the excess surface energy.¹⁴³

Unique physicochemical properties of nanoparticles and nanostructures make the design of functional nanomaterials based on them a quite interesting research avenue. Recently, particular emphasis has been placed on the magnetic and semiconductor nanomaterials. This is due to great practical value of these classes of materials for the development of information technologies. For instance, superparamagnetic materials based on transition-metal (e.g., Fe, Co, Ni) nanocrystals are used in memory devices with ultrahigh recording density.¹⁴⁴ Nanomaterials based on, e.g., $\text{A}^{\text{IV}}\text{B}^{\text{VI}}$ and $\text{A}^{\text{IV}}\text{B}^{\text{VI}}$ semiconductors possess unique optical properties and are thought to be promising for active elements of tunable lasers, nonlinear optical elements and devices for nanoelectronics.¹⁴⁵

Advances in studies of nanosystems are closely related to the improvement of field-ion, tunnelling, atomic force and high-resolution electron microscopies that allow visualisation and determination of the properties of individual nanoparticles and to the development of computational methods that would permit computer simulation of molecular motions in large molecular ensembles.

Summarising the investigations of nanosystems,¹⁴⁶ the following conclusions were drawn.

1. Modern theoretical concepts of nanosystems are too rough to underlie the practical use of nanosystems. Essential development of the theory of nanosystems is required. Most nanosystems are far from the equilibrium state; their state is continuously changed with time. That is why the establishment of laws of the physicochemical evolution of nanosystems is of crucial importance. The available data on this evolution are scarce as yet.

2. Methodologically, the properties of nanosystems should be studied by combining experimental studies and mathematical modelling. It is a combination of 'full-scale experiments and

computer simulation' that was used to obtain essential, unambiguously interpretable information on nanosystems.

3. Characterisation of nanosystems is still a challenge. Quantitative data on the properties of individual nanoparticles are hard to obtain. Information on the behaviour of nanoparticles in the measuring devices is of great importance. The most informative studies have been carried out by those research groups, which not only use but can also modify their measuring devices and adjust them in the course of measurements.

4. Currently, the emphasis has been placed on the following avenues of research on nanosystems:

- elaboration of theoretical foundations of preparation and operation of nanomaterials including superstrong metals and alloys, ceramics, film compositions and materials possessing specific optical, magnetic and electrical properties;

- elaboration of physicochemical foundations of nanotechnologies, including development of methods for preparation and characterisation of technological nanosystems and investigation of their behaviour under the operating conditions;

- development of nanopharmacology and nanomedicine, including elaboration of methods for the synthesis and characterisation of ultradispersed forms of pharmaceuticals and investigations of the mechanisms of their interaction with living organisms;

- creation of ecological nanophysicochemistry, which would study the mechanisms of formation and transformations of natural and technogenic air and water pollutants (aerosols and hydrosols, respectively); development of methods for cleaning the environment of nanoparticles.

Experiments with hydroxyapatite, acetylsalicylic acid and phthalocyanines showed that going to ultradispersed forms of these compounds causes dramatic changes in their therapeutic effects and opens up prospects for the formation of pharmaceuticals immediately inside invaded tissues. Therefore, the development of concepts of physicochemical evolution of ultradispersed pharmaceuticals from their formation in chemical reactors or in tissues to complete excretion is of paramount importance. Melikhov¹⁴⁶ posed a problem of development of physicochemical evolution of nanopharmaceuticals, which should provide methods for solving the following applied tasks.

1. Creation of materials possessing osteoinductive properties (inductors of osteogenesis), osteoporosis remedies and carriers for pharmaceuticals based on ultradispersed hydroxyapatite. For instance, the 'Ostim-100' osteoplastic material (ultradispersed form of hydroxyapatite) was proved to be highly efficient in acceleration of bone tissue regeneration. This opens up prospects for preparation of compositions containing this material and hormones or broad-spectrum antibiotics. However, this requires that hydroxyapatite nanoparticles be capable of forming 'complexes' with macromolecules of different nature.

2. Creation of 'nanofluids' based on hydroxyapatite and hydroxalcite doped with iron oxides for magnetic-field driven, directed transportation and delivery of pharmaceuticals in organisms. Preliminary experiments showed that both the interplanar space of hydroxalcite microcrystals and the aggregates of two-dimensional hydroxyapatite crystals can be intercalated with large amounts of various pharmaceuticals and with magnetic nanoparticles of iron oxides, thus making such materials magnetically sensitive. Therefore, studies on the possibility of creating pharmaceuticals based on these composites would be appropriate.

3. Development of methods for the preparation of nanostructured alloys based on nitinol to create materials for implants and medical instruments. Experiments revealed significant improvement of the consumer properties of the products made of nanostructured alloys. However, to meet all medical requirements, one should study the physicochemical evolution of the alloy.

4. Elaboration of methods for tumour therapy by sonostimulated inhibition and destruction of malignant cells using ultradispersed substances; search for compounds which can selectively crystallise and accumulate within malignant cells. There are experimental grounds to believe that tumour cells containing a rather

large amount of phthalocyanine nanoparticles can be killed by exposing to a weak acoustic field. Studies on crystal sensorics revealed that the frequency of formation of solid nanoparticles in cells can increase upon minor variations of the compositions and molecular structures of the substances present in the cells. Therefore, a promising avenue of pharmacological research consists in search for compounds, which can selectively form nanoparticles in tumour cells and thus provide a route to cell destruction using acoustic fields that is innocuous for normal tissues.

Returning to the role of nonlinear processes and self-organisation in the chemistry of nanomaterials, it should be emphasised that self-organisation is possible in different stages of their synthesis and exploitation, from the formation of nanocrystallites or nanoclusters to long-term operation of nanostructures in various technical, technological and biomedical systems.^{147, 148}

Indeed, in most cases nanoparticles (nanoclusters) are formed under strongly nonequilibrium conditions, which provides the necessary ratio of the rate of spontaneous nucleation to the seed growth to particular sizes. Historically, nanoparticles were first prepared using methods of colloid chemistry, which allowed the synthesis of particles of size 1 nm to 100 μm . In Fig. 21 we compared the linear dimensions of various colloidal systems, which are most often used in practice.

In 1968, Stöber, Fink and Bohn¹⁴⁹ first demonstrated that polycondensation methods are also efficient in the preparation of monodispersed silica particles. They hydrolysed a solution of tetraethylorthosilicate in alcohol at high pH values and obtained homogeneous spherical particles of amorphous SiO_2 . The particle size could be varied from 50 nm to 2 μm by varying only one parameter (reagent concentration). Matijevic *et al.*^{150–154} and the authors of Refs 155–157 also have made large contributions to the development of polycondensation methods. Methods of preparation of colloidal particles using polycondensation in solutions both in the presence and in the absence of surfactants (inhibitors of aggregation) have also been analysed.¹⁵⁸

The next group of methods for the preparation of nanoparticles comprises high-energy methods based on rapid condensation of vapours under such conditions that exclude aggregation and growth of the particles thus formed. These methods mainly differ in the procedures employed for evaporation of the starting compound and stabilisation of nanoparticles. Evaporation can be achieved by plasma excitation, laser methods, arc melting, heat treatment, *etc.*^{159–161} Condensation can occur either in the presence of a surfactant (adsorption of surfactant on the surfaces of particles hampers their growth) or on a cold substrate (here, the growth of particles is limited by diffusion rate).¹⁶²

Yet another group of methods involves the use of spatially confined systems, or the so-called synthesis in nanoreactors (micelles, droplets, films, *etc.*).¹⁶³ Here, one deals with the synthesis in reversed micelles, Langmuir–Blodgett films, adsorption layers, *etc.*^{164–167} Clearly, the particles thus obtained cannot be larger than the size of the corresponding nanoreactor; therefore, these methods allow preparation of monodispersed systems.¹⁶⁸ Biomimetic and biological approaches, which involve the use of biomolecules (proteins, DNA, *etc.*) as nanoreactors,^{169–171} can also be placed into this group.

Synthesis in colloidal nanoreactors permits not only the preparation of nanoparticles with very narrow and controllable size distribution but also particles of different shape and anisotropy (including small particles) as well as coated particles. This technique can be employed to prepare virtually all classes of nanostructures, from single-component metal to multicomponent oxide nanostructures.^{172–174}

It should be noted that the use of free nanoparticles as materials is strongly complicated by the fact that matter in the nanocrystalline state exhibits metastable properties. As mentioned above, this is due to an increase in the specific surface area of particles with decreasing linear size down to the nanometre scale, which leads to an increase in the reactivity of a compound and enhanced aggregation of nanoparticles. The method most

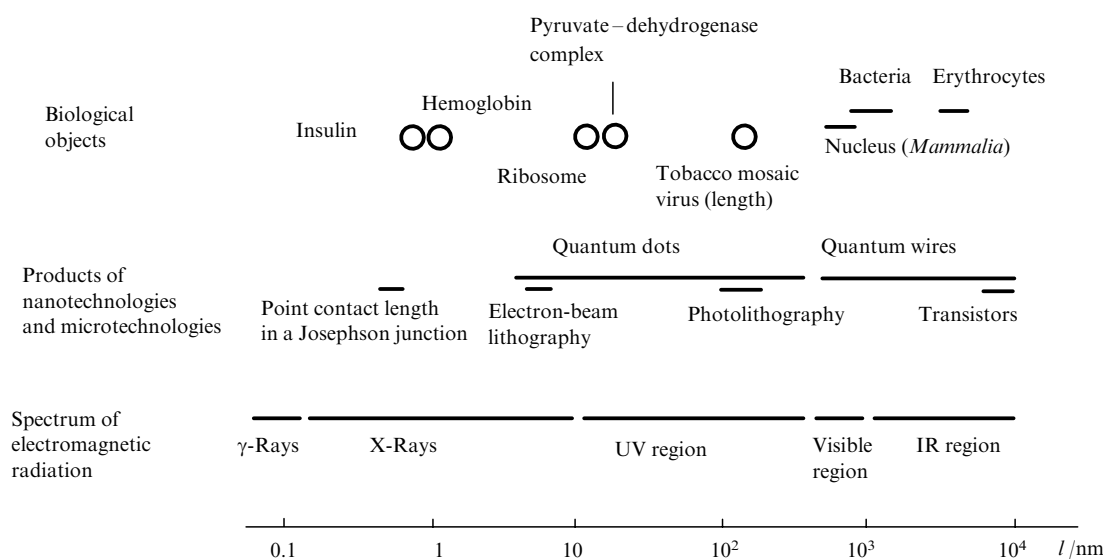


Figure 21. Linear dimensions of various colloidal objects.

widely used to solve this problem involves fabrication of nanocomposites (*i.e.* nanoparticles encapsulated in a chemically inert matrix).¹⁷⁵ This approach provides a way to eliminate aggregation of nanoparticles and protect them from external conditions (*e.g.*, from oxidation by air oxygen), which significantly facilitates the practical use of nanomaterials.

Nearly ten methods of matrix isolation of nanoparticles have been proposed to date. They can be conventionally divided into two groups. The first group comprises methods for the preparation of free nanoparticles followed by their incorporation into an inert matrix. The second group includes methods of formation of nanostructures in the bulk of the matrix during its chemical modification.^{176, 177} Methods from the first group are simple but impose strong limitations on the choice of matrix. Usually, organic polymers are employed as matrices, but these substances do not possess high thermal stability and sometimes do not exhibit the necessary physical properties (*e.g.*, high optical transparency).¹⁷⁸ Besides, incorporation of nanoparticles does not exclude their aggregation.¹⁷⁹ The second approach not only allows one to eliminate these problems but also provides a way of controlling the parameters of nanoparticles immediately in the matrix during their formation and even changing these parameters in the course of exploitation of the material. In this case, the matrix must contain some structural voids, which can be filled with appropriate compounds; subsequent modification of these fillers should cause the formation of nanoparticles in the voids.¹⁸⁰ In other words, these voids should confine the zone of the reaction involving the incorporated compounds, *i.e.*, act as a specific kind of nanoreactor. Clearly, by choosing compounds with different shapes of structural voids it is possible to synthesise nanostructures with different morphologies and anisotropies.

The best known example for this approach is the synthesis of nanomaterials using porous oxide matrices (usually, SiO₂ or Al₂O₃).^{181, 182} In this case, pores are filled with various compounds, which are then chemically modified. However, disordered porous structure and broad pore size distribution preclude preparation of good nanosystems. As a rule, such materials are used in catalysis, where the requirements imposed on the particle size distribution and particle morphology are not too strong.¹⁸³ A possible solution to the problem is provided by using porous materials with ordered pore structure, such as mesoporous silica and zeolites having 1D-channels or 2D-voids.^{184–186} In this case, it is possible to obtain whiskers, plate-like or spherical nanoparticles (depending on the type of the porous structure) with narrow particle size distribution.^{187, 188} Sometimes, rapid directed

formation of nanoparticles in the matrix is achieved by exposing the system to, *e.g.*, sonication, microwave and laser irradiation.^{189–191} However, a rigid porous structure precludes variation of the particle size and morphology during synthesis. As a rule, these parameters are strongly dependent on the pore size and morphology.¹⁹²

The use of structures with variable void sizes seems to be a convenient version of this method. A recently proposed technique involving compounds with layered aluminosilicate structures also seems to be promising.¹⁹³ In these compounds the layers are linked together through weak van der Waals forces, which allows one to change the volume of the interplanar space with ease. Besides, a layered structure permits considerable acceleration of gas diffusion in the interplanar space, thus facilitating chemical modification of layered compounds.^{194, 195}

Several tens of communications on the preparation of nanocomposites *via* layered compounds have been reported so far.^{196–200} Most of them are concerned with aluminosilicates, which have negatively charged layers and cations located in the interplanar space. However, these compounds usually have non-stoichiometric compositions and are highly hydrated and cross-linked, which strongly complicates the synthesis of nanomaterials and has a negative effect on the reproducibility of their properties.^{201, 202}

A large surface area and, hence, an excess surface energy of nanoclusters make aggregation processes unavoidable. They are directed towards a decrease in the Gibbs free energy, occur spontaneously and can be described in the framework of the model of conservative self-organisation in the absence of kinetic difficulties. Figure 22 presents a micrograph of a nearly spherical colloidal gold particle obtained after spontaneous aggregation of nanocrystals of average size 35 ± 5 nm.²⁰³ It was quite correctly pointed out²⁰⁴ that formation of nanostructures from nanoclusters is similar to the formation of bulk crystals from atoms, but the fundamental difference between these processes is that, unlike atoms, clusters are characterised by real surfaces and intercluster boundaries. What is more, cluster-cluster interactions produce strain as well as excess energy and excess pressure at the cluster boundaries. The excess energy per dislocation can be calculated by the formula

$$E_d = \frac{Gb^2}{4\pi(1-\nu)} \ln \frac{r}{r_0}$$

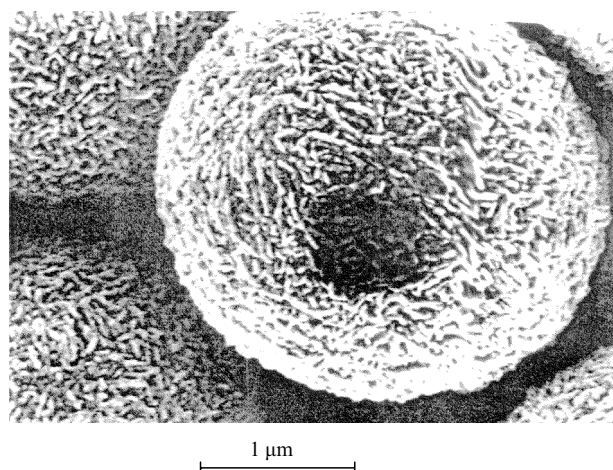


Figure 22. Micrograph of a colloidal gold particle formed upon spontaneous aggregation of nanocrystallites of average size 35 ± 5 nm.

where G is the shear modulus, b is the Burgers vector, which characterises the displacement of the edge dislocation, ν is the Poisson coefficient (usually, $\nu = 0.3$), r is the range of the effect of dislocations and r_0 is the minimum dislocation size. Assuming that the concentration of dislocations in the cluster is determined by the surface-to-volume ratio, the density of the excess energy of a cluster is given by the following expression

$$\varepsilon = \frac{Gb^2}{4\pi(1-\nu)R} \ln \frac{r}{r_0},$$

where R is the cluster size.

Thus, the density of the excess energy decreases with an increase in the cluster size R and equals zero for the bulk material.

Considering the effect of defects and dislocations on the properties of nanosystems comprised of nanoclusters of arbitrary sizes, one should start from the thermodynamic concentration of defects and dislocations, which includes the chemical potential and excess energy of the cluster surface. The excess energy causes the production of excess pressure, which can be estimated at $\sim 10^9$ Pa for clusters of size 1 nm.¹³⁶ Ignoring the difference between the pressure within the cluster and at its surface, the concentration of defects in the cluster (c_0) can be calculated by the formula

$$c_0 = \frac{a(3R^2 - 3aR + a^2)}{R^3},$$

where a is the thickness of the surface layer.

Taking into account the difference between the pressure within the cluster and at its surface, the following expression was derived¹³⁶

$$c = c_0 \exp \left(-\frac{2\alpha V/R}{kT} \right),$$

where α is the surface stress and V is the volume of the defect.

The dependence of c on the cluster size is plotted in Fig. 23. The maximum in the c - $f(R/a)$ curve is observed at $R/a = 25$, which corresponds to $R = 10$ – 50 nm. This range of cluster sizes provides the maximum concentrations of defects and excess energies, and such clusters are involved in the formation of nanosystems.

Nanostructures comprised of molecular clusters CO_2 , N_2 and SF_6 exhibit an increase in strain with increasing cluster size.²⁰⁵ X-Ray diffraction studies of nanosystems revealed the effect of the cluster size and interfacial strain on the structure of nanosystems.²⁰⁶ Analysis of nanocrystalline samples of Al, Ru, Cu and

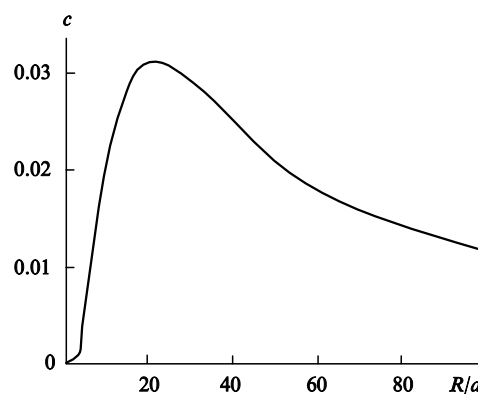


Figure 23. Defect concentration in clusters plotted vs. cluster size.

AlRu showed^{207,208} that their deformations lie between 1% and 3%, which much exceeds the deformation of coarse-grain metals. Small clusters do not contribute to elastic deformation of the crystal lattice, which is due to interfacial dislocations.²⁰⁹ The major contribution comes from large nanoclusters. Hence, there is some intermediate range of cluster sizes, corresponding to maximum effect of interfacial strain, which is in agreement with the conclusions drawn based on the thermodynamic model of the influence of structural defects.

Nanosystems possess unusual mechanical properties. At room temperature, their microhardness is 2–7 times higher than that of the corresponding bulk materials. The Vickers microhardness of a cluster is given by the expression²¹⁰

$$H_V \approx H_0 + kR^{-1/2}$$

and increases with a decrease in the cluster size R . Experiments showed that a decrease in the size of Ag, Cu, Pd, Fe and Ni clusters is accompanied by an increase in the hardness of nanosystems.²¹¹ The microhardness of a nanosystem also depends on the treatment conditions, which affect the interface structure, cluster–cluster interactions and the cluster size. For instance, relaxation and annealing of interfacial defects at a constant size of $\text{Al}_{98.5}\text{Mg}_{1.5}$ clusters ($R \approx 150$ nm) cause a decrease in the microhardness from 1.7 to 1.45 GPa.²¹² However, annealing has a much more pronounced effect on R . In particular, heat treatment of a nanosystem comprised of palladium clusters at 475–600 K results in an increase in the cluster sizes and, correspondingly, in a nearly three-fold decrease in the microhardness of the system.

Yet another remarkable feature of nanosystems is their superplasticity, which was observed²¹³ for nanocrystalline Ni and Ni_3Al at 470 and 450 °C, respectively (this is nearly one third of the melting temperatures of these compounds). Superplasticity of oxide ceramics is of considerable interest for both theoretical studies and practical implementation. This property manifests itself at cluster sizes lying between 1 nm and 1 μm; the cluster size should not change on heat treatment.²¹⁴ The presence of amorphous phases can influence the superplasticity effect.²¹⁵

Structural transformations in nanosystems also attract considerable attention. It was established²¹⁶ that nanoclusters comprised of thermodynamically unstable γ -Fe phase are stable even at room temperature, whereas bulk samples are stable only at 800 °C. Cadmium sulfide nanoclusters with a rock salt structure are also known;²¹⁷ a bulk sample of CdS with the same structure is stable at high pressure only. Stabilisation of nonequilibrium (at a given temperature) structures due to formation of small clusters ($R < 10$ nm) can be explained by the effects of the surface energy and the surface pressure, which can be as high as several GPa for clusters of size 1–2 nm.

Thermodynamic features of the behaviour of nanosystems including surface phenomena, phase transformations and aggregation of free molecules or ions into various supramolecular structures have also been studied.^{218,219}

IX. Fractal, epitaxial, template structures and nanocomposites

The evolution of any physicochemical systems existing under nonequilibrium conditions can involve formation of various structures (including fractal, epitaxial and template ones) and nanocomposites.

Formation of fractal structures in macroscopic and nano-systems is due to manifestation of dissipative self-organisation under such conditions where the driving force of the process (*e.g.*, the temperature or chemical potential gradient) exceeds a critical value corresponding to the bifurcation point. Many materials have fractal structures in different stages of preparation and exploitation.^{220, 221} A classical example is provided by the formation of fractal particles during aggregation in solutions and gases.^{222–224} The formation of dendritic structures in the course of, *e.g.*, nonequilibrium electrochemical deposition of metals, solidification of alloys under strong supercooling conditions or phase separation processes is also well known.^{224–227} The surface structures of many catalysts and adsorbents are also described in terms of fractal geometry.²²⁸ Finally, cracks and surfaces, which develop on fracture of many materials, also have a fractal structure.^{229–231} Clearly, periodic geometric patterns characteristic of fractal objects strongly affect their behaviour in various physicochemical processes, among which the most important for materials science are heat treatment processes, catalytic and surface phenomena and solid-phase reactions. The fractal structure also influences the characteristics of diffusion in such objects.

The main laws and peculiarities of diffusion processes and reactions in fractal media, which do not involve changes in the fractal structure, have been studied in considerable detail.^{232–235} Much less attention has been paid to the effects of excess surface energy and to significant geometric nonuniformity on the thermodynamic and kinetic properties of fractal objects (in particular, on their behaviour during ageing, sintering, *etc.*). Here, of particular interest for materials science is the evolution of dendritic inclusions on annealing, as well as crack healing in ceramic materials, structural changes in composites at elevated temperatures, *etc.* A common property of these processes is that they occur with a constant amount of matter in the system (*i.e.*, at a conserved order parameter). This differs from dissolution of particles in reactive media or etching.

A computer simulation of the evolution of fractal particles in systems with a conserved order parameter during ageing and sintering has been reported.²³⁶ The fractal cluster was generated by the diffusion limited aggregation (DLA) mechanism with preset joining probabilities assuming that the change in the density at each point of the cluster is described by the Cahn–Hilliard equation

$$\frac{dc}{dt} = \nabla^2 c - V(c),$$

where c is the dimensionless density ($0 \ll c \ll 1$); $V(c) = K(c^2 - c)^2$ is the potential whose minima correspond to the bulk ($c = 1$) and free ($c = 0$) phases and K is a constant. At different stages of evolution, the geometry of the structure of the particles thus obtained was characterised using the box-counting method and by analysing the correlation functions. It was found that the observed evolution pattern is strongly dependent on the geometry of the seed particles, which is prescribed by the ratio of the upper and lower fractality boundaries, $R_{\max}/R_{\min}$, and by the fractal dimension D .

It was also found²³⁶ that, depending on the self-similarity range of the ‘seed,’ the evolution of the fractal cluster can occur in different manners, namely, with and without fragmentation of the initial particles (long-range and short-range cases shown in Figs 24 and 25, respectively).

The principle of orientational and dimensional correspondence, which was first formulated by Konobeevskii and then by

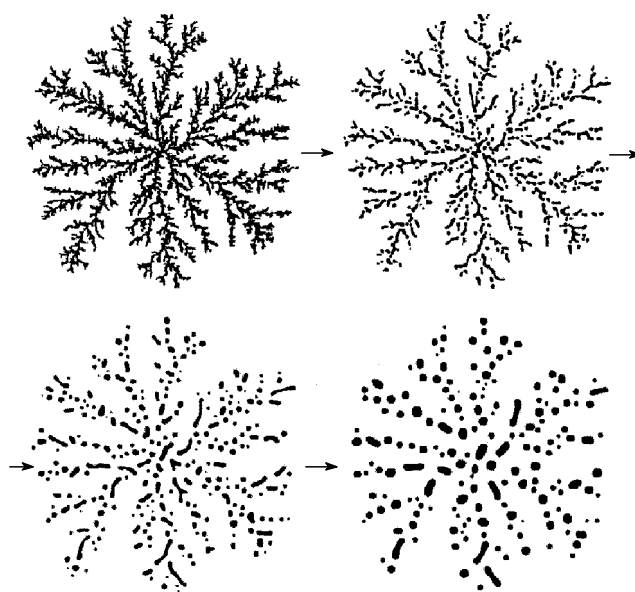


Figure 24. Evolution of a fractal cluster involving fragmentation.

Dankov (see Ref. 237), serves as the basis for the growth of epitaxial structures. According to this principle, the shape and orientation of the seeds of new phases crystallising in an anisotropic medium should correspond to the free energy minimum, which is achieved when the patterns of atomic arrangement in adjacent faces of the new and old phases are best matched. The condition for oriented crystallisation has the form of inequality

$$A + E - Z \leq A_1,$$

where A and E are respectively the work of formation and the energy of two-dimensional nucleus for oriented crystallisation; Z is the work of adhesion (adhesive forces are responsible for enhanced deformation); and A_1 is the work of formation of a three-dimensional nucleus in the case of spontaneous crystallisation. It was shown^{238, 239} that oriented crystallisation is possible if the parameters of the lattices to be matched differ by at most 18%.

It was established²⁴⁰ that epitaxial stabilisation is often followed by the formation of film structures, which are thermodynamically unstable in the absence of such a stabilisation. This can be exemplified by the formation of thin films of REE-containing nickelates and cobaltites on LaAlO_3 , SrTiO_3 and

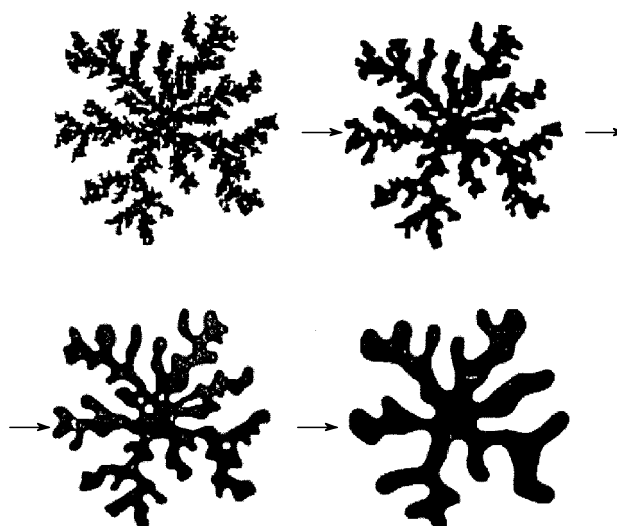
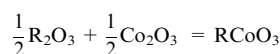
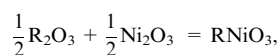


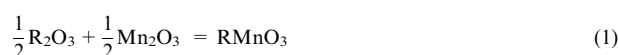
Figure 25. Evolution of a fractal cluster involving no fragmentation.

NdGaO₃ substrates, though the changes in the Gibbs free energy of the reactions



are positive and, hence, the bulk phases of the nickelates and cobaltites are thermodynamically unstable.

Stabilisation of epitaxial structures can also be exemplified by the behaviour of bulk samples of REE-containing manganites RMnO₃, which can be divided into two groups, namely, samples with a perovskite structure (*Pnma*) for the early REE (*R* = La–Dy) and samples with hexagonal structures (*P6₃mc*) for the late REE (*R* = Ho–Lu). Figure 26 presents the $\Delta_r G^\circ$ of the reaction



plotted vs. the ionic radius of REE, which confirms the above-mentioned structural evolution.²⁴¹

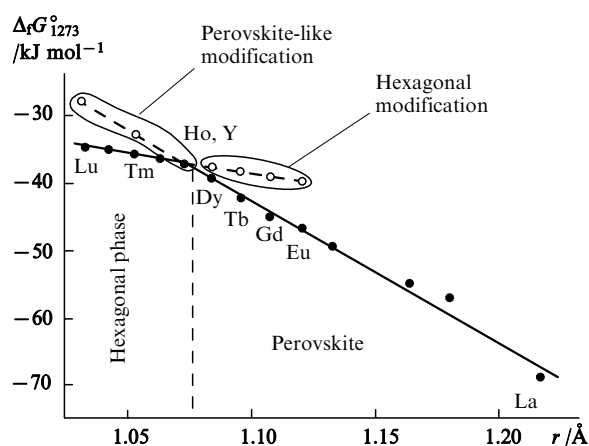


Figure 26. Plot of $\Delta_r G^\circ$ for reaction (1) vs. ionic radius of REE.²⁴¹

However, it is possible to grow thin films of (i) manganites of the late REE with the perovskite structure on substrates with the perovskite structure and (ii) manganites of the early REE with a hexagonal structure on substrates with the hexagonal structure under conditions of epitaxial growth. In other words, the oxide substrate can ‘force’ the film of the REE-containing manganite to grow following the epitaxial pattern, which is atypical of the manganite film under the equilibrium synthesis conditions.²⁴¹

It should be noted that heteroepitaxy of the vapour and liquid phases on single crystals or biaxially textured substrates is efficient only when preparing oriented films of thickness at most 1 μ m. Epitaxial effects dramatically weaken as the film thickness increases. Usually, thin epitaxial films exhibit record values of specific characteristics (e.g., the maximum critical current densities for superconducting cuprates). However, they cannot be

used to achieve high absolute values of operating parameters, as is the case of bulk ceramics, which, unfortunately, possesses poor mechanical properties (first of all, it is highly brittle). A way out was to use a hybrid method elaborated by researchers from the Aachen Centre for solidification in space (Germany) and the Department of Chemistry, M V Lomonosov Moscow State University. To obtain textured thick (50 to 100 μ m) superconducting films, the orientational effect of the substrate (formally, it is similar to the epitaxial effect in the case of thin films) was combined with the melt growth of large grains, which is typical of bulk materials.²⁴² Here, the substrate had an artificial symmetrical relief, which matched the symmetry (grooves or a square grid) and typical sizes (0.1–1 mm) of the crystallising YBa₂Cu₃O_x phase (Fig. 27), instead of short-range orientational effect (molecular epitaxy). By creating such a surface relief using strips made of cheap, untextured commercially available polycrystalline silver as the substrate it is possible to obtain up to 90% of the *ab*-biaxially textured, melt grown crystallites of high-temperature superconductors.

The origin of texture formation is based on various physico-chemical phenomena including wetting (some specific aspects), surface tension, meniscus, heterogeneous nucleation, redistribution of melt components, capillary effects, effects of crystallisation pressure and topographic wall effect of relief elements.^{242, 243} By analogy with ‘graphoepitaxy’ (a well-known thin-film process),^{243, 244} a ‘graphotexturing’ technique was developed, which can be employed in studies of various materials and arbitrary substrates. This approach can lead to virtually complete texturing of a polycrystalline layer in accord with the relief symmetry. The process occurs as a ‘self-assembly’ of the crystallite layer at the mesoscopic level. All tape fragments behave identically, so that the length of the tape crystallising per unit of time can be infinitely long provided that the entire sample is heat treated in the furnace.

Porous structures with pore sizes ranging from 10 nm to 10 μ m can be formed using template synthesis,^{245–248} which is exemplified by Fig. 28. Structural units of the matrix to be formed self-organise into a continuous framework around the template particles. The structure obtained after post-synthetic removal of the template contains channels, which exactly match the size and shape of the template. Once the framework is formed, the template (most often, polystyrene or silica beads) is removed. Namely, polystyrene beads are burnt out in air or dissolved in toluene, while silica beads are etched with hydrofluoric acid. Typical examples of template porous structures are shown in Fig. 29.²⁴⁹ Template synthesis is convenient for preparation of mesoporous, metal,^{250, 251} metal oxide,^{252–254} chalcogenide,^{255, 256} polymeric²⁵⁷ and silica^{253, 258} materials. This method is of prime interest for the formation of photonic crystals (periodic structures comprised of fragments with different dielectric constants). The most important feature of photonic crystals is the forbidden photon energy band, which excludes passage of photons with a particular wavelength through the crystal. Photonic crystals are similar to semiconductor crystals but manipulate photons rather than electrons, thus opening new prospects for development of photonic applications.

In contrast to semiconductor crystals that are characterised by spontaneous formation of periodic atomic structure, photonic



Figure 27. Biaxial texturing of superconducting phase YBa₂Cu₃O_x on a silver substrate with artificial relief.

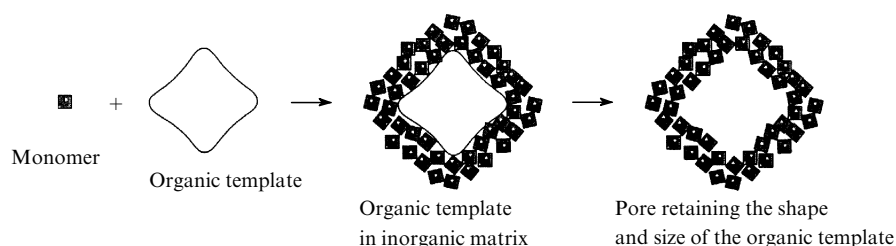


Figure 28. Scheme of the template synthesis of porous structures.

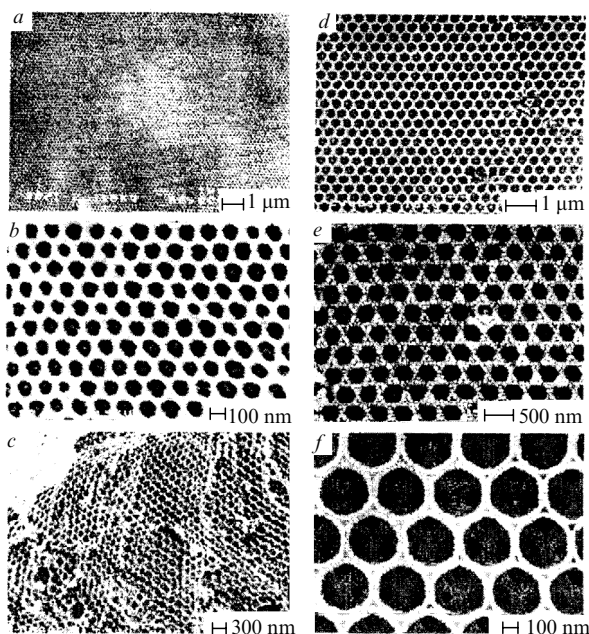


Figure 29. Typical examples of porous template structures in polyurethane-based polymeric materials (a–c) and in ceramics based on SiO₂ (d), SnO₂ (e) and TiO₂ (f).

crystals are produced artificially using specific methods of template synthesis. The 'lattice' constant of a photonic crystal is comparable with the wavelength of light (of the order of 1 μm), which is more than three orders of magnitude larger than typical lattice constants of 'normal' crystals. At the same time, this value is nearly two orders of magnitude smaller than the diameter of a human hair. A version of template synthesis of photonic silicon crystals elaborated by Vlasov *et al.*²⁵⁹ is illustrated in Fig. 30. The technique is based on self-organisation of colloidal spherical silica particles that act as an ordered template. The starting point is ordered, temperature gradient driven self-organisation of silica particles on the surface of a vertical silicon plate due to surface tension by evaporation of solvent (Fig. 30 a). The temperature gradient permits minimisation of undesired sedimentation processes. The space between spherical silica particles is uniformly filled with silicon using a CVD technique (Fig. 30 b). Then, silica is etched with hydrofluoric acid to leave a photonic crystal, *i.e.*, a periodic three-dimensional structure comprised of a porous silicon framework adjacent to the silicon chip (Fig. 30 c). Thus, self-organisation processes play a key role in the formation of template structures including photonic crystals.²⁶⁰ Two-dimensional photonic structures, *e.g.*, alumina films (Fig. 31), are also of interest. Here, the ordered pore system is formed as a result of self-organisation of alumina films during the oxidation of aluminium.²⁶¹

As mentioned in the preceding Section, nanocomposites (*i.e.*, composites comprised of nanoparticles encapsulated in a chemi-

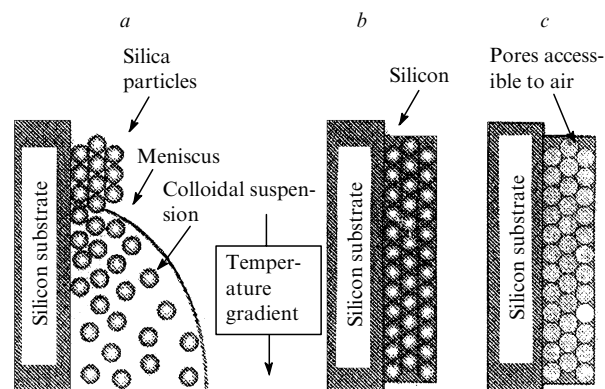


Figure 30. Scheme of the template synthesis of photonic silicon crystals (for details, see text).

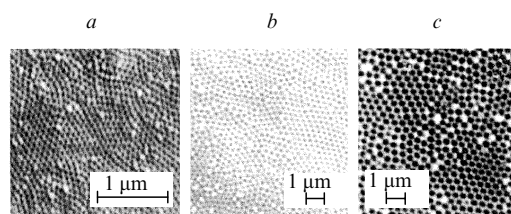


Figure 31. Micrographs of porous alumina film prepared by anodic oxidation of aluminium foil under different conditions. H₂C₂O₄, 40 V (a); H₃PO₄, 140 V (b); and H₃PO₃, 195 V (c).

cally inert matrix) belong to those promising materials whose formation is strongly affected by self-organisation processes. In this case, the matrix allows one to avoid uncontrollable aggregation of nanoparticles and protect them from external factors (*e.g.*, oxidation by air oxygen), thus facilitating practical use of such materials. Considerable attention has been paid to the method for preparation of nanocomposites,^{196, 262–264} which is based on chemical modification of layered double hydroxides (LDH). The LDH are compounds of the compositions $[M_{1-x}^{2+}M_x^{3+}(\text{OH})_2]^{A+} \cdot [(A^{n-})_{A/n} \cdot m \text{H}_2\text{O}]$, where $A = x$ at $z = 2$ and $A = 2x - 1$ at $z = 1$, M^{2+} is the metal in the oxidation state +2 or Li⁺, M^{3+} is the metal in the oxidation state +3 and A^{n-} is any anion incapable of forming stable complexes with these cations.²⁶⁵ The structure of LDH comprises positively charged hydroxide layers $[M_{1-x}^{2+}M_x^{3+}(\text{OH})_2]^{A+}$ and anions present in the interplanar space (Fig. 32), which is usually filled with labile water molecules too. This structure was named hydrotalcite after a natural mineral of the composition $\text{Mg}_{1-x}\text{Al}_x(\text{OH})_2[(\text{CO}_3)_{x/2} \cdot m \text{H}_2\text{O}]$ ($x \sim 0.25$, $m \sim 0.5$). The method for the synthesis of nanocomposites is based on chemical modification of the anions present in the interplanar space of LDH. The reaction zone is confined by the hydroxide layers, which makes the conditions for the synthesis of

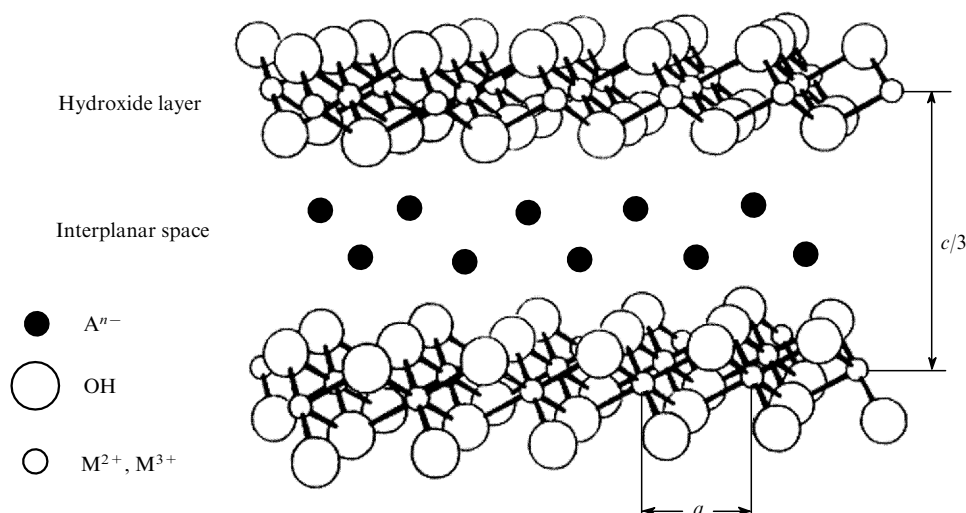


Figure 32. LDH structure.

nanophase similar to the conditions for the synthesis in two-dimensional nanoreactors.

Compounds like clays, zeolites and Chevrel's phases also have layered structures; however, only the LDH possess some unique properties that are of great importance for directed synthesis of nanomaterials.²⁶⁶ On the one hand, the LDH containing a very broad range of cations and anions (compounds with $M^{2+} = \text{Mg}^{2+}, \text{Zn}^{2+}, \text{Fe}^{2+}, \text{Co}^{2+}, \text{Ni}^{2+}, \text{Cu}^{2+}, \text{Cd}^{2+}, \text{Mn}^{2+}$ and $M^{3+} = \text{Al}^{3+}, \text{Cr}^{3+}, \text{Mn}^{3+}, \text{Fe}^{3+}, \text{Co}^{3+}, \text{Ni}^{3+}, \text{Sc}^{3+}, \text{Ga}^{3+}, \text{Ln}^{3+}$ have been characterised to date) retain stable layered structures and the interplanar space of the Mg-Al LDH can be intercalated with various anions of sizes 3 to 50 Å. On the other hand, the number of anions present in the interplanar space of the LDH is determined by the M^{2+}/M^{3+} ratio, which can be controlled with ease during the synthesis. This allows preparation of LDH with a prescribed stoichiometric composition and, hence, variation of the concentration of the reactive sites in the matrix. Besides, these compounds can retain the layered structure on thermal decomposition due to high rate of gas diffusion in the interplanar space. This permits chemical reactions involving the anions present in the interplanar space to be carried out at elevated temperatures (*e.g.*, hydrogen reduction, which is necessary for preparation of magnetic nanocomposites) without breaking the matrix that confines the reaction zone.

This synthetic approach was employed for the preparation of various LDH-based functional nanocomposites (*e.g.*, magnetic Fe- and Ni-containing nanocomposites).^{263,267} To this end, the Mg-Al LDH of various cationic compositions were intercalated

with anionic complexes of these metals [$\text{Fe}(\text{EDTA})^-$ and $\text{Ni}(\text{EDTA})^{2-}$]. The anion-substituted LDH thus obtained were reduced in a hydrogen flow at different temperatures (Fig. 33). It was shown that, depending on the LDH compositions and reduction conditions, the reaction results in one-, two- and three-dimensional metal nanostructures (Fig. 34). An increase in the content of the complex in the LDH matrix causes a decrease in the dimension of the newly formed nanostructures and an increase in the anisotropy factor. It should be noted that lowering the temperature has virtually no effect on the morphology of the nanoparticles thus formed. Namely, an increase in the reduction temperature leads to an increase in the average size of nanoparticles, while the ratio of their linear dimensions (anisotropy factor) varies only slightly. By varying the reduction temperature it is possible to vary the sizes of the newly forming nanoparticles over a rather wide range from several to several tens of nanometres. The results obtained show that magnetic nanocomposites thus obtained can be promising materials for memory devices with ultrahigh recording density.²⁶⁸

The possibility of using the LDH for preparation of semiconductor PbS nanoparticles coated with an amorphous sulfur shell is of considerable interest.^{269,270} The sulfur shell allows a substantial increase in the luminescence intensity and quantum yield. Usually, the preparation of such nanostructures requires multistage synthesis. The use of LDH allowed a single-stage synthesis of matrix isolated PbS/S nanostructures by photochemical modification of Mg-Al LDH intercalated with $[\text{Pb}(\text{S}_2\text{O}_3)_2]^{2-}$ anions (Fig. 35). Nanocomposites thus obtained possess unusual

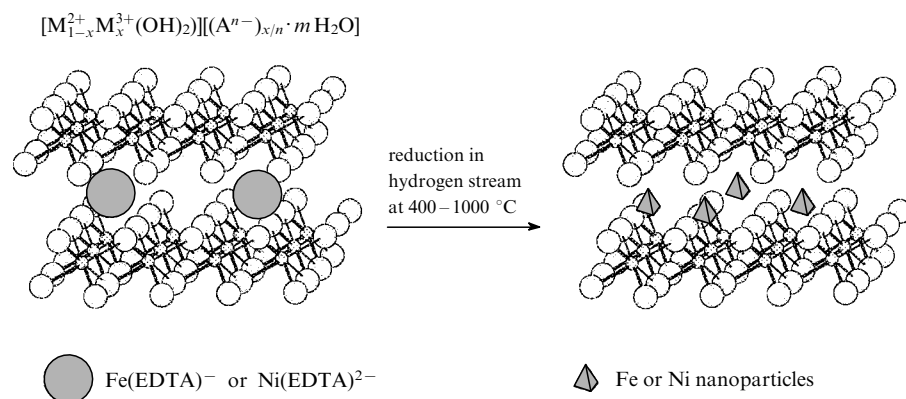


Figure 33. Scheme of preparation of nanocomposites based on iron or nickel.

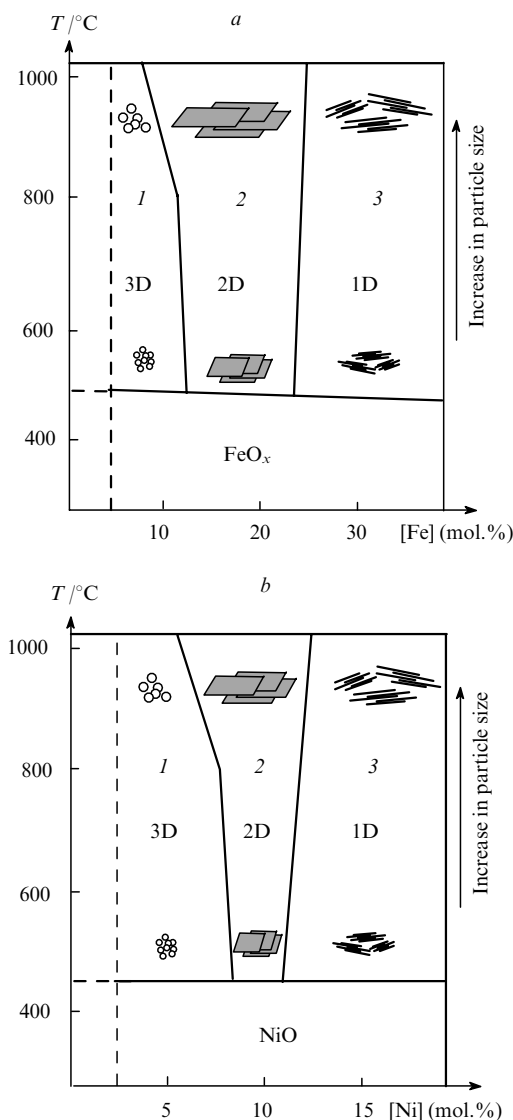


Figure 34. Diagrams showing the formation regions of different types of particles in Mg-Al-Fe(EDTA)^- (a) and $\text{Mg-Al-Ni(EDTA)}^{2-}$ (b) systems.

(a): Iron spheres of size 1–10 nm (1), iron plates 10–100 nm long and 1–3 nm thick (2) and iron wires 10–100 nm long and 1–5 nm thick (3); (b): nickel spheres of size 1–10 nm (1), nickel plates 10–70 nm long and 1–3 nm thick (2) and nickel wires 10–150 nm long and 1–5 nm thick (3).

optical properties (increased luminescence intensity, additional exciton bands in absorption spectra) due to modification of the surface of PbS nanoparticles with amorphous sulfur (Fig. 36). The use of Mg-Al LDH as precursors allows exact control of the amount of nanoparticles in the matrix by varying the Mg/Al ratio in the initial stage of the synthesis of LDH. This is of crucial importance for fabrication of optical devices based on quantum dots.

Platinum nanoparticles can be obtained in the LDH matrix in one stage.²⁷¹ Reduction of LDH intercalated with hexahydroxoplatinate(IV) anions is accompanied by the formation of platinum nanoparticles of a size of at most 10 nm. The specific catalytic activity of such nanocomposites in the oxidation of CO, hydrocarbons and alcohols is ten to fifty times higher than the activity of bulk platinum metal. As a consequence, these nanocomposites seem to be promising catalysts for the afterburning of exhaust gases. It should be noted that the approach involving LDH is not limited to preparation of the above-mentioned nanomaterials.

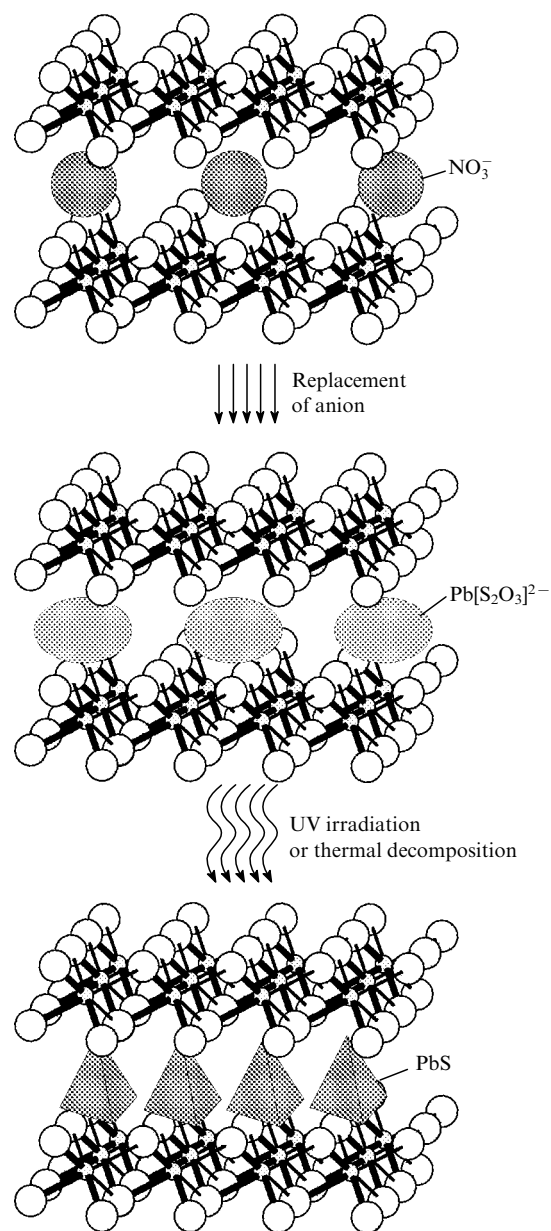


Figure 35. Scheme of the synthesis of PbS nanoparticles in a LDH matrix.

The availability of the starting compounds, simplicity and low cost of synthetic procedure, ease of control of the composition of both intermediates and end products, as well as the possibility of intercalating the LDH structure with various cations and anions make this method rather promising for the preparation of virtually all classes of nanocomposites.

Yet another method for the synthesis of nanocomposites is based on matrix stabilisation of metal and metal oxide nanoparticles of size less than 50 nm as a result of the polymerisation reaction proceeding within the solid phase.^{272, 273} In other words, the technique combines the formation of both nanoparticles and polymer matrix to stabilise them. The process proceeds as copolymerisation of metal-containing monomers that form the polymer matrix. Supramolecular organisation of nanocomposites is achieved as a result of controlled thermal transformation of the metal-containing monomers in an inert atmosphere. The main stages of this transformation are dehydration and thermal copolymerisation including self-propagating frontal polymerisation and controlled pyrolysis of the product obtained.

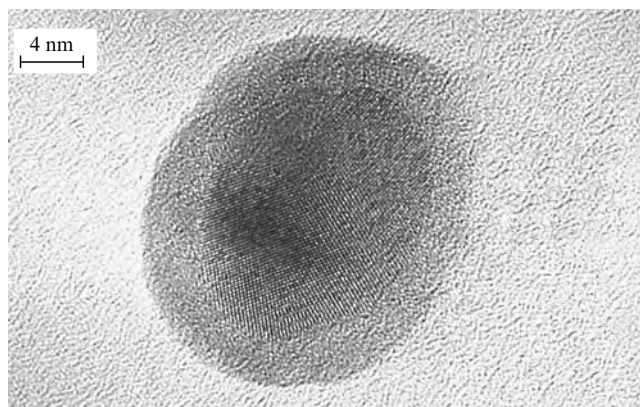


Figure 36. High-resolution electron micrograph of a PbS–amorphous sulfur core–shell nanoparticle in a LDH matrix.

By varying the copolymerisation conditions and pyrolysis temperature it is possible to prepare both nanoparticles of desired size and the necessary particle size distribution within the polymer matrix with controllable composition and thickness. The nanoparticles thus obtained are chemically bound to the polymer matrix in which they are present. Typical monomers are methacrylate, maleate and acrylamide complexes of d-metals (Co, Ni, Fe, Mn, Ti, Zr, Hf, *etc.*).

When preparing nanocomposites possessing synergistic properties, particular emphasis is placed on co-polycondensation of one or more monomeric metal complexes including both main-group (Ba, Zn, Cd, Pb) and rare-earth (Eu, La, Nd) elements. In particular, controlled thermolysis of $\text{Fe}_2\text{CoAcr}_5$ causes amorphisation of the starting crystalline phases, while the magnetic product (CoFe_2O_4) is formed in the last stage of the process. The nanocomposite thus obtained exhibits unusual properties (*e.g.*, a non-symmetric hysteresis loop and anomalous coupling between the antiferromagnetic and ferrimagnetic phases). Each magnetic particle of the nanocomposite is comprised of a spherical ferrimagnetic core (8–12 nm) and a spin glass shell 8 to 10 nm thick; ensembles of such particles can be an efficient magnetic medium.

A particular group of compounds comprises hybrid nanocomposites, which are formed from organic molecules or macromolecules (templates) and inorganic components containing optically active molecules or ions. Using methods of ‘soft chemistry’ and self-assembly at nanolevel, it is possible to create highly complex hierarchical structures with unique optical properties including high light emissive power and photochromic and electroluminescent effects.²⁷⁴

X. Biomimetism as route to advanced materials

One of the most attractive avenues in design of advanced materials involves the use of biomimetic approaches.^{275, 276} A living organism is a complex dynamic system, which exists due to continuous exchange with the environment. The exchange occurs by breathing, nourishment and excretion. In other words, dissipative self-organisation is intrinsic in any living organism.²⁷⁷ However, this does not exclude conservative self-organisation processes in certain regions of a complex system. And though the processes of conservative and dissipative self-organisation are to some extent the reverse of each other (conservative self-organisation is a result of the evolution of the system towards a decrease in the Gibbs free energy, which is achieved at high temperatures due to an increase in entropy, while dissipative self-organisation is a result of the evolution of the system towards a decrease in entropy), they likely co-exist and make different contributions to the vital activity of the complex system.^{30, 31}

Undoubtedly, both geological and biological evolution of matter obey the laws of nonlinear dynamics, but the interrelation between the processes of conservative and dissipative self-organisation changes in favour of the latter on going from inanimate to organised matter.²⁷⁸ Clearly, the pre-biological or geological evolution associated with transition from plasma to molecules, condensed phase and then to formation of simple and complex minerals is determined by processes of conservative self-organisation,²⁷⁹ whereas the phenomenon of life is intimately associated with dissipative self-organisation.²⁸⁰ Time is also of paramount importance for evolution.²⁸¹ Creating more or less complex artificial inorganic or organic structures, researchers accelerate particular processes by varying the temperature, pressure, chemical potentials of reagents, *etc.* Illustrative examples are provided by fabrication of synthetic diamonds, opals, complex oxides with spinel, perovskite, pyroxene, *etc.* structures. Considerable progress has been made towards hydrothermal synthesis of natural minerals,²⁸² which demonstrated high efficiency of approaches based on geomimetism.²⁸³ Some efforts have been undertaken, aimed at ‘adjusting’ nature by creating more perfect biological systems or their fragments by, *e.g.*, cloning. In the course of pre-biological evolution any system tends to reach a state that is most stable towards faults or fluctuations. At the same time, an increase in the complexity of a system accelerates the exchange of matter and energy, *i.e.*, biological evolution. This statement to some extent contradicts inferences about slowing down metabolism during the evolution of living systems in the course of natural selection. Nevertheless, approaches developed to create models of evolution can be employed for chemical engineering of various materials.²⁸⁴

One of the simplest methods involves the use of biomineralisation processes, in which the conditions for nucleation and crystal growth of inorganic phases are determined by the organised surface of an organic matrix. Biomineralisation processes allow preparation of various inorganic materials with nearly identical crystallites of particular compositions and structure at moderate supersaturations and temperatures.^{285, 286} A classical example is provided by the formation of oriented chains of monodomain magnetite crystals²⁸⁷ or metastable ferromagnetic based on iron sulfide involving magnetic bacteria.^{288, 289} This opens up a way towards cryochemical synthesis of advanced magnetic materials. As a rule, particles of the magnetic material are similar in size to one another and often have an unusual metastable structure.

Yet another feature of biomimetism is preferred crystallographic orientation of inorganic material relative to the organic matrix,²⁹⁰ which often represents a supramolecular structure and is comprised of polypeptide layers, polysaccharide matrices or protolipid membranes. Subsequent ordering of such organised inorgano-organic composites often causes formation of hierarchical structures,^{291, 292} which can be exemplified by mollusk shells. For instance, the shell of *Atrina sp.* comprises a layer of calcite crystals coated with an organic sheath and ordered with formation of a coherent structure. This structure is typical of many types of bioceramics and characterised by unusual structural properties. For instance, the tensile strength of bioceramics is several orders of magnitude higher than that of a material of the same composition prepared in a conventional manner.

The mechanism of the effect of an organic matrix on crystallisation of inorganic compounds was initially described in the framework of epitaxial relationships based on crystallographic similarity.²⁹³ More recently,^{294–296} it was shown that the mechanism of the influence of ordered organic matrix on the nucleation of inorganic compounds is more complicated, being a combination of at least three interfacial processes including adsorption and ordering of charged particles on the surface of the organic matrix, transcription of geometric information through ordered cations and the appearance of stoichiometric complementarity between the cations bonded to the head groups of adsorbed monolayer and

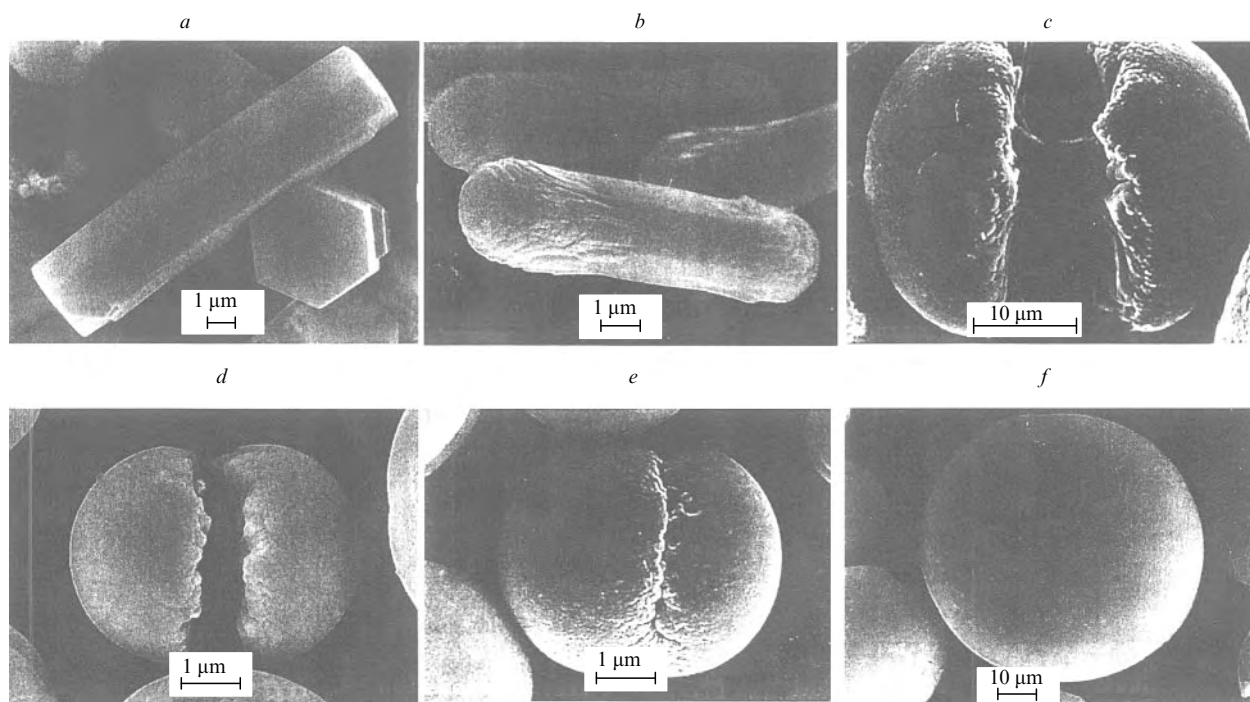


Figure 37. Electron micrographs obtained in different stages of morphogenesis of fluoroapatite aggregates. Initial stage, elongated hexagonal prismatic seeds 10 μm long (a); intermediate stages (dumb-bell aggregates) (b–d); and final stages (spheroaggregates) (e, f).³⁰¹

the local coordination environment of ions in the crystal structure of nuclei. Oriented nucleation of inorganic compounds is controlled by molecular recognition of the two-dimensional organic template and the nuclei of inorganic crystals.²⁹⁷

Of crucial interest are the results obtained in a study²⁹⁸ on the morphogenesis of fluoroapatite in denatured collagen (gelatin) matrix, which is in many ways similar to the growth of bone tissue and dentin.^{299, 300} The sequence of morphogenesis stages is shown in Fig. 37. The process begins with elongated hexagonal prismatic seeds, which are then transformed into dumb-bell structures by a fractal self-similarity mechanism, and is completed by the formation of spheroaggregates of size 150 μm . It is noteworthy that the surface of the spheroaggregates is comprised of needle-shaped fragments. Figure 38 presents the results of a two-dimensional computer simulation,³⁰¹ which clearly illustrates the possibility of fractal growth of the system from a seed to a closed fluoroapatite

spheroaggregate. The fractal mechanism of morphogenesis of the fluoroapatite particles was related to the assumption of the existence of intrinsic electric fields that control the crystal growth. This means that both crystalline seeds and products of morphogenesis are permanent dipoles. The polarity of collagen and the structural features of apatites $\text{Ca}_5\text{X}[\text{PO}_4]_3$ ($\text{X} = \text{F}^-, \text{Cl}^-, \text{OH}^-$),³⁰² in which the distribution of the anions X can be varied from centrosymmetrical to non-centrosymmetrical, confirm this model. It should be taken into account that extremely mild biomimetic growth conditions, which must favour a high degree of atomic ordering, cause an asymmetric displacement of the anions X from the equilibrium positions in the mirror plane³⁰³ and a (possible) reduction of symmetry from the centrosymmetrical point group $6/m$ to the pyroelectric point group 6. Finally, the polar organic component and inorganic crystals can exhibit synergism, thus forming an ordered composite structure in

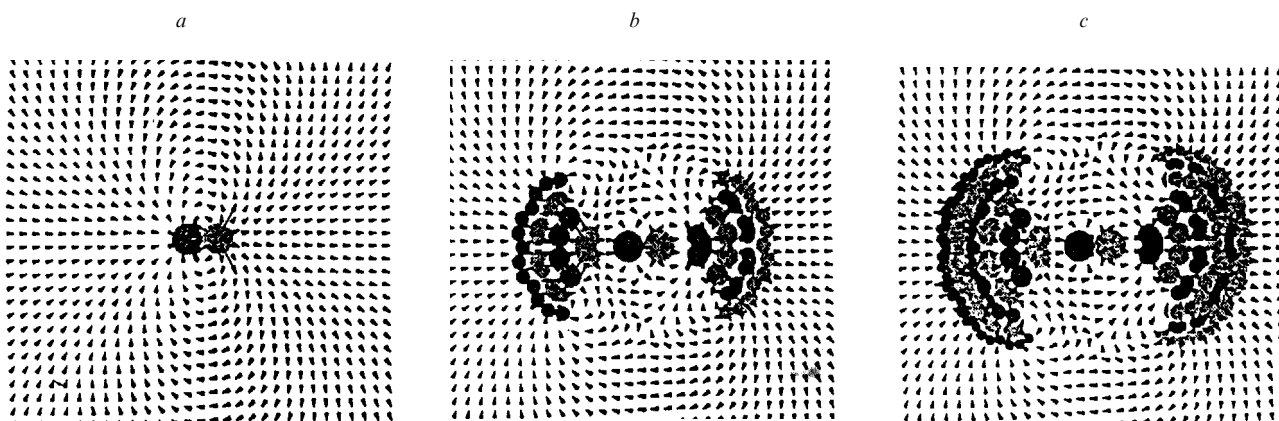


Figure 38. Two-dimensional evolution models of an intrinsic electric field around a growing fluoroapatite spheroaggregate. Each permanent dipole is represented by a combination of black and gray circles denoting the positive and negative charge, respectively; seeds (a); the growing spheroaggregate: seed + 2 generations (b) and seed + 3 generations (c). Arrows denote the directions of the electric field lines.³⁰¹

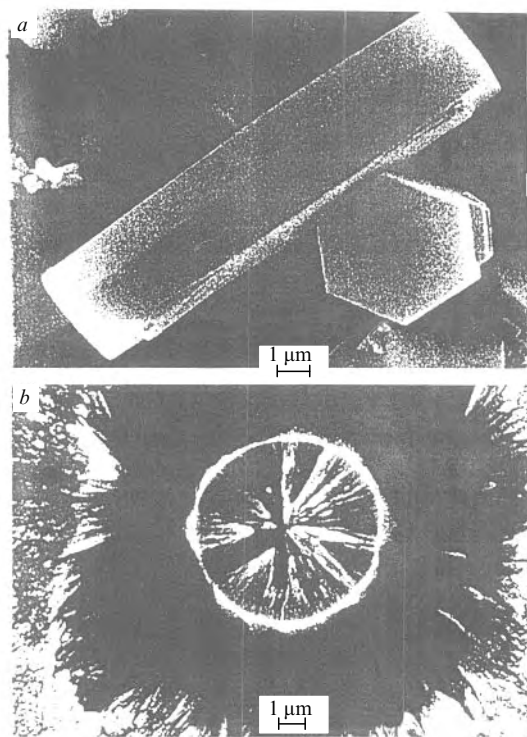


Figure 39. Electron micrographs of a hexagonal prismatic fluoroapatite seed (a) and its fracture area perpendicular to the seed axis (b).²⁹⁸

which the *c* axis of apatite crystals is oriented parallel to the long axis of collagen fibres.²⁷⁵

Returning to the morphogenesis of fluoroapatite, it should be noted that completion of the fractal growth (formation of spherical particles) is followed by formation of concentric shells comprised of elongated prismatic fluoroapatite seeds with nearly parallel orientation (the maximum diameter of the core + shell particle is 1 nm) and that the structure of the particle has much in common with the structure of dentin. Hexagonal prismatic seeds of fractal aggregates (see Fig. 39) are not single crystals, as is clearly demonstrated in the micrograph of the fracture area perpendicular to the seed axis. The cross-section shows that formation of the hexagonal prism begins with the central seed, which can be formed due to rearrangements of the gelatin molecules, which can serve as active nucleation centres of apatite. The size of apatite crystallites was not exactly determined, it can lie between nanoscale and mesoscopic levels. Thus, the hexagonal prismatic macroscopic seed is an inorgano-organic composite with an ordered hierarchical superstructure rather than a single crystal.

XI. Conclusion

Modern revolutionary changes in chemistry and technology of materials are closely related to the changes in the fundamental concepts of spatio-temporal evolution of materials.³⁰⁴

Self-organisation processes in the physicochemical systems used as precursors are of great importance for the design of advanced materials, since usually their evolution occurs under strongly nonequilibrium conditions. Conservative and dissipative self-organisation, which best manifest themselves in isolated and open systems, respectively, can accompany each other, thus making the description of the evolution of corresponding physicochemical systems much more complicated. Nonlinear patterns of evolution from precursor to the target solid-phase product complicates the optimum organisation of the reaction zone. Ideally, the precursor or the solid-phase intermediate from which

the solid-phase product is formed must be a composite comprised of a highly homogeneous amorphous matrix and a nanotemplate, which provides a necessary direction of bulk crystallisation.

Application of dissipative chaos models to poorly reproducible physicochemical systems allows valuable information on their dynamics to be obtained. Of crucial importance are the self-organisation processes with formation of supramolecular ensembles and supramolecular materials bonded through noncovalent intermolecular bonds.³⁰⁵

Research on self-organisation phenomena in nanosystems¹⁴⁷ provides an insight into the conditions for formation of various structures (from nanocrystals to nanocomposites). Particular emphasis should be placed on the formation of fractal, epitaxial and template structures as well as nanocomposites that are used in the design of functional materials.

The use of models of bio-evolution, biomimetism and biomineralisation opens up attractive prospects for the creation of smart materials that will be highly competitive with natural materials and in some cases be superior to them.^{306–308}

The author of this review would consider the goal sought in writing this review attained if he was able to show that the most promising and 'stylish' avenues of research in the field of materials science, which are associated with the design of seemingly quite different materials, have much in common. This first of all concerns the algorithm of description of complex open physicochemical systems, which exchange energy and matter with the environment but allow control of the evolution from precursors to target solid-phase products.

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Nucleophilic substitution of the nitro group, fluorine and chlorine in aromatic compounds

V M Vlasov

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Abstract. The published data on the comparative activities of the nitro group, fluorine and chlorine in aromatic nucleophilic substitution reactions are generalised and systematised. The factors influencing the relative activities of these substituents, viz., the structure of the substrate, the nature of the nucleophile and reaction conditions, are discussed. The synthetic applications and possible mechanisms of nucleophilic substitution of the nitro group, fluorine and chlorine in aromatic compounds are considered. The bibliography includes 265 references.

I. Introduction

Nucleophilic aromatic substitution is still the field of organic chemistry that is the most intensively developed^{1,2} owing to the diversity of reaction mechanisms^{1–4} and high synthetic potentials of these reactions.^{5–7} Nucleophilic substitution of hydrogen (S_N^H) in arenes is an efficient approach to their functionalisation,^{1,2,8,9} but *ipso*-substitution (S_N^{ipso}) of the nucleofugal group in aromatic compounds is of no less importance, since it allows regioselective synthesis of not only *ortho*- and *para*-isomers, but also of their *meta*-derivatives.¹ The present review is mostly concerned with the S_N^{ipso} reactions of arenes under the conditions where the role of a nucleofuge is played by the nitro group or halogens (fluorine and chlorine).^{1,10–12} The popularity of these leaving groups is due primarily to the high accessibility of the corresponding derivatives^{13–16} and activity of these groups in aromatic nucleophilic substitution reactions.^{1,10–12,17}

Some physicochemical characteristics of the Ar–X bonds and the leaving groups X, where X = NO₂, F and Cl, are given in Table 1. The C–F bond is much shorter, more stable and less polarisable than the C–NO₂ and C–Cl bonds. The NO₂ and F groups are characterised by a strong polar effect (*cf.* relatively high values of the constants σ_X and σ_F), but the steric (E_S) and polarisability (σ_X) effects for the NO₂ group are much stronger

than those for fluorine (the minus sign designates an enhancement of the corresponding effect). Chlorine is the most polarisable and the least electronegative among the substituents mentioned. These characteristics of the leaving groups X have a pronounced effect on their relative activities in nucleophilic substitution reactions. The rates and directions of these reactions depend on the structure of the starting arene, the nature of the nucleophile and the experimental conditions. A combination of these factors determines the reaction mechanism.^{11,12,17,23} For this reason, an analysis of kinetic data on the comparative activities of a nitro group, fluorine and chlorine bound to an aromatic ring is very important for the correct choice of the most efficient approaches to the synthesis of functionalised arenes.¹⁶

Nucleophilic substitution of the aromatic nitro group has been reviewed previously²⁴ with the main emphasis on the synthetic results. The present review is devoted to the analysis and systematisation of the data on comparative activities of the NO₂, F and Cl groups in arenes under the action of various nucleophilic agents published in the past 10–15 years. The main emphasis is laid on reactions of NO₂-, F- or Cl-substituted aromatic compounds with anions as nucleophiles.

Table 1. Characteristics of the Ar–X bonds and groups X in substituted arenes.

Parameter	Group X			Ref.
	NO ₂	F	Cl	
Bond length /Å	1.4982	1.305	1.766	15, 18
Bond dissociation energy /kJ mol ^{–1}	298.0	525.4	400.0	19
Refraction of the Ar–X bond /cm ³	6.9	1.43	6.62	20
Constants:				
electronegativity (σ_X)	0.46	0.70	0.16	21
polarisability (σ_X)	–0.26	0.13	–0.43	21
field (σ_F)	0.65	0.44	0.45	21
resonance (σ_R)	0.18	–0.25	–0.17	21
steric (E_S) (see ^a)	–0.75	0.49	0.18	22

^a The constant of the *ortho*-substituent X ($E_S = 0$ for the CH₃ group) is given.

V M Vlasov N N Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, prosp. Akad. Lavrent'eva 9, 630090 Novosibirsk, Russian Federation.
Fax (7-383) 234 47 52. Tel. (7-383) 234 38 33.
E-mail: vmvlasov@nioch.ncs.ru

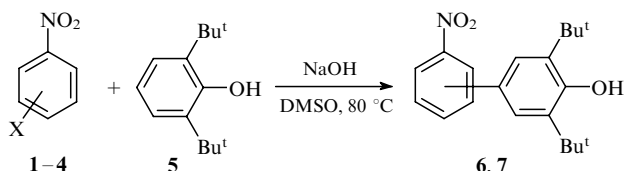
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II. Reactions with carbanions

The methods for the formation of a new carbon–carbon bond in arenes, particularly through aromatic nucleophilic substitution of the nitro group, fluorine and chlorine under the action of carbanions, have been discussed previously.^{7,25} We shall dwell only on specific features of carbanions in the reactions from the standpoint of relative activities of the substituents mentioned.

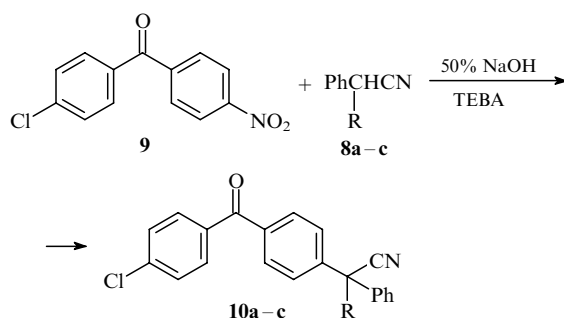
Thus the arylation of 4- and 2-substituted nitrobenzenes **1–4** under the action of a 2,6-di-*tert*-butylphenol anion (**5**), which acts as a C- rather than an O-nucleophile due to steric hindrance, yields 4- and 2-nitro-substituted biphenyls **6** and **7** according to the S_NAr mechanism.



Compound	X	Reaction time /h	Product	Yield (%)
1	4-NO ₂	3	6	77
2	2-NO ₂	17	7	64
3	2-F	18	7	97
4	2-Cl	24	7	71

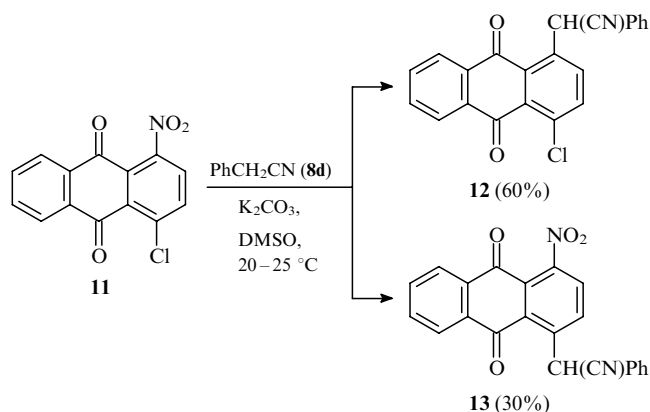
Although the results of this study are purely qualitative,²⁶ it is nevertheless evident that the activity of fluorine is higher than that of the nitro group or chlorine. Obviously, steric hindrance in the 1,2-disubstituted substrate **2** decreases the activity of the nitro group making it similar to that of chlorine. Therefore, the activity of the nitro group in sterically non-hindered 1,4-dinitrobenzene (**1**) is much higher.²⁶

Under conditions of phase-transfer catalysis, carbanions of disubstituted acetonitriles **8a–c** attack 4-chloro-4'-nitrobenzophenone (**9**) exclusively with the substitution of the nitro group and the formation of the chloro derivatives **10a–c**.²⁷



R = Me (**8a**; **10a**, 75%), Prⁿ (**8b**; **10b**, 78%), Bn (**8c**; **10c**).

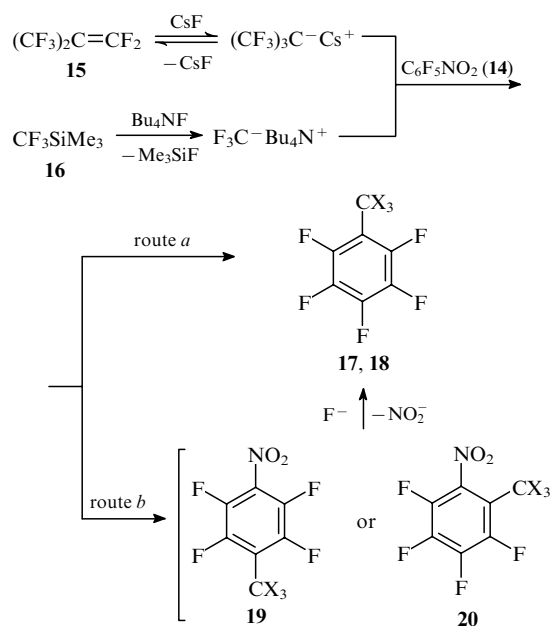
Similarly, a higher activity of the nitro group in comparison with chlorine was observed in the reaction of a tricyclic 1-chloro-4-nitrobenzene analogue **11** with the phenylacetonitrile carbanion **8d** (R = H), the yield of 1-chloro-4-(α -cyanobenzyl)anthraquinone (**12**) being twice as high as that of 1-(α -cyanobenzyl)-4-nitroanthraquinone (**13**).²⁸



These results can be explained by the softness of the carbanions **8** which preferentially attack the carbon atom of the C–NO₂ group which makes a more significant contribution to LUMO (orbital control) than the carbon atom of the C–Cl group which bears a higher positive charge (charge control).²⁹

Reactions of pentafluoronitrobenzene (**14**) with perfluoro-*tert*-butyl and trifluoromethyl anions [these are generated from perfluoroisobutylene (**15**) and trifluoromethyltrimethylsilane (**16**), respectively under the action of the fluoride ion] afford formally the substitution products of the nitro group **17** and **18**.^{30–32} However, the mechanism of direct nucleophilic substitution (route *a*) can be argued (Scheme 1).

Scheme 1

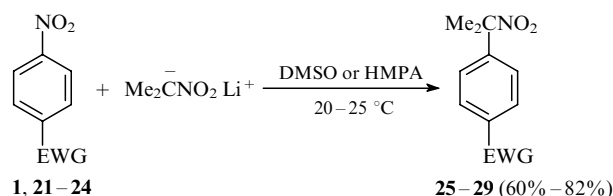


X = CF₃ (**17**, 65.5%), F (**18**, 90%).

Indeed, in the reactions of pentafluoronitrobenzene with nucleophilic reagents (hard N- and O- or soft S-anions) it is the fluorine atom in position 2 or 4 that is usually replaced whereas the nitro group remains unaffected.^{33,34} It is therefore more likely that this reaction occurs according to the route *b* where the additionally activated nitro group in the intermediate compounds **19** and **20** is replaced by the fluoride ion resulting in perfluoro-*tert*-butylbenzene (**17**) or perfluorotoluene (**18**).^{30,35} Supporting evidence in favour of this route can be derived from the yields of

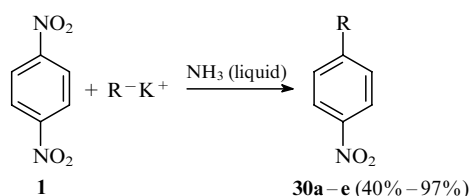
compounds **17** and **18**: the yield of a direct substitution product according to the route *a* is smaller for the more nucleophilic perfluorobutyl anion. Moreover, the more electron-withdrawing CF₃ group in the intermediates **19** and **20** significantly facilitates the substitution of F for the NO₂ group.

The nitro group in compounds **1**, **21–24**, which is activated by an electron-withdrawing substituent, is readily replaced even by weakly basic nitroalkane anions in aprotic polar solvents to give compounds **25–29**.^{36–38}



EWG = NO₂ (**1**, **25**), CN (**21**, **26**), SO₂Ph (**22**, **27**), CO₂Me (**23**, **28**), CPh (**24**, **29**).

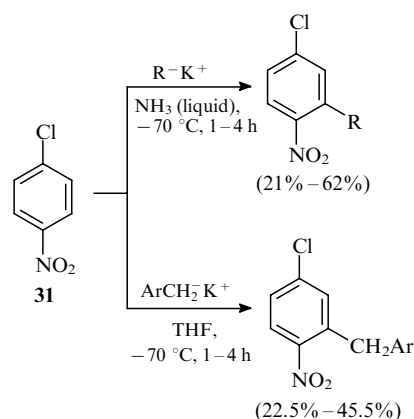
The bulky tetrabutylammonium cation can be used as a counterion for accelerating these reactions and promoting better separation of the ion pairs.^{39,40} A similar effect is observed when the reactions of compound **1** with stabilised carbanions of different basicities are carried out in liquid ammonia;⁴¹ this reaction gives nitroarenes **30a–e**.



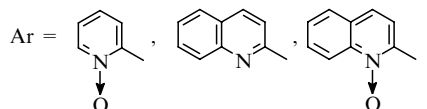
R = CH₂COMe (**a**), CH(Me)COEt (**b**), CH₂CO₂Et (**c**), CH₂CN (**d**), CH(Ph)CN (**e**).

As a rule, the reactions of carbanions with substitution of the nitro group, fluorine and chlorine in arenes proceed according to the S_NAr mechanism with formation of a σ-complex in the limiting step. This is corroborated by the results of kinetic studies of reactions of 9-substituted fluorenyl anions with *para*-halonitrobenzenes in DMSO, the activities of the leaving groups changing in the following order: F > Cl > Br ≈ I; the ratio of the reaction rate constants (*k*_F/*k*_{Cl}) is 3.5–8.0 (see Ref. 42). Free ions or solvent-separated ion pairs are more reactive than contact ion pairs (for reactions in THF).⁴³

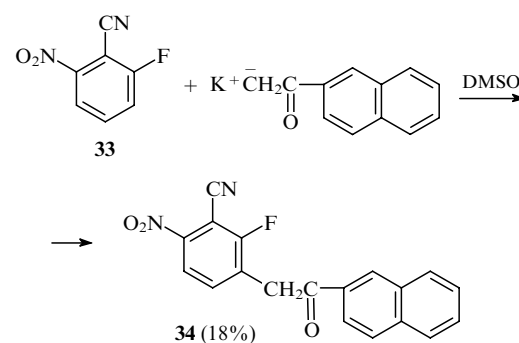
The formation of stable anionic σ-complexes at unsubstituted positions of the aromatic ring is a distinguishing feature of reactions of some carbanions with substituted halogeno- and nitroarenes; their further conversions yield S_N products as a result of oxidation or vicarious nucleophilic substitution with retention of the nucleofugal groups.^{9,25,44} This route is realised not only for low-active substrates, such as nitro-⁴⁵ and 1,3-dinitrobenzenes,²⁶ 1-nitro-^{46,47} and 1,8-dinitronaphthalenes⁴⁸ and 9-nitroanthracene,⁴⁹ but also for substrates with highly reactive nitro groups and halogens, *e.g.*, 1,3,5-trinitrobenzene,⁵⁰ 4-nitrophthalonitrile,⁵¹ 4-chloro- (**31**) and 4-fluoronitrobenzenes (**32**), 1,4-dinitrobenzene (**1**), halo-2,4-dinitrobenzenes^{25,44,52,53} and 3,6-dichloropyridazine as well as 2-chloro-3- and -5-nitropyridines.⁵⁴ The direction of the substitution of the leaving group or hydrogen in arenes under the action of carbanions depends not only on the structure of the substrate but also on the nature of the nucleophile and the reaction conditions. Thus compound **31**, in contrast to the 1,4-dinitro derivative **1**,⁴¹ reacts with some stabilised carbanions in liquid ammonia or THF with substitution of hydrogen rather than halogen. In this case, the starting nitro compound seems to serve as an oxidant of the corresponding σ-complex.^{55,56}



R = CH₂COMe, CH(Me)COPh, CH₂CN, CH₂CO₂But⁴¹;

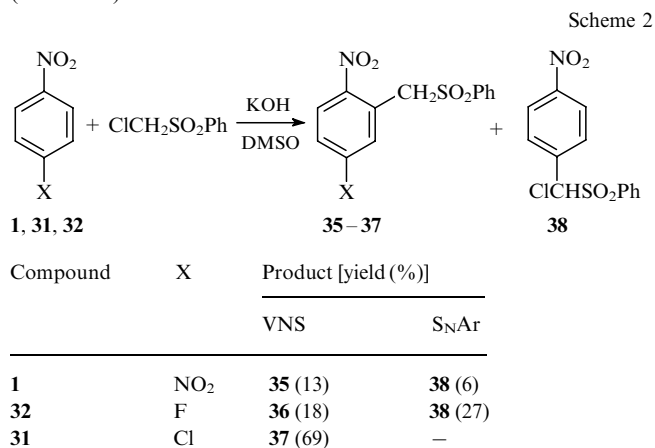


Similarly, the main reaction product of 2-acetylnaphthalene anion with 2-fluoro-6-nitrobenzonitrile (**33**) in DMSO retains all the functional groups in the benzene ring, *viz.*, 2-fluoro-3-(2-naphthoylethyl)-6-nitrobenzonitrile (**34**).⁵⁷



The activated nitro group is unaffected under these conditions, which may be ascribed to the steric effect.

Under conditions of vicarious nucleophilic substitution (VNS), the substrates **1** and **32** containing reactive NO₂ and F groups react with chloromethylphenyl sulfone according to both VNS and S_NAr mechanisms. At the same time, 4-nitrochlorobenzene **31** reacts exclusively according to the vicarious route (Scheme 2).^{44,52}

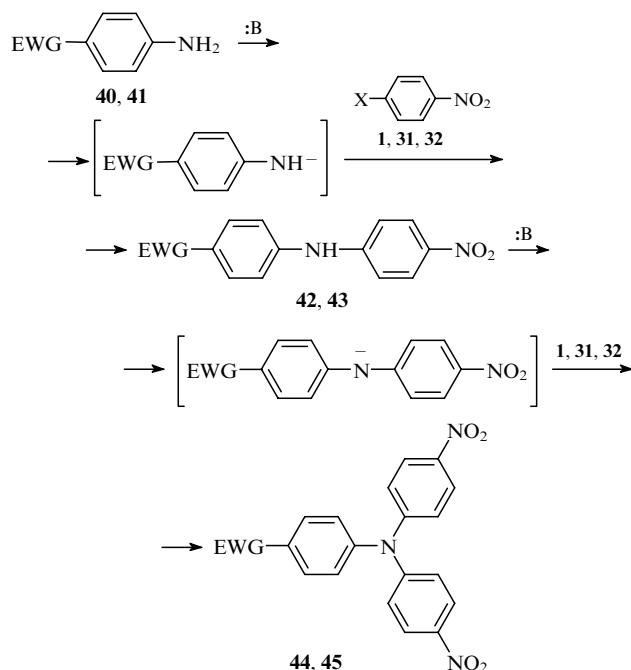


In those cases where VNS is to be employed for the preparation of products with preservation of nucleofuges in the aromatic ring, it is desirable that the starting arene contains neither activated nitro group nor fluorine.

In conclusion it may be mentioned that reactions of structurally different carbanions with arenes most often result in the substitution of the most active nucleofuges NO₂ and F according to the S_NAr mechanism. The substitution of chlorine in arenes under the action of the same C-anions according to the S_N^{ipso} mechanism proceeds at a much slower rate and shows a tendency for hydrogen substitution (the S_N^H mechanism).

III. Reactions with N- and P-anions

Like carbanions, N- and P-anions naturally manifest certain specificity with respect to the substitution of the nitro group, fluorine and chlorine in arenes. The differences in the activity, *i.e.*, the ratios of the rate constants of the substitution reactions[†] of fluorine and chlorine in arenes under the action of N-anions **39a,b**, are usually of about two orders of magnitude (Table 2)⁴² and the activity of fluorine in these reactions is similar to that of the nitro group.⁵⁸ Presumably, steric hindrance in the N-anion should decrease the activity of the bulky nitro group in arenes and make it similar to the activity of chlorine. Thus the reactions of N-anions of 4-cyanoaniline (**40**) or 4-nitroaniline (**41**) with 4-substituted nitrobenzenes **1**, **31** and **32** afford di- (**42**, **43**) and triarylamines (**44**, **45**); their ratios depend on the nature of the leaving group X (Table 3).^{58–60}

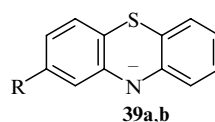


EWG = CN (**40**, **42**, **44**), NO₂ (**41**, **43**, **45**);

:B is base; X = NO₂ (**1**), Cl (**31**), F (**32**).

Under the action of the N-anions of anilines **40** and **41**, the relative activities of the leaving groups X in compounds **1**, **31** and **32** decrease in the following order: F ≥ NO₂ > Cl.⁵⁹ However, the activities of the same substituents under the action of the N-anions of diarylamines **42** and **43** decrease in the following order: F ≫ NO₂ ≈ Cl.⁵⁸ The sharp (in comparison with the activity of fluorine in the latter reaction) decrease in the activity of the nitro

Table 2. Basicities of N-anions (pK_B)

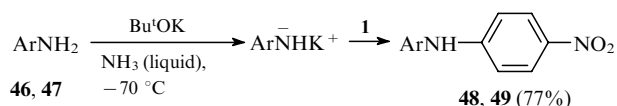


and the rate constants for the halogen substitution reactions in compounds **31** and **32** (DMSO, 25 °C; the counterion is K⁺).⁴²

Anion	R	pK _B	Compound	X	k ₂ /litre mol ⁻¹ s ⁻¹	k _{rel} = k ₂ ^F /k ₂ ^{Cl}
39a	H	22.72	31	Cl	9.95 × 10 ⁻³	94.5
			32	F	0.941	
39b	Cl	20.79	31	Cl	4.35 × 10 ⁻⁴	214
			32	F	9.31 × 10 ⁻²	

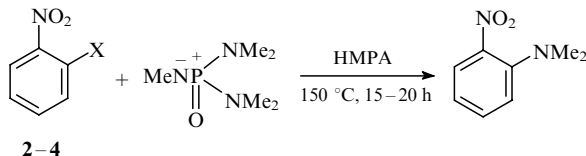
group, which is similar to that of chlorine, seems to be due to its steric (but not polar) effect⁵⁸ (see Table 1).

Obviously, it is for this reason that the reactions of the N-anions generated from aniline (**46**) and 2-aminopyridine (**47**) with 1,4-dinitrobenzene (**1**) give exclusively diarylamines **48** and **49** in high yields.⁴¹



Ar = Ph (**46**, **48**), 2-Py (**47**, **49**).

Reactions of the dimethylamide anion (from HMFTA) with *ortho*-substituted nitrobenzenes corroborate the fact that in the absence of steric hindrance in the N-anion the activity of the nitro group is high and comparable to that of fluorine.⁶¹ In this case, the activities of the NO₂, F and Cl groups were determined from the degree of conversion of the starting compounds **2–4** after 5 h (GLC and NMR).



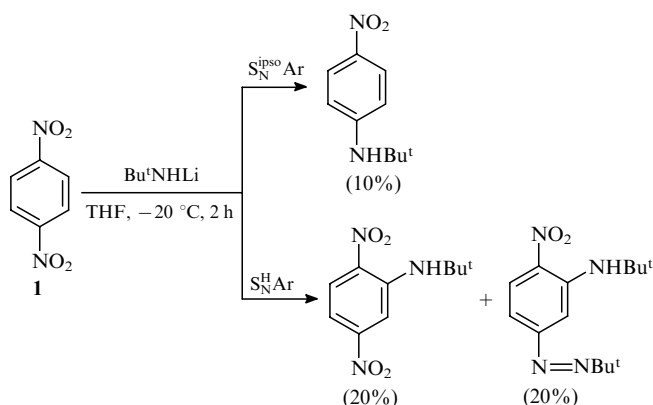
Compound	X	Conversion of compounds 2–4 (%)	
		GLC	NMR
2	NO ₂	93	86
3	F	84	83
4	Cl	41	40

Steric hindrance in the N-anion changes the direction of the reaction, which sharply decreases the yields of the substitution products of the nitro group. Thus the substitution of the nitro group in the reaction of lithium *tert*-butylamide with 1,4-dinitrobenzene (**1**) proceeds with a rather small yield (10%), while the substitution of the hydrogen atom occurs to a larger extent. In this case, the nitrite ion generated in the S_N^{ipso} Ar reaction⁶² behaves as an oxidant of the corresponding σ-complex in the substitution of the hydrogen atom.⁶² This occurs in parallel with partial reduction of the nitro compound formed by the hydride ion liberated in the reaction and condensation with *tert*-butylamine.

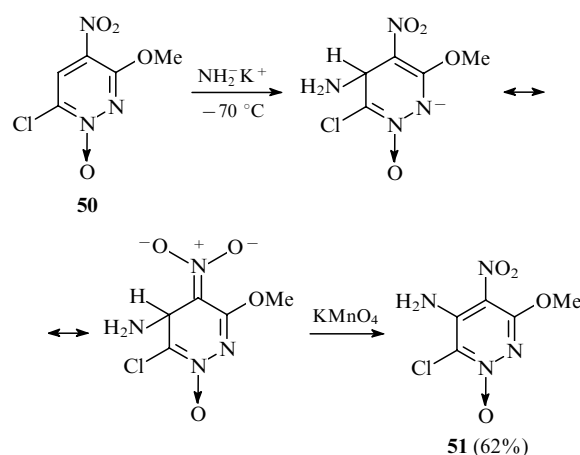
[†] This parameter is always indicated for identical conditions.

Table 3. Ratios of the yields of di-(**42**, **43**) and triarylamines (**44**, **45**) in the reaction of 4-substituted anilines **40** and **41** with nitrobenzenes **1**, **31** and **32**.^{58–60}

Nitroarene	X	Aniline	:B	Solvent	Temperature /°C	Time /h	Reaction products [yield (%)]	
							diarylamine	triarylamine
1	NO ₂	40	K ₂ CO ₃	DMSO	120–130	5	42 (50)	44 (3)
32	F	40	K ₂ CO ₃	DMSO	120–130	5.5	42 (5)	44 (64)
31	Cl	41	K ₂ CO ₃	DMSO	145–150	5	43 (71)	45 (1–2)
31	Cl	41	NaH	DMF	100	2	43 (38)	—

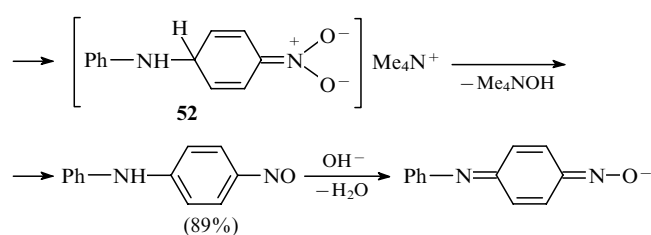
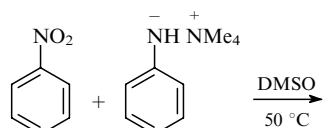


Substitution reactions of hydrogen in (het)arenes, which occur with retention of the halogens and/or the nitro group in the ring, are very typical of N-anions. They involve the intermediate formation of a σ^H -complex which can react with an external oxidant to give a substituted (het)arene.^{2,63} Thus the reaction of 6-chloro-3-methoxy-4-nitropyridazine *N*-oxide (**50**) with potassium amide yields a σ -complex at the unsubstituted position 5 of the ring; this complex is further oxidised to the aromatic amine **51**.⁶⁴

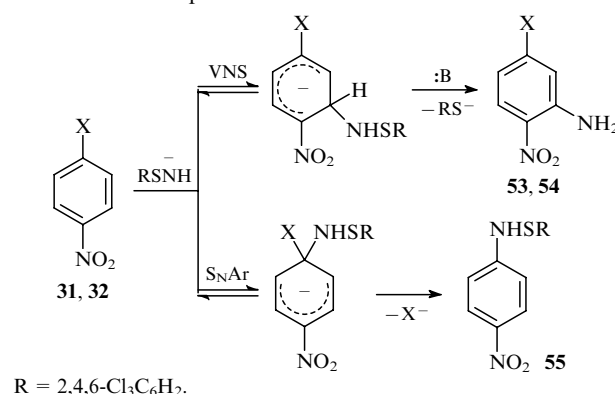


Other examples of nucleophilic hydrogen substitution with retention of the nitro group and the chlorine atom in the azine ring have been described.^{2,63}

Intramolecular oxidation of a σ -complex is also possible. Thus the oxidation of the σ -complex **52** by the nitro-group oxygen is the main direction in the reaction of the anilide ion with nitrobenzene.⁶⁵



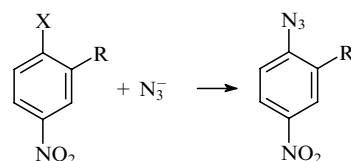
The conversion of the σ -complex can also proceed according to the vicarious substitution route. In this case, the N-nucleophile should contain a good leaving group, e.g., a triazole,⁶⁶ an ammonium⁶⁸ or a sulfide group.⁶⁹ However, in contrast to chlorine, the substitution of fluorine in arenes follows the S_NAr mechanism rather than VNS. The formation of compounds **53–55** is an example.⁶⁹



R = 2,4,6-Cl₃C₆H₂.

Compound	X	Products [yield (%)]
31	Cl	53 (60), 55 (0)
32	F	54 (7), 55 (66)

The relative activities of the nitro group, fluorine and chlorine in reactions of arenes with the azide ion change in the following order: NO₂ ≥ F ≫ Cl (see Ref. 11, p. 165; Refs 70 and 71). This dependence was established for the substitution of the 4-nitrobenzene derivatives **1**, **31**, **32** and **56–59** (Table 4):



1, **31**, **32**, **56–59**

R = H: X = NO₂ (**1**), Cl (**31**), F (**32**), I (**56**);

R = NO₂: X = F (**57**), Cl (**58**), I (**59**).

The nitro group activated by the electron-withdrawing substituents in the arene is readily replaced by a small-size azide ion in *N*-methyl-3,5-dinitroththalimide,⁷² 3-nitrothioxanthone deriva-

Table 4. Rate constants for the reactions of 1-X-4-nitrobenzenes (**1**, **31**, **32**, **56**) and 1-X-2,4-dinitrobenzenes (**57–59**) with the azide ion.^{11,70,71}

Compound	R	X	Solvent	Temperature /°C	$10^4 k_2$ /litre mol ⁻¹ s ⁻¹	$k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$
1	H	NO ₂	MeOH	100	5.31	78.7 ^a
32	H	F	MeOH	100	2.32	68.8
			PhCl	80	649	54.1
31	H	Cl	PhCl	80	9.5	0.79
56	H	I	MeOH	100	0.0338	1
			PhCl	80	12	1
57	NO ₂	F	MeOH (25%)	25	400	432
58	NO ₂	Cl	MeOH (25%)	25	0.79	0.85
59	NO ₂	I	MeOH (25%)	25	0.925	1

^a With allowance for the statistical factor.

tives,⁷³ 2,5-dinitro-4-trifluoromethyl- and 5-chloro-2-nitrobenzonitriles⁷⁴ and 2-chloro-1-nitroanthraquinone.⁷⁵ In the case of 1-chloro-2-nitro- and 2-chloro-3-nitroanthraquinones containing a less active nitro group, it is only chlorine that is substituted.⁷⁶

Some ambident ions (NO₂⁻, SCN⁻) react as N-anions in S_NAr reactions. The activities of the substituted groups in 1-X-4-nitrobenzenes **1**, **31** and **32** in their reactions with the nitrite ion decrease in the following order: F > Cl ≈ NO₂,[‡] while those in 1-X-2,4-dinitrobenzenes **57**, **58** and **60** change as follows: NO₂ > Cl > F (Table 5).^{77,78} The reason for the change in the activities of substituents is that the limiting step of the reaction of low-reactive substrates with the nitrite ion is the formation of the σ-complex, in the reaction with highly reactive substrates it is its decomposition.⁷⁸ Thus, it is reasonable to use chlorine as a leaving group (especially in the case of highly reactive arenes) for the introduction of the nitro group into arenes according to the S_NAr mechanism. This has recently been demonstrated for the synthesis of 1,2,4-trinitrobenzene (**60**) from 2,4-dinitrochlorobenzene (**58**) and KNO₂ under the conditions of phase-transfer catalysis (yield 71%).⁷⁹ Substitution of the nitro group for fluorine is especially efficient in the case of low-reactive arenes, *e.g.*, penta- or hexafluorobenzenes.⁸⁰

Table 5. Rate constants for the reactions of 1-X-4-nitrobenzenes **1**, **31** and **32** and 1-X-2,4-dinitrobenzenes **57**, **58** and **60** with the nitrite ion (DMSO).^{77,78}

Compound	X	Temperature /°C	$10^2 k_2$ /litre mol ⁻¹ s ⁻¹	$k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$
1	NO ₂	100	158	0.89
32	F	100	1290	7.25
31	Cl	100	178	1
60	NO ₂	25	680	17
57	F	25	3.2	0.08
58	Cl	25	40	1

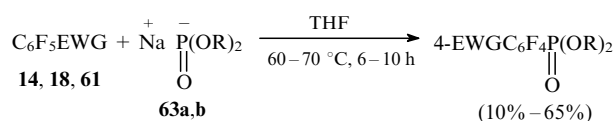
In the case of the thiocyanate ion, the activities of the leaving groups in the S_NAr reaction with 2,4-dinitrobenzenes **57**, **58** and **60** change in the following order: F ≈ NO₂ > Cl (Table 6).⁸¹ The formation of the σ-complex is the limiting step of this reaction.

P-Anions react with nitro- and haloarenes to form preferably hydrogen substitution products rather than functional-group substitution products. Hydrogen substitution is observed not only for activated arenes, *e.g.*, trinitrobenzene⁸² and 1-chloro-4-nitronaphthalene,⁸³ but also for less reactive substrates, such as 1-amino- and 1-methoxy-4-nitronaphthalenes⁸⁴ and 1-nitronaph-

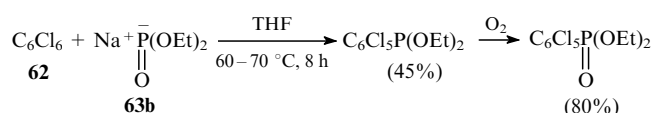
Table 6. Rate constants for the reactions of 1-X-2,4-dinitrobenzenes **57**, **58**, **60** with the thiocyanate ion SCN⁻ (DMSO, 75.2 °C).⁸¹

Compound	X	$10^3 k_2$ /litre mol ⁻¹ s ⁻¹	$k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$
60	NO ₂	1	50
57	F	1	50
58	Cl	0.0199	1

thalene.⁸⁵ However, S_NAr-substitution of fluorine and chlorine in activated polyhaloarenes **14**, **18**, **61** and **62** under the action of the dialkyl phosphite ions **63** is also possible in moderate yields.^{86,87} These reactions are usually carried out in weakly polar aprotic solvents (*e.g.*, ethers, hydrocarbons).



EWG = NO₂ (**14**), CF₃ (**18**), CN (**61**); R = Me (**63a**), Et (**63b**).



Thus the N-anions of amines and the P-anions of dialkyl phosphites replace hydrogen in reactions with arenes, which is mainly due to steric factors. Compact inorganic azide, nitrite and thiocyanate ions readily replace the nitro group, fluorine and chlorine in activated arenes according to the S_NAr mechanism; in the case of the nitrite ion, the electrophilicity of the substrate determines the limiting step of the process.

IV. Reactions with O- and S-anions

The majority of papers devoted to nucleophilic substitution of the nitro group, fluorine and chlorine in arenes deal with their reactions with O- and S-anions. Many such reactions have been reviewed previously,^{1,7,10–12,20,24} but a series of important kinetic studies in this area has appeared only in the past 10–15 years. The main differences in the relative activities of aromatic substituents under the action of hard O- or soft S-anions are determined by the different nature of the nucleophiles.^{20,88} S-Anions are much more reactive in both S_N2⁸⁹ and S_NAr reactions^{20,42} carried out in solutions than O-anions with similar basicities. This is due to the smaller solvation of S-anions in comparison with O-anions;^{90,91} therefore, the reactivities of S- and O-anions of equal basicities in the gas-phase S_N2-reactions differ only insignificantly.^{92,93} Consequently, the enhanced reactivity of S-anions in solution is not their intrinsic property (*cf.* Ref. 89).

Unfortunately, there are still no literature data on the quantitative aspects of nucleofugicities of leaving groups in arenes in the gas phase (with the exception of fluorine).^{94,95} Therefore, comparative activities of the aromatic nitro group, fluorine and chlorine with respect to the O- and S-anions are discussed exclusively for reactions carried out in solutions.

The data on the relative activities of the nitro group, fluorine and chlorine in structurally different arenes in their reactions with O- and S-anions are given in Table 7. The table contains both the kinetic characteristics and the most interesting synthetic results which altogether provide more detailed information about the dependence of the nucleofugicities of these groups on various factors.

First of all, it is worth comparing the activity series of the nitro group, fluorine and chlorine for those cases where substitution occurs according to the S_NAr mechanism with σ-complex for-

‡ The substitution of the nitrite ion for the nitro group is an example of a degenerate reaction.

Table 7. Activities of the leaving groups X = NO₂, F and Cl in the reactions of ArX with O- and S-anions.

Ar	Entry	Nucleophile	Reaction conditions		Rate constant k_2^{Cl} /litre mol ⁻¹ s ⁻¹	Relative activity $k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$ at X		Yield (%) ^a for X			Ref.
			solvent	temperature /°C				NO ₂	F	Cl	
						NO ₂	F				
4-NO ₂ C ₆ H ₄	1	MeONa	MeOH	25	3.78×10^{-7}	224 ^b	473	—	—	—	96, 97
	2	MeONa	MeOH	50	8.46×10^{-6}	183 ^b	312	—	—	—	70, 98, 99
	3	MeONa	MeOH	50	8.46×10^{-6}	378 ^b	—	—	—	—	100, 101
	4	EtONa	EtOH	50	2.38×10^{-5}	500 ^b	360	—	—	—	100, 101
	5	Pr ⁱ OK	Pr ⁱ OH	75	1.2×10^{-5} (see ^c)	—	250	—	—	—	102
	6	PhONa	DMSO	25	2.0×10^{-3}	—	260	—	—	—	103, 104
	7	PhONa	DMSO	90	—	—	—	77	—	—	105
	8	2,6-Br ₂ -4-MeC ₆ H ₂ ONa	DMSO	90	—	—	—	65	8	—	105
	9	1-C ₁₀ H ₇ ONa	DMSO	90	—	—	—	89	—	—	105
	10	MeSNa	Pr ⁱ OH	40	1.09×10^{-3} (see ^c)	—	—	—	—	100 (1.5)	106
	11	MeSNa	Pr ⁱ OH	25	—	—	—	—	100	—	106
	12	Pr ⁱ SNa	Pr ⁱ OH	40	2.41×10^{-4} (see ^c)	—	—	—	—	96	106
	13	PhSNa	MeOH	25	2.1×10^{-5}	—	10	—	—	—	20
	14	PhSNa	MeOH	50	3.2×10^{-4}	556 ^b	7.2	—	—	—	107, 108
	15	PhSNa	Pr ⁱ OH	40	1.59×10^{-4} (see ^c)	—	—	—	—	96	106
	16	NaNO ₂	DMSO	100	0.89×10^{-4}	1.11	3.55	—	—	—	77, 78
	17	PhCH = NONa	DMSO	30	—	—	—	78	79	—	109
2-NO ₂ C ₆ H ₄	18	MeONa	MeOH	50	2.52×10^{-6}	252 ^b	718	—	—	—	110, 111, 112
	19	CF ₃ CH ₂ ONa	HMPA	150	—	—	—	98 (2)	93 (2)	95 (2)	113
	20	Pr ⁱ OK	Pr ⁱ OH	75	8.1×10^{-5} (see ^c)	—	395	—	92	98	102
	21	MeSNa	Pr ⁱ OH	40	0.778×10^{-3} (see ^c)	—	—	—	—	95	106
	22	Pr ⁱ SNa	Pr ⁱ OH	40	0.231×10^{-3} (see ^c)	—	—	—	—	95	106
	23	PhSNa	Pr ⁱ OH	40	0.098×10^{-3}	—	—	—	—	95	106
3-NO ₂ C ₆ H ₄	24	MeONa	MeOH	49.55	1.59×10^{-7} (see ^d)	—	—	—	—	—	114, 115
	25	MeONa	HMPA	25	—	—	—	83	—	—	36
	26	CF ₃ CH ₂ ONa	HMPA	25	—	—	—	93	78	—	116
	27	PhONa	DMSO	80	—	—	—	18	—	—	26
	28	PhOK	DMF	135	—	1.5 ^e	1	98	60	—	117
	29	3-NO ₂ C ₆ H ₄ OK	DMF	135	—	1.9 ^e	1	55	34	—	117
	30	PhSK	DMF	90	—	1.3 ^e	1	98	97	—	117
	31	PhSNa	HMPA	25	—	—	—	88	—	—	36
	32	Pr ⁱ SNa	HMPA	25	—	—	—	86	—	—	118
	33	MeONa	DMF	25	—	—	—	92	—	—	119
4-CNC ₆ H ₄	34	CF ₃ CH ₂ ONa	HMPA	25	—	—	—	95 (1.5)	58 ^f	64 ^g	116
	35	PhCH = NONa	DMSO	25	—	—	—	94	—	—	109
	36	PhONa	DMSO	50	3.39×10^{-2} (see ^h)	—	—	93	—	—	120
	37	PhONa	DMSO	100	64.3×10^{-2} (see ^h)	—	—	—	—	—	121
	38	CF ₃ CH ₂ ONa	HMPA	50	—	—	—	84	—	57 ^g	116
3-CNC ₆ H ₄	39	PhONa	DMSO	100	1.2×10^{-2} (see ^h)	—	—	—	—	—	121
	40	MeONa	MeOH	50	1.6×10^{-4}	690	160	—	—	—	122
4-CF ₃ SO ₂ C ₆ H ₄	41	PhSNa	MeOH	50	1.03×10^{-4}	1300	8.6	—	—	—	123

Table 7 (continued).

Ar	Entry	Nucleophile	Reaction conditions		Rate constant k_2^{Cl} /litre mol ⁻¹ s ⁻¹	Relative activity $k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$ at X		Yield (%) ^a for X			Ref.
			solvent	temperature /°C				NO ₂	F	Cl	
						NO ₂	F				
C ₆ H ₅ COC ₆ H ₄	42	MeONa	DMSO	20	—	—	—	100	—	—	124
4-NO ₂ C ₆ H ₄ COC ₆ H ₄	43	MeONa	DMSO	20	—	—	—	100	—	—	124
2,4-(NO ₂) ₂ C ₆ H ₃	44	MeONa	MeOH	25	2.9 × 10 ⁻²	531	610	—	—	—	20, 125
							(562) ⁱ				126
	45	PhSNa	MeOH	0	3.89	100	26.5	—	—	—	107
							(33) ⁱ				127
	46	PhSNa	MeOH	25	21.0	1857	37	—	—	—	20
	47	2,4-(NO ₂) ₂ C ₆ H ₃ SK	MeOH	30	3.63 × 10 ⁻²	1585	17.8	—	—	—	81
	48	NaNO ₂	DMSO	25	0.6	13.3	0.23	—	—	—	77, 78
	49	KSCN	DMF	75.2	1 × 10 ⁻²	199.5	0.25	—	—	—	81
	50	C ₁₆ H ₃₃ P ⁺ Bu ₃ NCS ⁻	PhCl	60	2.3 × 10 ⁻³	—	1.4	—	—	—	71
4-NO ₂ -2-CNC ₆ H ₃	51	MeONa	MeOH	25	24.2 ^g	—	—	—	—	—	126
2-NO ₂ -5-ClC ₆ H ₃	52	MeONa	MeOH	25	7.28 × 10 ⁻³ (see ^h)	—	—	—	—	—	10, 128
3-Cl-2-CNC ₆ H ₃	53	MeONa	DMF-H ₂ O	25	—	—	—	67	—	—	74
	54	MeSK	DMF-H ₂ O	25	—	—	—	83	—	—	74
3-Cl-6-CNC ₆ H ₃	55	KSCH ₂ COOMe	DMF-H ₂ O	0	—	—	—	84	—	—	129
	56	Na ₂ S	DMF-H ₂ O	0	—	—	—	66	—	—	130
2-SO ₂ CF ₃ -5-ClC ₆ H ₃	57	MeONa	MeOH	65	—	—	—	61	—	—	131
	58	PhONa	MeOH	65	—	—	—	49	—	—	132
4-SO ₂ CF ₃ -3-ClC ₆ H ₃	59	MeONa	MeOH	65	—	—	—	96.3	—	—	129
3-NO ₂ -4-SO ₂ CF ₃ C ₆ H ₃	60	MeONa	MeOH	25	—	—	—	70	—	—	129
	61	PhONa	MeOH	25	—	—	—	32	—	—	130
	62	PhSNa	MeOH	25	—	—	—	(see ^j)	—	—	130
3,5-(NO ₂) ₂ C ₆ H ₃	63	MeONa	MeOH	25	2.57 × 10 ⁻⁴ (see ^d)	—	—	—	—	—	97
	64	MeONa	MeOH	40	4.1 × 10 ⁻⁴ (see ^h)	—	—	—	—	—	133
	65	MeONa	MeOH	49.55	4.19 × 10 ⁻³ (see ^d)	—	—	—	—	—	114
	66	MeONa	MeOH	100	4.06 × 10 ⁻¹ (see ^d)	—	—	—	—	—	115
	67	MeOK	MeOH	65	—	—	—	65 (0.3)	—	—	134
	68	MeONa	MeOH	65	—	—	—	—	—	(see ^k)	135
	69	Na ₂ CO ₃	EtOH (60%)	25	1.02 × 10 ⁻³ (see ^d)	—	—	—	—	—	97
3-NO ₂ -5-SO ₂ CF ₃ C ₆ H ₃	70	MeONa	MeOH	65	—	—	—	62 (1.5)	—	—	134
	71	PhSNa	MeOH	25	—	—	—	35	—	—	134
3-NO ₂ -5-CNC ₆ H ₃	72	MeOK	MeOH	25	—	—	—	90	—	—	136
3-NO ₂ -5-CF ₃ C ₆ H ₃	73	MeOK	MeOH	65	—	—	—	89 (0.3)	—	—	137
	74	MeONa	MeOH	100	3.23 × 10 ⁻² (see ^d)	—	—	—	—	—	115
	75	3-NO ₂ -5-CF ₃ C ₆ H ₃ OK	DMF	80	—	0.59 ^e	1	—	—	—	138
3,5-(SO ₂ CF ₃) ₂ C ₆ H ₃	76	MeONa	MeOH	25	—	—	—	31.4 (20)	92.5 (1)	0 (2)	139
	77	MeONa	MeOH	50	—	—	—	58.5 (2)	—	10.8 (2)	139
	78	PhSNa	MeOH	25	—	—	—	77 (1.5)	58.6 (2)	16.2 (2)	139
3,5-(CF ₃) ₂ C ₆ H ₃	79	MeONa	MeOH	100	1.17 × 10 ⁻³ (see ^d)	—	—	—	—	—	115
	80	PhSNa	HMPA	25	—	—	—	92	—	—	36

Table 7 (continued).

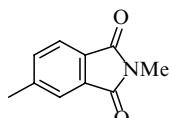
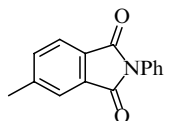
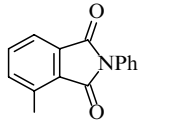
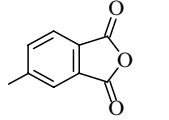
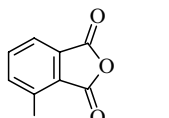
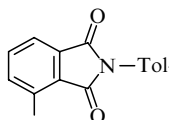
Ar	Entry	Nucleophile	Reaction conditions		Rate constant k_2^{Cl} /litre mol ⁻¹ s ⁻¹	Relative activity $k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$ at X		Yield (%) ^a for X			Ref.
			solvent	temperature /°C				NO ₂	F	Cl	
						NO ₂	F				
	81	PhONa	DMSO	25	—	37 ¹	4	—	—	—	140
	82	4-MeC ₆ F ₄ SNa	DMSO	25	—	250 ¹	8	—	—	—	141
	83	PhONa	DMSO	25	—	130 ¹	20	—	—	—	140
	84	4-MeC ₆ H ₄ SNa	DMSO	25	—	93.8 ¹	4.8	—	—	—	141
	85	PhONa	DMSO	25	—	520 ¹	65	—	—	—	140
	86	4-MeC ₆ H ₄ SNa	DMSO	25	—	2667 ¹	31.7	—	—	—	141
	87	4-MeC ₆ H ₄ SNa	DMF	25	—	66.7 ¹	6.7	—	—	—	142
	88	4-MeC ₆ H ₄ SNa	DMF	25	—	1400 ¹	20	—	—	—	142
	89	4-MeC ₆ H ₄ ONa	THF	0	—	—	—	77	—	—	72
	90	PhSNa	DMSO	25	—	—	—	95	—	—	72

Table 7 (continued).

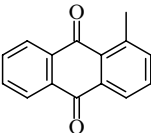
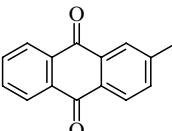
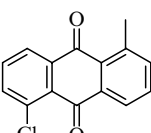
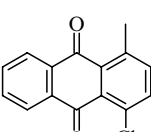
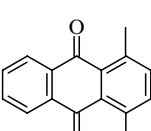
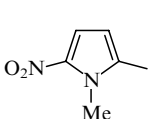
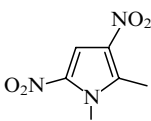
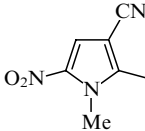
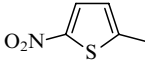
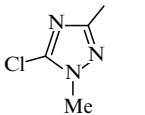
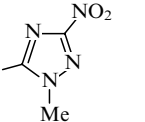
Ar	Entry	Nucleophile	Reaction conditions		Rate constant k_2^{Cl} /litre mol ⁻¹ s ⁻¹	Relative activity $k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$ at X		Yield (%) ^a for X			Ref.
			solvent	temperature /°C				NO ₂	F	Cl	
						NO ₂	F				
	91	MeONa	MeOH	50	3.2×10^{-6}	214	535	—	—	—	143
	92	MeONa	MeOH	50	2.53×10^{-6}	713	783	—	—	—	143
	93	PhSNa	EtOH	80	—	—	—	90	—	—	144
	94	PhSNa	DMSO	20–25	—	—	—	80	—	—	29
	95	4-NO ₂ C ₆ H ₄ ONa	DMSO	60–70	—	—	—	—	—	90	29
	96	4-NO ₂ C ₆ H ₄ ONa	DMSO	65	—	—	—	—	77	—	145
	97	MeONa	MeOH	25	1.22×10^{-4}	11.1	—	—	—	—	96
	98	MeONa	MeOH	25	20.7 ^h	—	—	—	—	—	126

Table 7 (continued).

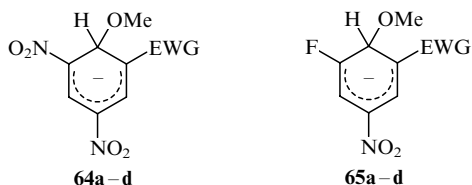
Ar	Entry	Nucleophile	Reaction conditions		Rate constant k_2^{Cl} /litre mol ⁻¹ s ⁻¹	Relative activity $k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$ at X		Yield (%) ^a for X			Ref.
			solvent	temperature /°C		NO ₂	F	NO ₂	F	Cl	
	99	MeONa	MeOH	25	6.3 ^g	—	—	—	—	—	126
	100	PhSNa	MeOH	20	1.26×10^{-1}	1032	80	—	—	—	146
	101	MeONa	MeOH	25	0.42×10^{-4} (see ^h)	—	—	—	—	—	147
	102	MeONa	MeOH	25	1.24×10^{-2}	—	—	—	—	—	147

^a In parentheses, the reaction time /h. ^b With allowance for the statistical factor. ^c The pseudo-first order constant /s⁻¹. ^d k_2^{F} . ^e The activity relative to fluorine, determined from competitive reactions. ^f At 50 °C. ^g At 150 °C. ^h $k_2^{\text{NO}_2}$. ⁱ The value for fluorine calculated relative to chlorine. ^j Substitution of the SO₂CF₃ group (yield 95%). ^k Substitution of the nitro group (yield 10%). ^l Determined from competitive reactions.

mation in the limiting step. For O-anions, the activities of the leaving groups decrease in the following order: $F > NO_2 > Cl$ (Table 7, entries 1–3, 16, 18, 44, 75–77, 91, 92, 97), whereas those for S-anions change as follows: $NO_2 > F > Cl$ (entries 14, 30, 47, 78, 82, 84, 86–88, 93, 94, 100). The activity series of the leaving groups NO_2 , F and Cl present no peculiarities for various derivatives of 2- and 4-nitrobenzenes, 2,4- and 3,5-dinitrobenzenes, 3,5-bis(trifluoromethylsulfonyl)benzenes, 1- and 2-anthraquinones, 1-methyl-5-nitropyrroles and 5-nitrothiophenes and are attributable to different polarisabilities of O- and S-anions.²⁰ At the same time, in the case of 3-nitrobenzene, 3- and 4-cyanobenzene, 4-trifluoromethylsulfonylbenzene and 3- and 4-phthalimide derivatives (entries 26, 28–30, 34, 38, 40, 41, 81–86), the activity series of the leaving groups are the same for both O- and S-anions: $NO_2 > F > Cl$. However, for some compounds of this group the differences in the relative activities of the nitro group and fluorine for S-anions are more significant: $NO_2 \gg F$.^{123, 141, 142}

It is known that in some compounds of the benzene series the electron-withdrawing substituents favour the replacement of the leaving group by the O- and S-anions in the order: *ortho* $\geq$ *para* $>$ *meta* (entries 5 and 20, 12 and 22, 15 and 23, 34 and 38). The degree of activation depends not only on the electronic properties of the substituent in the *ortho*- or *para*-positions relative to the leaving group (entries 2 and 40, 14 and 41, 6 and 36, 97–99), but also on the steric effect of the *ortho*-substituent. Thus steric hindrance due to the *ortho*-nitro group is smaller than that of the *ortho*-nitro group in 2-substituted 1,4-dinitrobenzenes. Therefore, substitution of the methoxy group for the nitro group occurs faster in nitrile derivatives (entries 44 and 51). The activating effects of electron-withdrawing substituents in the *meta*-position of the benzene ring are strong enough for the substitution of the nitro group, fluorine and chlorine by both O- and S-anions (entries 25, 26, 28–32, 38, 39). In the case of simultaneous activation of the nitro group and chlorine by electron-withdrawing substituents in the *ortho*- and/or *para*-position(s) of the benzene ring, the activity of the nitro group exceeds markedly that of chlorine for both O- and S-anions (entries 52–59).

Substitution in the case of activation by electron-withdrawing substituents in the *meta*-position of the benzene ring has a number of specific features. Thus substitution of the nitro group under the action of methoxide occurs more easily in the case of activation by *meta*-CN or $-CF_3$ substituents than by *meta*- NO_2 - or $-SO_2CF_3$ groups in 5-derivatives of 1,3-dinitrobenzenes (entries 67, 70, 72, 73). The situation is different if the leaving group is fluorine. The activation by a *meta*- NO_2 substituent is more efficient than that by the *meta*- CF_3 group in the same reaction (entries 66 and 74). The reason for the reversal of the substituent effects is the formation of more stable σ -complexes at the unsubstituted positions of the benzene ring **64a–d** (especially for EWG = NO_2 and SO_2CF_3) in comparison with the σ -complexes **65a–d** (see Ref. 148; pp. 173, 276 and 292).

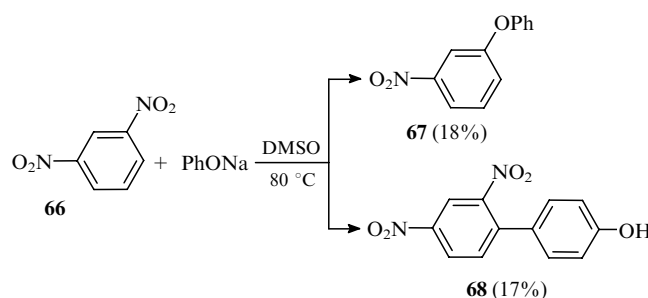


EWG = NO_2 (a), SO_2CF_3 (b), CN (c), CF_3 (d).

The σ -complexes **65a–d** are significantly less stable; therefore, the activation occurs in an ordinary way in accordance with the Hammett constant, which reflects the effect of the electron-withdrawing *meta*-substituent (EWG) on the reaction centre (σ_M). The greater ease of substitution of the thiolate anion for the nitro group in 1-nitro-3,5-bis(trifluoromethyl)benzene in comparison with 1,3-dinitro-5-trifluoromethylsulfonylbenzene in the same

reaction (entries 71 and 80) and the greater activity of fluorine in 3-nitro-5-trifluoromethylfluorobenzene in comparison with 3,5-bis(trifluoromethyl)fluorobenzene in the reaction with sodium methoxide (entries 74 and 79) can be explained in a similar way.

The lower activity of chlorine in comparison with the nitro group is also observed in the case of their simultaneous activation by an electron-withdrawing *meta*-substituent. Thus only the nitro group is substituted in 3,5-dinitrochlorobenzene under the action of methoxide (entry 68). Moreover, the nitro group in 1,3-dinitrobenzene (**66**) can be substituted under the action of the phenolate ion resulting in 3-nitrodiphenyl ether (**67**). The phenolate ion, being an ambident anion, also acts as a C-nucleophile and attacks the non-substituted position of the benzene ring to yield 2,4-dinitro-4'-hydroxybiphenyl (**68**) (entry 27).²⁶ In the latter case, the starting dinitrobenzene **66** acts as an oxidant of the intermediate σ -complex.²⁶



There are some other examples of the dependence of the direction of the substitution reaction on the nature of the nucleophile. Thus the reactions with O-anions result in the substitution of the nitro group in 2,4- (entries 60 and 61) and 3,5-dinitro-1-trifluoromethylsulfonylbenzene (entry 70), whereas reactions with S-anions result predominantly in the substitution of the trifluoromethylsulfonyl group in these compounds (entries 62, 71). The orientation of the substitution reactions in 1-chloro-4-nitroanthraquinone and 1-chloro-5-nitroanthraquinone also depends on the nature of the nucleophile: chlorine is predominantly substituted by O-anions, whereas the nitro group is substituted by S-anions (entries 93–95). Similarly, in 4-chloro-3,5-difluoronitrobenzene fluorine is substituted under the action of sodium methoxide, whereas chlorine is substituted under the action of the benzenethiolate anion.¹⁴⁹ The change in the reaction route on going from hard O-anions to soft easily polarisable S-anions seems to be caused by a transition from charge control to orbital control.^{29, 149, 150} However, fluorine is more easily replaced in 1-fluoro-4-nitroanthraquinone irrespective of the nature of the nucleophile, which is consistent with charge control of the reaction.^{29, 145}

The ease of substitution of the nitro group, fluorine and chlorine is also determined by the structure of the substrate. Thus the activities of these substituents in reactions with both O- and S-anions are much higher for 3-substituted phthalic acid derivatives than for 4-substituted derivatives (entries 83–88). This is corroborated by the selective substitution of the 3-nitro group in 3,5-dinitro-*N*-arylphthalimide under the action of both O- and S-anions (entries 89 and 90). The activities of the nitro group and fluorine in 2-substituted anthraquinone are somewhat higher than in the 1-isomer, whereas those of chlorine are virtually identical in these compounds (entries 91 and 92). It was found also that the nitro group in 5-chloro-1-methyl-3-nitro-1,2,4-triazole is almost 300 times less active than chlorine in a reaction with methoxide (entries 101 and 102). These data corroborate the fact that different activities of substituents with respect to the same nucleophile are determined by different electronic and steric effects in the substrate.

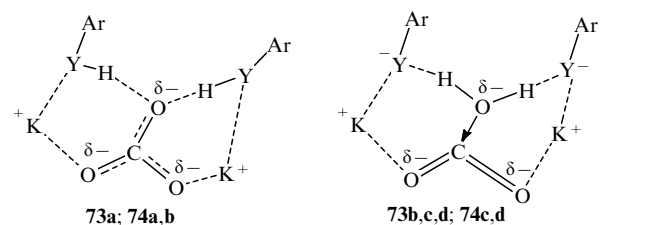
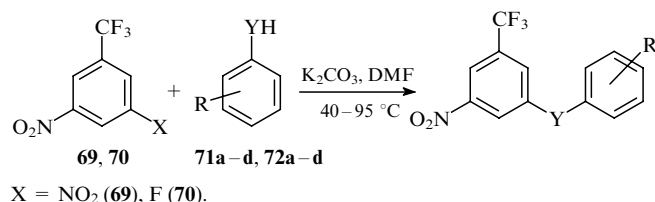
The data on the activities of the nitro group, fluorine and chlorine in the above-described reactions with O- and S-anions are

related to the S_NAr mechanism with the σ -complex formation as a limiting step. If the limiting step is the decomposition of the σ -complex, the activities of the leaving groups in reactions with O- and S-anions will be as follows: $NO_2 > Cl > F$ (entries 48 and 49). This series corresponds to the increase in the dissociation energy of the $Ar-X$ bond on going from $X = NO_2$ to $X = F$ (see Table 1).

In some substitution reactions by aryloxide anions, the nitro group manifests higher activity (entries 7–9) than fluorine and chlorine (entries 6 and 8). However, the addition of a radical trap to a reaction mixture containing 1,4-dinitrobenzene (**1**) and the 2,6-dibromo-4-cresolate anion inhibits completely the substitution of the nitro group. Presumably, the substitution of the nitro group in compound **1** occurs predominantly according to the electron transfer mechanism.¹⁰⁵

It is known that the energies of bimolecular S_NAr reactions depend on the nature of the leaving group and the nucleophile,¹ whereas the reactivities in these processes are under enthalpy control.¹¹ Entropy control itself is effective in fast bimolecular reactions occurring in solution involving radicals ($k_2 = 10^6$ – 10^8 litre mol⁻¹ s⁻¹ from -85 to -10 °C),¹⁵¹ carbenes ($k_2 = 10^4$ – 10^9 litre mol⁻¹ s⁻¹ at 25 °C)¹⁵² or carbocations ($k_2 = 10^{-1}$ – 10^8 litre mol⁻¹ s⁻¹ from -70 to -30 °C)¹⁵³ where the contribution of enthalpy is either very small or constant as a result of which the transition state is shifted to earlier position on the reaction coordinate.^{152, 153}

Recently, it has been found that the selectivity of substitution of the nitro group and fluorine in S_NAr reactions is connected with entropy control,^{154, 155} although bimolecular S_NAr reactions occur at a relatively slow rate ($k_2 = 10^{-4}$ – 10^{-1} litre mol⁻¹ s⁻¹ at 25 °C in DMSO or DMF).¹⁵⁶ However, the relative activities of the nitro group and fluorine in the competitive reactions between nitrobenzotrifluorides **69** and **70**, phenols **71a–d** and arenethiols **72** in the presence of K_2CO_3 in DMF (40 – 95 °C) are controlled by the entropy of the activation, since $T\Delta S^\ddagger > \Delta\Delta H^\ddagger$ in all cases (Table 8).^{154, 155} It was shown¹⁵⁷ that compounds **71** and **72** yield complexes **73** and **74** of the type $(2 ArYH) \cdot K_2CO_3$ in the reaction with K_2CO_3 in DMF. The structures of these complexes depend on the nature of the substituent in the benzene ring.



Compound	Y	R	Compound	Y	R
71a, 73a	O	H	72a, 74a	S	H
71b, 73b	O	4-Cl	72b, 74b	S	4-MeO
71c, 73c	O	3-NO ₂	72c, 74c	S	3-CF ₃
71d, 73d	O	4-CN	72d, 74d	S	4-NO ₂

As the changes in the entropy $\Delta\Delta S^\ddagger$ are positive, the reactions of the fluoro derivative **70** with complexes **73** and **74** are more organised in comparison with analogous reactions of the dinitro-substituted compound **69**. Therefore, the S_NAr -substitution of the nitro group in compound **69** is characterised by an earlier

Table 8. Relative activities of the nitro group and fluorine and the activation parameters for the competitive reactions of compounds **69** and **70** with phenols **71a–d** and arenethiols **72a–d** in the presence of K_2CO_3 (DMF, 70 °C).^{154, 155}

Compound	$k_{rel} = k^{NO_2}/k^F$	$\Delta\Delta H^\ddagger$ (see ^a) /kJ mol ⁻¹	$T\Delta\Delta S^\ddagger$ (see ^b) /kJ mol ⁻¹
71a	1.11	18.1	18.2
71b	1.20	21.8	22.0
71c	1.38	27.6	28.7
71d	1.58	80.3	82.8
72a	10.1	69.1	72.3
72b	6.73	60.6	63.2
72c	32.8	94.1	98.6
72d	116.2	124.8	130.9

^a $\Delta\Delta H^\ddagger = \Delta H^\ddagger_{NO_2} - \Delta H^\ddagger_F$, ^b $\Delta\Delta S^\ddagger = \Delta S^\ddagger_{NO_2} - \Delta S^\ddagger_F$.

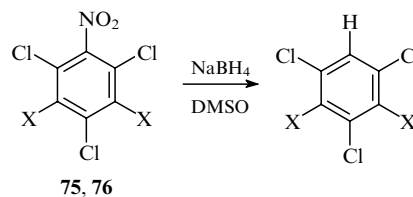
transition state on the reaction coordinate than the substitution of fluorine in compound **70**.^{154, 155}

Summing up the results of the discussion of the reactivities of O- and S-anions, special mention should be made of the following items. First of all, it is obvious that the reactions of O- and S-anions are very sensitive to the nature of both the substrate and the leaving group in the arene. Soft S-anions usually react with those centres in the arene which carry highly polarisable leaving groups owing to the orbital control of the reaction. The reactions of hard O-anions are characterised by charge control. As a result, the activity series of the leaving groups changes from $NO_2 > F > Cl$ (RS^-) to $F > NO_2 \geq Cl$ (RO^-) within the framework of the same reaction mechanism. It should be stressed that the selectivity of substitution of the nitro group and halogens under the action of O- and S-anions may depend on the transition from enthalpy to the entropy control as the nature of the nucleophile is changed.

V. Reactions with hydride and halide ions

S_NAr substitution of the nitro group and halogens in arenes under the action of hydride and halide ions has been described in a number of reviews.^{7, 148, 158} Here, it seems expedient to emphasise only some peculiarities of activities of aromatic substituents with respect to these nucleophiles.

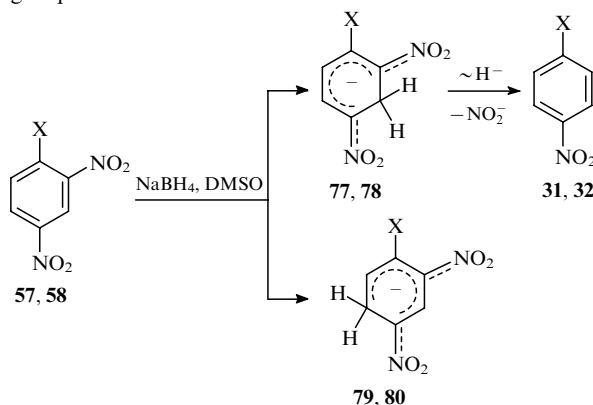
The activity of the nitro group is somewhat higher than that of chlorine in the reaction of *para*-substituted nitrobenzenes with the hydride ion in DMSO,¹⁵⁹ which is also characteristic of other hard anions, *e.g.*, N- and O-anions (see Sections III and IV). However, the nucleofugicity of the nitro group in arenes is increased drastically if it becomes non-coplanar with the aromatic ring under the influence of steric factors. Thus only the nitro group is replaced by hydrogen in the reaction of pentachloronitrobenzene (**75**) or 1,3,5-trichloro-2,4,6-trinitrobenzene (**76**) with sodium borohydride.^{160, 161}



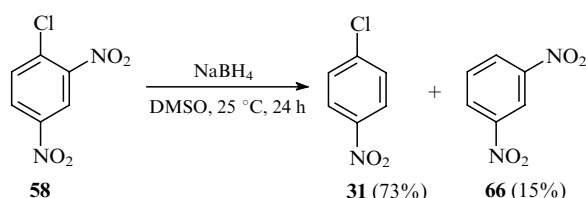
$X = Cl$ (**75**), NO_2 (**76**).

The enhanced activity of the aromatic nitro group (in comparison with fluorine and chlorine) with respect to the hydride ion may be due to a predominant attack on the unsubstituted position of the aromatic ring. Thus the reaction of compounds **57** and **58** with sodium borohydride in DMSO occurs *via* the anionic σ^H -complexes **77**–**80**. It is noteworthy that the conversion of the

σ -complexes **77** and **78** into halonitrobenzenes **31** and **32** proceeds as the intramolecular substitution of the hydride ion for the nitro group.¹⁵⁹



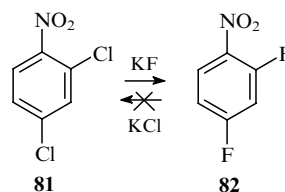
Owing to such a vicinal attack, the yield of the substitution product of the nitro group (compound **31**) in the case of the chloro derivative **58** markedly exceeds the yield of the substitution product of chlorine (compound **66**),¹⁵⁹ which is formed upon a significant increase in the reaction time.



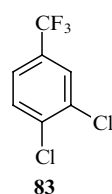
Recently, it has been shown that reactions of nitroarenes with the hydride ion (NaBH_4) strongly depend on the spatial structures of the substituents adjacent to the reaction centre.^{162, 163} Moreover, one should not rule out the possibility that the predominant substitution of the nitro group in comparison with halogens in the reactions of halonitroarenes with the borohydride anion is due to the steric features of the nucleophile.

Substitution of chlorine and the nitro group in arenes under the action of the fluoride ion is a main route to the introduction of fluorine into the aromatic ring;^{14, 15, 164} this approach has a

considerable preparative significance.^{165–169} The nucleophilicity of the halide ions in $\text{S}_{\text{N}}\text{Ar}$ reactions occurring in dipolar aprotic solvents changes in the following order: $\text{F} \gg \text{Cl} > \text{Br} > \text{I}$.^{77, 78, 170} Thus the rate of the substitution of the fluoride ion (DMSO, 25 °C) for the nitro group in compound **60** exceeds 320-fold the rate of an analogous reaction with the chloride ion.⁷⁷ The halogen exchange in 2,4-dichloro- (**81**) and 2,4-difluoro-nitrobenzenes (**82**) under the action of KF and KCl, respectively (DMF, 125 °C) is yet another example of a higher nucleophilicity of the fluoride ion.¹⁷¹



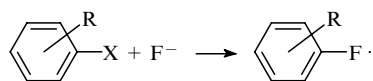
If the substitution of chlorine for fluorine in compound **82** does not take place, compound **81** reacts with KF to give product **82** in a quantitative yield; the rate constant of this pseudo-first order reaction (k_1) is $3.43 \times 10^{-4} \text{ s}^{-1}$ (125 °C).¹⁷¹ This value is similar to the value of the rate constant ($k_1 = 1.1 \times 10^{-4} \text{ s}^{-1}$) for the substitution of fluorine for chlorine in 3,4-dichlorobenzotrifluoride (**83**)



under the action of KF (sulfolane, 180 °C) in the presence of Ph_4PCl .¹⁷² However, the nucleophilicity of the chloride ion in the substitution of the nitro group in compound **76** (LiCl in acetone) is high enough [$k_2 = 0.525 \text{ litre mol}^{-1} \text{ s}^{-1}$ (25 °C)].¹⁷³ The high substitution rate and the low activation energy of the latter reaction are due to alleviation of steric strain on going from the starting compound to the intermediate σ -complex.¹⁷³

Relative activities of the nitro group, fluorine and chlorine in various disubstituted arenes with respect to the fluoride ion are listed in Table 9. The activity series of these substituents in the

Table 9. Activities of the leaving groups X in reactions of compounds ArX with the fluoride ion.



R	Entry	Reagent	Reaction conditions	Temperature /°C	Time /h	k_2^{Cl} /litre mol ⁻¹ s ⁻¹ [$k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$]	Yield (%) at X		Ref.
							NO ₂	Cl (F)	
4-NO ₂	1	RbF	DMSO	150	0.5	[500(NO ₂), 1(Cl), 50(F)] ^a	—	—	35
	2	RbF	DMSO	110	0.5	—	87	—	35, 174
	3	RbF	DMSO	165	0.25	—	—	35–50	175
	4	CsF	DMSO	80	0.3	1.0×10^{-4} (see ^b)	50	—	176
	5	RbF	DMSO	25	—	0.92×10^{-4} (see ^c)	—	—	177
	6	KF	DMSO	190	14	—	—	72	178
2-NO ₂	7	RbF	DMSO	150	0.5	[1.3(NO ₂), 1(F)] ^d	—	—	35
	8	RbF	DMSO	150	0.3	—	58	—	35, 174
	9	RbF	DMSO	25	—	3.12×10^{-4}	—	—	177
	10	KF	DMSO	185	4.5	—	—	38	178
	11	Bu ₄ NF	THF	20–25	1.5	—	100	25	179
3-NO ₂	12	RbF	DMSO	150	0.3	—	17.4	—	35
	13	KF	NMP ^e	180	48	—	40–45	—	125

Table 9 (continued).

R	Entry	Reagent	Reaction conditions	Temperature /°C	Time /h	k_2^{Cl} /litre mol ⁻¹ s ⁻¹ [$k_{\text{rel}} = k_2^{\text{X}}/k_2^{\text{Cl}}$]	Yield (%) at X		Ref.
							NO ₂	Cl (F)	
4-CN	14	KF	Sulfolane, PDC ^f	200	72	—	70	—	180
	15	KF	Sulfolane, PDC, Me ₄ NCl	160	8	—	94	—	181
	16	KF	Sulfolane, PDC, Ph ₄ PBr	180	3	—	89	—	182
	17	KF	Sulfolane, PDC, Ph ₄ PBr	220	5.5	—	—	16 ^g	182
	18	Me ₄ NF	DMSO	100	4	—	70	—	183
	19	Me ₄ NF · HF	DMA ^h	140	2	—	66	—	184
	20	RbF	DMSO	150	0.3	—	81	—	35
	21	RbF	DMSO	165	0.25	—	50	30	175
	22	CsF	DMSO	80	0.33	1.58×10^{-7}	7	—	176
	23	KF	DMSO	180	0.16	—	75	—	185
2-CN	24	KF	DMI ⁱ	290	2	—	—	91	186
	25	RbF	DMSO	150	0.3	—	86	—	35, 174
	26	KF	DMI	290	2	—	—	76	186
	27	Me ₄ NF	DMSO	80	1	—	100	—	183, 187
2-CF ₃	28	Me ₄ NF	DMSO	80	24	—	95	—	187
2-CHO	29	Me ₄ NF	DMSO	80	1	—	60	—	187
3-CN	30	KF	Sulfolane, PDC, Ph ₄ PBr	210	2.5	—	86	—	182
	31	KF	DMI	290	8	—	—	70	186

^a The activities of groups X relative to chlorine, determined from competitive reactions. ^b $k_2^{\text{NO}_2}$ (25 °C). ^c k_2^{F} . ^d The activities of groups X relative to fluorine. ^e NMP is *N*-methylpyrrolidone. ^f PDC is phthaloyl chloride. ^g 1-Chloro-3-fluorobenzene is also formed (yield 27%). ^h DMA is *N,N*-dimethylacetamide. ⁱ DMI is 1,3-dimethylimidazolidin-2-one.

reactions of 1,4-disubstituted benzenes **1**, **31** and **32** with Rb¹⁸F (DMSO, 150 °C) changes in the following order: NO₂ > F >> Cl (Table 9, entry 1).³⁵ However, the activities of the nitro group and fluorine in an analogous reaction of 1,2-disubstituted benzenes **2** and **3** are markedly approximated (entry 7).³⁵ A comparison of the activation parameters ($\Delta H^\ddagger$ and $\Delta S^\ddagger$) for the substitution of the nitro group and fluorine in compounds **1** and **32** under the action of the ¹⁸F-labelled fluoride ion in DMSO showed that the selectivity of substitution of these groups ($k^{\text{NO}_2}/k^{\text{F}}$ ratio) is controlled by the entropy of activation.^{176, 177} Obviously, in this case, too, the substitution of the nitro group in compound **1** is characterised by an earlier transition state on the reaction coordinate than the substitution of fluorine in compound **32** (cf. Refs 154 and 155). At the same time, the substitution of the nitro

group in 1,4-dinitro- (**1**) and 1-cyano-4-nitrobenzenes (**22**) under the action of the fluoride ion in DMSO (entries 4 and 21) is subject to enthalpy control despite the fact that a decrease in the electrophilicity of the substrate **22** results in a more positive value of $\Delta S^\ddagger$ in comparison with compound **1** (see Ref. 176).

The data listed in Table 9 corroborate the fact that fluorode-nitration is an efficient procedure for the introduction of fluorine into the aromatic ring in both activated (entries 2, 4, 8, 11, 20, 21, 23, 25, 27–29) and low-reactive substrates (entries 13–16, 18, 19 and 30).

Some synthetic implications of reactions of complex chloro-(nitro)aromatic compounds with the fluoride anion are presented in Table 10; these are analysed in subsequent paragraphs with regard to the previously established kinetic, thermodynamic and

Table 10. Activities of the leaving groups NO₂ and Cl in reactions of chloronitroarenes with the fluorine ion resulting in fluoroarenes.

Compound	Entry	Reagent	Reaction conditions	Temperature /°C	Time /h	Reaction products	Yield (%)	Ref.
2-NO ₂ -4-ClC ₆ H ₃ CO ₂ Me	1	Me ₄ NF	DMSO	80	1.5	2-F-4-ClC ₆ H ₃ CO ₂ Me	76	183, 187
	2	R ₃ NMeF · 2 H ₂ O ^a	DMSO	100	2	2-F-4-ClC ₆ H ₃ CO ₂ Me, 2-NO ₂ -4-FC ₆ H ₃ CO ₂ Me	50, 6	188
	3	KF	DMSO, Ph ₄ PBr	130	27	2-F-4-ClC ₆ H ₃ CO ₂ Me, 2-NO ₂ -4-FC ₆ H ₃ CO ₂ Me	72, 1	189
4-NO ₂ -2-ClC ₆ H ₃ CO ₂ Me	4	Me ₄ NF	DMSO	80	3	4-F-2-ClC ₆ H ₃ CO ₂ Me	44	187
	5	KF	DMSO, Ph ₄ PBr	130	24	4-F-2-ClC ₆ H ₃ CO ₂ Me	60	189
2-NO ₂ -4-ClC ₆ H ₃ CN	6	KF	DMSO, Ph ₄ PBr	130	0.5	2-F-4-ClC ₆ H ₃ CN	100	189
4-NO ₂ -2-ClC ₆ H ₃ CN	7	KF	DMSO, Ph ₄ PBr	130	1	4-F-2-ClC ₆ H ₃ CN, 2,4-F ₂ C ₆ H ₃ CN	90, 10	189
2-NO ₂ -4-ClC ₆ H ₃ CF ₃	8	KF	DMSO, Ph ₄ PBr	130	20	2-F-4-ClC ₆ H ₃ CF ₃	31	189
4-NO ₂ -2-ClC ₆ H ₃ CF ₃	9	KF	DMSO, Ph ₄ PBr	130	5	4-F-2-ClC ₆ H ₃ CF ₃	48	189
2-NO ₂ -4-ClC ₆ H ₃ SO ₂ CF ₃	10	KF	DMSO, Ph ₄ PBr	130	0.5	2-F-4-ClC ₆ H ₃ SO ₂ CF ₃ , 2,4-F ₂ C ₆ H ₃ SO ₂ CF ₃	64, 26	189
4-NO ₂ -2-ClC ₆ H ₃ SO ₂ CF ₃	11	KF	DMSO, Ph ₄ PBr	130	0.1	4-F-2-ClC ₆ H ₃ SO ₂ CF ₃ , 2,4-F ₂ C ₆ H ₃ SO ₂ CF ₃	78, 5	189
	12	Bu ₄ NF	THF	78	0.5	4-F-2-ClC ₆ H ₃ SO ₂ CF ₃	98	189
2-NO ₂ -4-ClC ₆ H ₃ NO ₂	13	R ₃ NMeF · 2 H ₂ O	DMSO	60	0.1	2-F-4-ClC ₆ H ₃ NO ₂ + 2-F-5-ClC ₆ H ₃ NO ₂	95	188

Table 10 (continued).

Compound	Entry	Reagent	Reaction conditions	Temperature /°C	Time /h	Reaction products	Yield (%)	Ref.
2-NO ₂ -6-ClC ₆ H ₃ CN (84)	14	RbF	DMSO	150	0.3	2-F-6-ClC ₆ H ₃ CN, 2-NO ₂ -6-FC ₆ H ₃ CN (33)	55, 17	35, 174
	15	Bu ₄ NF	THF	25	1.5	2-F-6-ClC ₆ H ₃ CN, 2,6-F ₂ C ₆ H ₃ CN	75, 25	179
	16	Me ₄ NF·HF	DMA	60	3	2-F-6-ClC ₆ H ₃ CN	84	184
4-ClC ₆ H ₄ SO ₂ C ₆ H ₄ NO ₂ -4	17	R ₃ NMeF·2 H ₂ O	DMSO	100	0.5	4-ClC ₆ H ₄ SO ₂ C ₆ H ₄ F-4	75	188
3,5-(NO ₂) ₂ -4-ClC ₆ H ₂ CF ₃	18	KF	Sulfolane, TPDF ^b	150	2	5-NO ₂ -3,4-F ₂ C ₆ H ₂ CF ₃	70	181
1,2,4-(NO ₃) ₃ C ₆ H ₃ (58)	19	KF	Sulfolane, PDC, Me ₄ NCl	160	1.5	3,4-F ₂ C ₆ H ₃ NO ₂	51	181
3-NO ₂ -4-ClC ₆ H ₃ CF ₃	20	KF	Sulfolane, PDC, Ph ₄ PBr	180	7	3,4-F ₂ C ₆ H ₃ CF ₃	65	181
3-NO ₂ -4-ClC ₆ H ₃ CN	21	KF	Sulfolane, PDC, Ph ₄ PBr	180	2	3,4-F ₂ C ₆ H ₃ CN	65	182
3-NO ₂ -6-ClC ₆ H ₃ CN	22	KF	Sulfolane, PDC, Ph ₄ PBr	220	8	2,5-F ₂ C ₆ H ₃ CN	25	182
C ₆ Cl ₅ NO ₂ (75)	23	KF	DMF	150	4	C ₆ Cl ₅ F	10	178
2,3,5,6-Cl ₄ C ₆ HNO ₂ (85)	24	Bu ₄ NF	THF	25	1.5	2,3,5,6-Cl ₄ C ₆ HF	70	179
	25	Me ₄ NF	MeCN	50	3	2,3,5,6-Cl ₄ C ₆ HF	86	187
2,3,4,5-Cl ₄ C ₆ HNO ₂	26	R ₃ NMeF·2 H ₂ O	DMSO	100	0.1	2,3,4,5-Cl ₄ C ₆ HF	84	188
2,4-(NO ₂) ₂ C ₆ H ₃ CO ₂ Me	27	Me ₄ NF	DMSO	60	1	2-NO ₂ -4-FC ₆ H ₃ CO ₂ Me, 4-NO ₂ -2-FC ₆ H ₃ CO ₂ Me	66, 20	183, 187
2,4-(NO ₂) ₂ C ₆ H ₃ CF ₃	28	Me ₄ NF	DMSO	80	4	4-NO ₂ -2-FC ₆ H ₃ CF ₃ , 2,4-F ₂ C ₆ H ₃ CF ₃	63, 31	187
2,4-(NO ₂) ₂ C ₆ H ₃ CN	29	Me ₄ NF	DMSO	80	0.2	2,4-F ₂ C ₆ H ₃ CN	100	187
1,3,5-(NO ₂) ₃ C ₆ H ₃	30	KF	Sulfolane, PDC	180	12	3,5-F ₂ C ₆ H ₃ NO ₂	77	180
3,5-(NO ₂) ₂ C ₆ H ₃ CO ₂ Me	31	RbF	DMSO	150	0.3	5-NO ₂ -3-FC ₆ H ₃ CO ₂ Me	34	35
N-Methyl-4-nitro-phthalimide	32	KF	—	300	5	N-methyl-4-fluoro-phthalimide	28	190
4-Nitrophthalic anhydride	33	KF	—	220	2	4-fluorophthalic anhydride	62	191

^a R₃N is hexamethylenetetramine (urotropin). ^b TPDF is tetrafluorophthaloyl fluoride.

topological peculiarities. High yields of fluoro derivatives can be achieved by varying the source of the fluoride ion (Table 9, entries 11, 18, 19, 28 and 29), solvents and traps for the leaving nitrite ion (Table 9, entries 15, 16 and 30).¹⁶⁴

The lower activity of chlorine in comparison with the nitro group (Table 9, entries 11, 17, 21, 30 and 31) allows selective fluorodenitration in nitrochloroarenes where these substituents are additionally activated by an electron-withdrawing group (Table 10, entries 1–17). Under these conditions, the effect of the phase-transfer catalyst on the exchange of the nitro groups and chlorine is more pronounced in weakly polar aprotic solvents than in strongly polar solvents.¹⁹² Using the reaction of 2-chloro-6-nitrobenzonitrile (**84**) with KF as an example, a number of solvents were tested to ensure the highest selectivity of substitution of the nitro group in comparison with chlorine: DMSO > NMP > sulfolane > MeCN > 1,2-dimethoxyethane (1,2-DME).¹⁹³ The order of substitution of the NO₂ and Cl groups in chloronitroarenes containing no activating group changes to the opposite (Table 10, entries 18–22). In this case, both functional groups are substituted for fluorine.¹⁶⁴

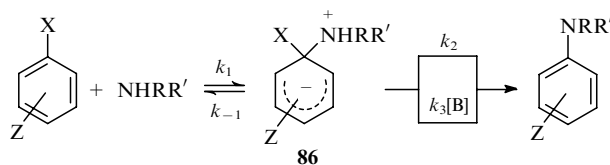
In polychloronitroarenes, the rate of substitution of the nitro group increases under the action of the fluoride ion due to both its exit from the plane of the aromatic ring and the inductive effect of chlorine (entries 24–26).¹⁷⁹ Naturally, the fluorodenitration reaction proceeds especially smoothly in nitroarenes where the nitro group is activated by more than one electron-withdrawing substituent (entries 27–33).

The relative nucleofugicities of the nitro group and chlorine within the same molecule were studied using semi-empirical methods (AM1 and PM3) for the reaction of 2,4-dichloronitrobenzene (**81**) with a free fluoride ion and a fluoride ion bound to

the counterion Me₄N⁺. A comparison of the transition state enthalpies for these reactions demonstrated a certain preference for fluorodenitration in the case of the free fluoride ion,¹⁹⁴ whereas fluorodechlorination occurs preferentially with Me₄N⁺ as a counterion. In addition, it was found experimentally^{187, 194} that the effect of the solvent on the predominant substitution of the nitro group or chlorine under the action of Me₄NF in 2,3,5,6-tetrachloronitrobenzene (**85**) can be used for estimating the contribution of solvation effects to the structure of the transition states of these reactions.

VI. Reactions with amines

Among other neutral nucleophiles used for aromatic substitution of the nitro group and halogens, only amines have been studied in detail.^{1, 165, 195–199} In contrast to reactions with charged nucleophiles, S_NAr reactions with primary and secondary amines can be catalysed by bases; the role of a base can be played by the second molecule of the amine.



The experimental second-order rate constant k_A is calculated from the conventional mechanism of S_NAr reactions with amines at a steady-state concentration of the σ -complex **86**.^{1, 195, 196}

$$k_A = \frac{k_1(k_2 + k_3[B])}{k_{-1} + k_2 + k_3[B]}$$

Depending on the ratio of the rate constants k_1 , k_{-1} , k_2 and $k_3[B]$ in reactions with amines, the following variants are possible:

(a) if $k_2 + k_3[B] \gg k_{-1}$, there is no catalysis and $k_A = k_1$, *i.e.*, the formation of the σ -complex **86** is the limiting step;

(b) if $k_2 + k_3[B] \ll k_{-1}$, the rapid formation of the intermediate **86** is followed by the rate-determining step of its decomposition, and the expression for k_A appears as $k_A = k_1 \times k_2 / k_{-1} + k_2 \times k_3[B] / k_{-1}$, which predicts that the basic catalysis will be characterised by a linear dependence of k_A vs $[B]$;

(c) if $k_2 + k_3[B] \approx k_{-1}$, the dependence of k_A on $[B]$ will be more complex, *viz.*, at low $[B]$, the dependence of k_A on $[B]$ will be linear, whereas at high $[B]$ it will reach a plateau where $k_A = k_1$. Depending on the nature of the aromatic compound, the amine, the base and the solvent, different substitution mechanisms of the nitro group, fluorine and chlorine in arenes under the action of amines will be realised,^{1, 195, 196, 200, 201} as a result of which the substitution rate constant k_A for these groups will change substantially.

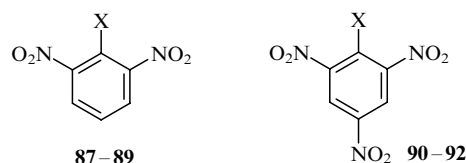
The data on the relative activities (rate constants k_A) of the nitro group, fluorine and chlorine in various arenes under the action of primary and secondary amines in protic, aprotic polar and nonpolar solvents are given in Table 11. The activity series of the leaving groups in reactions of 1,4-disubstituted nitrobenzenes **1**, **31** and **32** with piperidine in aprotic dipolar solvents appear as: $F \gg NO_2 > Cl$ (Table 11, entries 1–3). This order is obviously preserved in reactions of more electrophilic 1-X-2,4-dinitrobenzenes (**57**, **58**, **60**) with piperidine in both protic (MeOH) and aprotic polar solvents (MeCN): $F > NO_2 \gg Cl$ (entries 10 and 11). Presumably, this order of the relative activities of the leaving groups is observed in the absence of the amine catalysis where $k_A = k_1$ and the formation of the intermediate **86** is the limiting step.^{1, 211, 217}

At the same time, the differences in the activities of the nitro group, fluorine and chlorine in reactions of compounds **1**, **31** and **32** with piperidine in aprotic weakly polar solvents are less

apparent, and the order of their activities varies from $F > Cl > NO_2$ (Table 11, entry 4) to $F > NO_2 > Cl$ (entry 5). The activity series of the leaving groups on going to more electrophilic arenes **57**, **58** and **60** in reactions with piperidine under identical conditions appear to be different: $NO_2 > F > Cl$ (entries 12 and 13).

The reason for such variations in the relative activities of these groups is the change of the limiting step of the reaction. If the reaction of compounds **58** and **60** with piperidine in benzene is not subject to catalysis by the amine, the formation of the σ -complex **86** is the limiting step of the reaction.^{205, 213} The reaction of 1-fluoro-2,4-dinitrobenzene (**57**) is catalysed by piperidine.^{211, 214} This is confirmed by the observation of a kinetic isotope effect in a reaction where deuteriopiperidine²¹⁴ and the ¹⁸F-labelled starting compound **57** were used.²¹⁸ Obviously, in this case the decomposition of the σ -complex of the type **86** is the limiting step of this reaction.^{211, 214} A comparison of k_A values for the substitution of fluorine and chlorine in reactions of compounds **57** and **58** with piperidine revealed that the k_A^F/k_A^{Cl} ratio was rather small.^{211, 214} Quite probably, the small values of the $k_A^{NO_2}/k_A^{Cl}$ and k_A^F/k_A^{Cl} ratios in the reactions of nitrobenzenes **1** and **32** with this amine also suggest that the decomposition of the σ -complex **86** is the limiting step in the substitution of the nitro group and fluorine (entries 4 and 5).

The relative activities of the leaving groups in reactions of di- and trinitrobenzenes **57**, **58** and **60** with the primary aromatic amine, *viz.*, aniline, in ethanol decrease in the following order: $NO_2 > F > Cl$,²⁰⁹ which becomes $NO_2 \gg F \gg Cl$ for an analogous reaction of more electrophilic arenes, *viz.*, 2,6-dinitro- (**87–89**) and 2,4,6-trinitrobenzenes **90–92** (entries 16 and 17).



X = NO₂ (**87**, **90**), F (**88**, **91**), Cl (**89**, **92**).

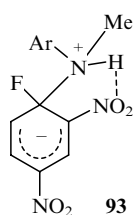
Table 11. Activities of the leaving groups X (X = NO₂, F, Cl) in reactions of substituted arenes ArX with amines.

Ar	Entry	Amine	Solvent	Temperature / °C	k_A^{Cl} /litre mol ⁻¹ s ⁻¹	$k_{rel} = k_A^X/k_A^{Cl}$ at X		Ref.
						NO ₂	F	
4-NO ₂ C ₆ H ₄	1	C ₅ H ₁₀ NH	DMSO	50	6.6×10^{-5}	8.7	412	202
	2	C ₅ H ₁₀ NH	DMSO	50	2.28×10^{-5}	6.7	325	203
	3	C ₅ H ₁₀ NH	MeCN	50	5.5×10^{-6}	3.4	209	203
						(2.6) ^a	—	204
	4	C ₅ H ₁₀ NH	MeCOEt	50	9.3×10^{-6}	0.25	24	203
2-NO ₂ C ₆ H ₄	5	C ₅ H ₁₀ NH	MeCO ₂ Et	50	0.32×10^{-6}	5.6	134	203
	6	C ₅ H ₁₀ NH	C ₆ H ₆	25	1.44×10^{-4} (see ^b)	—	—	205
				60	1.05×10^{-5}	—	—	206
	7	C ₅ H ₁₀ NH	n-C ₆ H ₁₄	27.4	1.67×10^{-4} (see ^b)	—	—	207
2,4-(NO ₂) ₂ C ₆ H ₃	8	Pr ⁱ NH ₂	C ₆ H ₅ CH ₃	60	1.71×10^{-5} (see ^c)	—	—	208
	9	PhNH ₂	EtOH	50	2.69×10^{-4}	188	62	209
	10	C ₅ H ₁₀ NH	MeOH	0	1.95×10^{-3}	207	769	210
	11	C ₅ H ₁₀ NH	MeCN	15	0.291	—	375	211
				25	0.422	—	214	212
	12	C ₅ H ₁₀ NH	MeCO ₂ Et	15	0.183	—	85	211, 213
	13	C ₅ H ₁₀ NH	C ₆ H ₆	15	4.0×10^{-2}	—	92	211, 213
				25	8.05×10^{-2}	143	29	205, 214
2,6-(NO ₂) ₂ C ₆ H ₃	14	4-MeOC ₆ H ₄ NH ₂	C ₆ H ₆	30	0.21×10^{-5}	—	33	215
	15	4-MeOC ₆ H ₄ NHMe	C ₆ H ₆	30	0.43×10^{-5}	—	0.3	215
2,6-(NO ₂) ₂ C ₆ H ₃	16	PhNH ₂	EtOH	50	1.98×10^{-4}	1646	44	216
2,4,6-(NO ₂) ₃ C ₆ H ₂	17	PhNH ₂	EtOH	50	3.34	1260	100	209

^a The experimental value for the nitro group was calculated relative to chlorine. ^b Substitution of the nitro group. ^c Substitution of fluorine.

For polynitroarenes, the higher activities of the nitro group (compounds **60**, **87** and **90**) and fluorine (compounds **57**, **88** and **91**) in comparison with chlorine (compounds **58**, **89** and **92**) are due to the fact that the limiting step of these reactions is the formation of the σ -complex **86**.^{1, 10, 199, 205} The activity of the nitro group in compounds **87** and **90** is higher than that of fluorine (compounds **88** and **91**) due to the steric effect of two *ortho*-nitro groups in the vicinity of the reaction centre (*cf.* entries 9, 16 and 17).²¹⁶ The weaker spatial effect of a primary amine in comparison with the secondary amine causes a reversal of the relative activities of the nitro group and fluorine in reactions of compounds **60** and **57** with aniline and piperidine in alcohols where the formation of the intermediate **86** (entries 9 and 10) is the limiting step.²¹⁷ Moreover, steric effects in amines can even change the limiting step of the substitution in arene **57** with a small-sized leaving group (the fluoride ion). Thus the reaction of the ¹⁸F-labelled compound **57** with 2-methylaniline (DMSO, 30 °C) manifests a pronounced kinetic isotope effect which suggests the abstraction of the fluoride ion at the rate-determining step.²¹⁹ However, no such effect is observed in an analogous reaction with 4-methylaniline where the formation of the σ -complex **86** is the limiting step²¹⁹ (*cf.* Ref. 220). Naturally, the steric effects of primary and secondary amines in their reactions with arenes in weakly polar media disappear, if the decomposition of the σ -complex **86** is the limiting step. The low values of the k_A^F/k_A^{Cl} ratio in reactions of compounds **59** and **60** with piperidine and 4-anisidine in benzene where the former undergoes catalysis by the corresponding amine (entries 13 and 14) is supporting evidence for this hypothesis.^{214, 215}

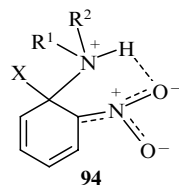
The reasons for the higher activity of fluorine in reactions of arenes with amines in weakly polar media in comparison with chlorine under conditions of basic catalysis were discussed in some recent publications.¹⁹⁹ The formation of a hydrogen bond with the amino group is a possible explanation for the faster abstraction of the fluoride ion from the σ -complex **86**. This means that the abstraction of the fluoride ion requires an additional molecule of the amine, *i.e.*, a catalytic step takes place.¹⁹⁹ This is confirmed by a decrease in the activity of fluorine in comparison with chlorine in reactions of halogeno-2,4-dinitrobenzenes **57** and **58** with *N*-methyl-4-anisidine in benzene; the efficiency of catalysis in the reaction of compound **57** (X = F) with a secondary amine markedly decreases due to increased stability of the intermediate **93**.²¹⁵



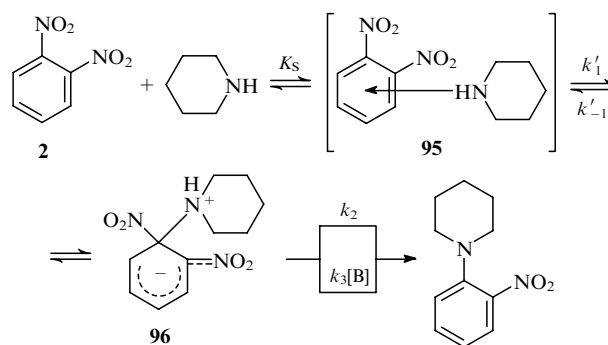
The formation of a molecular complex of an arene and an amine that is more reactive than the arene itself may be regarded as yet another reason for the higher activity of fluorine in comparison with chlorine under catalytic conditions. This is supported by high negative values of ρ obtained in the analysis of the Hammett equation for the reaction of compound **57** with substituted anilines.¹⁹⁹ Both molecular complexes of reactants and aniline dimers, which are more reactive nucleophiles^{221, 222} may be formed on the reaction coordinate of compounds **57** and **58** with aniline in a weakly polar solvent.

It should be emphasised that the activities of the nitro group, fluorine and chlorine in *ortho*-substituted benzenes **2–4** exceed those of the *para*-substituted compounds **1**, **32** and **33** in reactions

with piperidine in weakly polar solvents due to intramolecular solvation in the transition state of the reaction, *i.e.*, in the intermediate **94** (Table 11, entries 4, 5 and 6).^{1, 206, 208}



The reactions of compounds **2–4** with amines are not catalysed by a base and the formation of the σ -complexes **86** is the limiting step.^{205, 206, 208} In contrast, similar reactions of compounds **1**, **32** and **33** are catalysed by a base and decomposition of the corresponding σ -complexes is the limiting step. The amine-catalysed reaction of 1,2-dinitrobenzene (**2**) with piperidine in non-polar *n*-hexane is an exception.²⁰⁷ The kinetics of this reaction involves the equilibrium constant K_S for the formation of the π - π electron-donor complex **95** prior to the formation of the σ -complex **96**; the decomposition of the latter is the limiting step of this reaction (entry 7).²⁰⁷ Recently, it has been shown that no complexes of the type **95** are formed upon substitution of benzene for *n*-hexane, which results in the deceleration of the reaction of arene **58** with amines.²²³

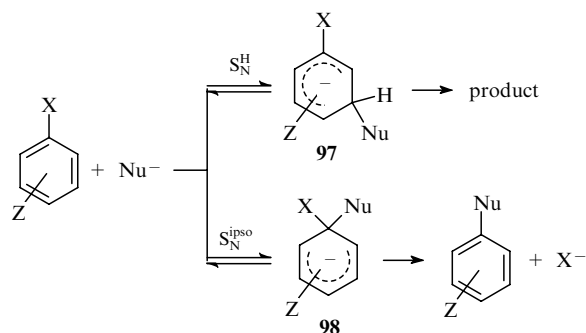


Thus, the substitution reactions of the nitro group, fluorine and chlorine in arenes under the action of amines under various reaction conditions are multistep processes. In-depth studies of their mechanisms in weakly polar and nonpolar media are currently under way.^{224–228} Such reactions are also being investigated for five-membered heterocycles, *e.g.*, thiophene derivatives.^{229, 230}

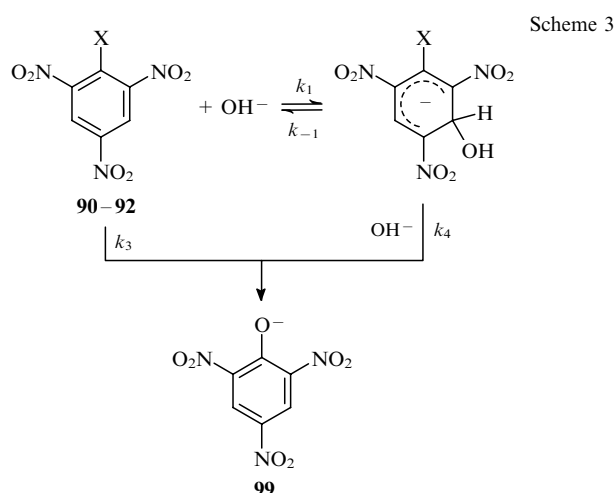
VII. The role of the reaction mechanisms

Although the nucleophilic substitution mechanism S_NAr (addition–elimination) in arenes and heteroarenes has become classical in organic chemistry long ago,^{1, 7, 10, 11} some alternative mechanisms can also be used. These may be divided into several groups, *viz.*, electron-transfer reactions (SET),³ photochemical reactions,^{6, 231–233} vicarious hydrogen substitution reactions (VNS),^{2, 9} *kine*- and *tele*-substitutions,^{6, 234} ring opening–closure reactions, mainly for heterocyclic compounds (ANRORC)^{2, 64} and reactions catalysed by transition metals.^{235, 236}

It is known that the formation of σ -complexes of the type **97** at nonsubstituted positions of activated aromatic rings proceeds much faster and the stabilities of these complexes strongly depend on the nature of the nucleophile, the substrate and some other factors.^{1, 2, 5, 9, 25, 44, 148} Therefore, S_N^H and S_N^{ipso} substitutions always compete with one another due to the reversibility of formation of the σ -complexes **97** and **98**.



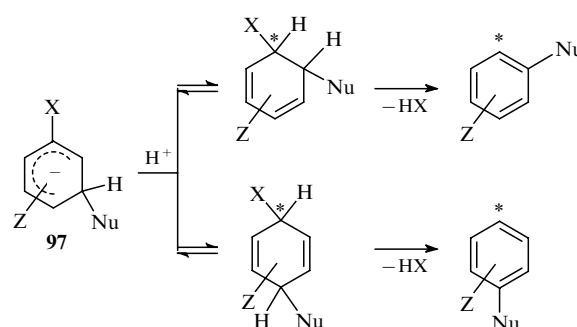
If σ -complexes of the type **97** can be transformed further (e.g., according to VNS or an oxidative route^{2,9}), the S_N^H route will prevail over S_N^{ipso} substitution. Such a competition has already been discussed in this review (Sections III–V) (see also Ref. 237). It is of note that steric and electronic factors can also influence the regioselectivity of substitution of the nitro group, fluorine and chlorine.^{5,20} Thus compounds **90** and **92** react with the hydroxide



Compound	X	k_1 /litre mol ⁻¹ s ⁻¹	k_3 /litre mol ⁻¹ s ⁻¹
90	NO ₂	1450	140
91	F	50	750
92	Cl	6	0.40

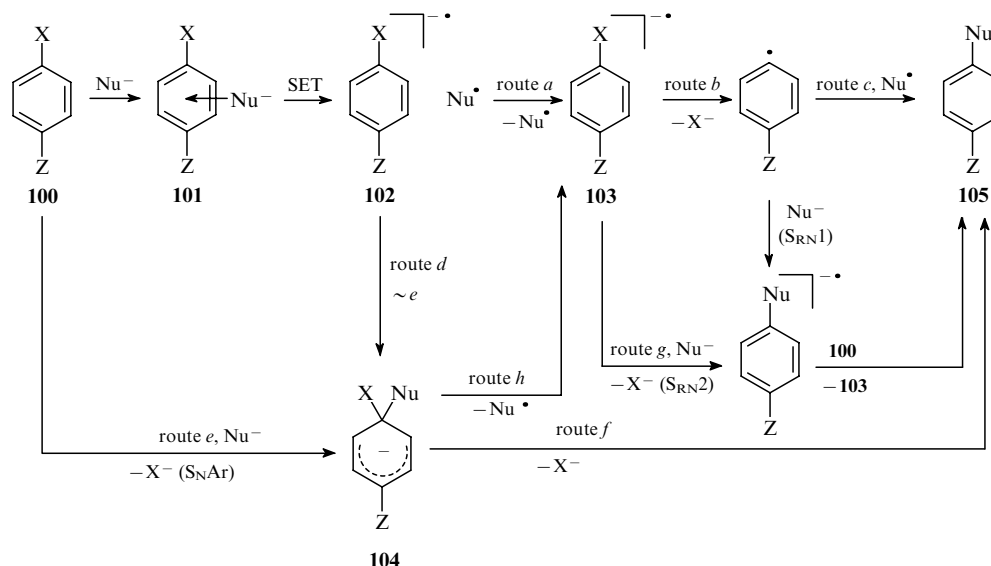
ion in water more readily according to the S_N^H route than according to the S_N^{ipso} route, whereas picryl fluoride **91** undergoes preferably *ipso*-substitution in this reaction.^{238,239} Presumably, the stereo-electronic effects in the reaction of compound **91** with the hydroxide ion in the *ipso*-position favour fast formation of the picrate ion **99** (Scheme 3).^{5,20}

Steric effects in a nucleophile may become crucial as regards the regioselectivity of substitution. Thus compounds **3** and **4** react with the 2-phenylthio-1,3-dithiane carbanion exclusively according to the VNS mechanism.²⁴⁰ Recently, it has been shown that the S_N^H substitution becomes prevalent over S_N^{ipso} substitution in reactions of 1,3-dinitrobenzene (**66**) and its 5-fluoro- and 5-chloro derivatives with potassium methoxide with an increase in the excess of the nucleophile relative to the substrate.²⁴¹ The competition between the S_N^{ipso} and S_N^H routes may result in *kine*- and *tele*-substitution due to faster conversion of the σ -complex of the type **97**. Various *kine*- and *tele*-substitution reactions of the nitro group were generalised in the reviews.^{6,234}



Aromatic nucleophilic substitution reactions are characterised by an immense diversity of intermediates formed (Scheme 4). Introduction of a nitro group into the aromatic ring significantly facilitates the formation and increases the stability of the corresponding radical anions because of a decrease in their LUMO energy. As a rule, *para*-substituted aryl halides **100** (X and/or Z = Hal) produce intermediate structures **101** and **102** and then free radical anions of the type **103**, which undergo fragmentation into aryl radicals and halide ions and can serve as substrates for $S_{NR}1$ reactions (routes *a* + *b*).^{3,242–244} The $S_{NR}1$ mechanism is uncommon for nitro- and halogenonitroarenes. It was shown that substitution of fluorine and chlorine in compounds **57** and **58** under the action of a sterically hindered ethyl α -cyanophenylacetate carbanion in DMSO is induced by a solvated electron and occurs according to the $S_{NR}1$ mechanism.²⁴⁵ Previous studies have

Scheme 4



shown^{246, 247} that substitution of fluorine and chlorine in compounds **31** and **32** under the action of ethyl cyanoacetate carbanion in DMSO follows a non-chain radical mechanism (routes *a* + *c*) (cf. Ref. 105). However, it is believed²⁴⁸ that in the latter case the reactions proceed presumably with an electron transfer (route *d*) with an intermediate formation of the radical pair **102** inside the solvent cage. Subsequent coupling of the radical anion and the radical inside the cage yields the σ -complex **104**. The S_NAr mechanism (route *e*) cannot be excluded either.²⁴⁸

There is a great body of evidence in favour of the *ipso*-substitution mechanism in nitro- and halogenonitroarenes under the action of charged and neutral nucleophiles, which proceeds via an intermediate $n-\pi$ donor-acceptor complex of the type **101**. This is followed by an electron transfer resulting in the formation of the radical pair **102**.^{242, 243, 249–251} The further fate of the radical pair **102** depends largely on the nature of the nucleophile, although its further conversion according to the route *d* + *f* prevails.²⁵¹ Since the routes *d* and *e* leading to the formation of the reaction product **105** are kinetically indistinguishable, the S_NAr substitution mechanism is not ruled out either.²⁴⁸ If the radical pair **102** leaves the solvent cage, free radical anions of the type **103** can be detected by ESR.^{244, 249–252} The hypothesis that these radical anions lie on the coordinate of nucleophilic S_{NR2} substitution of the nitro group, fluorine and chlorine (route *g*)^{253, 254} met sound criticism on kinetic,^{255, 256} electrochemical^{256, 257} and theoretical grounds.^{3, 243} Most probably, the formation of radical anions of the type **103** and the substitution via the σ -complex **104** may occur in parallel and independently of one another.²⁴⁴ Using the reaction of 1,4-dinitrobenzene **1** with the cyanide ion in oxygen-free DMF as an example, it was shown that the radical anions **103** can be generated by homolytic fragmentation of the σ -complex **104** (route *h*)²⁵⁸ (cf. Ref. 257). Therefore, the *ipso*-substitution of the nitro group, fluorine and chlorine in nitro- and halogenonitroarenes follows mainly the SET or the S_NAr mechanism (routes *d*, *e* and *f*) (cf. Ref. 259).

Photochemical substitution reactions of fluorine and chlorine in arenes have been reviewed previously;²³¹ their mechanisms strongly depend on the nature of the arene and the nucleophile. However, photosubstitution of the nitro group in arenes has been little studied. It was shown²³¹ that the reaction of 4-nitroanisole with glycine ethyl ester occurs upon an attack of the substrate in the excited state by the nucleophile (the S_NAr^* mechanism).²⁶⁰ The SET mechanism is realised to a lesser degree²⁶⁰ (cf. Ref. 261). It is of note that photochemical transformations are more efficient for S_N^H substitution reactions in nitroarenes which proceed according to the VNS mechanism.^{232, 233}

Reactions according to the ANRORC mechanism are mostly related to S_N^H rather than S_N^{ipso} substitution.^{2, 63} The S_N^{ipso} reactions catalysed by transition metals (Cu, Ni, Pd, etc.), are of extreme importance and are being developed dynamically; they were studied mostly for the substitution of chlorine, bromine and iodine.^{168, 235, 236, 262–265}

* * *

A vast body of evidence has been accumulated on the activities (including relative activities) of the nitro group, fluorine and chlorine in aromatic nucleophilic substitution reactions in relation to the structure of the substrate, the type of the nucleophile and the medium and the reaction mechanism. This review is an attempt at a state-of-the-art generalisation of the results obtained in this area. The need for such generalisation is due to the fact that significant progress in the development of methods for functionalisation of arenes has become possible owing to the use of convenient nucleophilic *ipso*-substitution reactions ($S_N^{ipso}Ar$).

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Reactions of phosphorus ylides with acyl chlorides: pathways and preparative potential

V N Listvan, V V Listvan

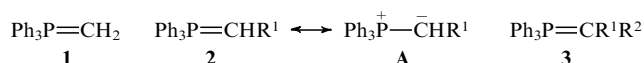
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Abstract. Data concerning the reactions of phosphorus ylides with acyl chlorides that occur by different pathways depending on the nature of the ylide or acyl chloride and on the reaction conditions are summarised and systematised. The products of these reactions are of interest as building blocks for the synthesis of other classes of compounds. The bibliography includes 131 references.

I. Introduction

Phosphorus ylides (or alkylidenephosphoranes, phosphonium methylides)^{1,2} are compounds with a P=C bond. They possess great synthetic potential and are used to obtain other classes of compounds. It is mostly triphenylphosphine derivatives, such as methylenetriphenylphosphorane (**1**) and substituted alkylidenephosphoranes **2** and **3**, that find practical use. The P=C bond in these compounds is polarised considerably in such a way that the electron density is shifted from the phosphorus atom to the carbon atom (structure **A**).



R¹, R² = Alk, Ar, COAlk, COAr, CO₂Alk, CN.

The presence of partial negative charge on the ylide carbon atom makes these compounds highly reactive, primarily with respect to electrophilic reagents.

Phosphorus ylides **2** and **3** containing alkyl or aryl substituents at the ylide carbon atom are the most reactive. They are sensitive to moisture and atmospheric oxygen; therefore, they are not isolated in pure form but are obtained in anhydrous solvents, usually in an inert atmosphere, just prior to the reaction. If electron-withdrawing groups (COR, CO₂R, CN) are present as substituents at the ylide carbon atom and the negative charge is partially shifted to them, the reactivity of the ylides decreases. Such compounds can be isolated in a free state and stored under ordinary conditions. Some of them are available commercially, e.g., acetylmethylenetriphenylphosphorane (**2**, R¹ = COMe), benzoylmethylenetriphenylphosphorane (**2**, R¹ = C(=O)Ph),

ethoxycarbonylmethylenetriphenylphosphorane (**2**, R¹ = CO₂Et), etc.

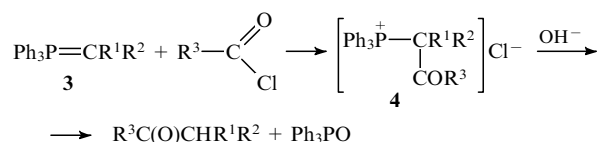
The reaction of phosphorus ylides with aldehydes (the Wittig reaction) is the most famous; it is widely employed in syntheses of unsaturated compounds. The Wittig reaction has been described in detail in a number of reviews and monographs,^{3–12} including one recent review¹³ dedicated to the 100th anniversary of this reaction's creator.

Wide circles of chemists are less aware of reactions of alkylidenephosphoranes with other electrophilic reagents, *inter alia*, acyl halides. Depending on the nature of the starting compounds and sometimes on the reaction conditions, the reactions of phosphorus ylides with acyl halides occur by different pathways and give different products. In the future, some of these transformations affording interesting organic products^{1,2,14} may become preparative methods for their synthesis. As of now, several examples of reactions of phosphorus ylides with acyl chlorides for possible preparative use are known: the formation of acylated ylides followed by their thermolysis into acetylene compounds or oxidation to give polycarbonyl derivatives; synthesis of allene compounds; synthesis of enol esters, etc.

Since the publication of the review by Bestmann and Zimmermann¹ and the monograph by Kolodyazhnyi² which cover the literature on reactions of phosphorus ylides with acyl chlorides reported before 1990, a lot of new publications have appeared that require generalisation and systematisation. Therefore, it seems expedient to cover this aspect of the chemistry of alkylidenephosphoranes in a separate review. The authors of this review tried to cover, as thoroughly as possible, the literature on reactions of phosphorus ylides with acyl chlorides for the period from 1990 to 2002. Moreover, the review considers the most significant publications of the preceding years.

II. Acylation of phosphorus ylides. Transylidation

Acylation occurs most readily with acyl chlorides and alkylidenephosphoranes **3**, which contain no hydrogen atoms at the ylide carbon atom: the acyl residue adds to the ylide carbon atom to give C-acylated phosphonium salts **4**.^{15–17} Alkaline hydrolysis of the latter results in ketones.



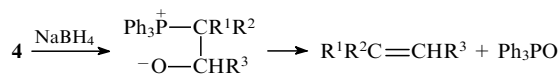
R¹, R² ≠ H.

V N Listvan, V V Listvan I Franko Zhytomyr State Pedagogical University, ul. B Berdichevskaya 40, 10008 Zhytomyr, Ukraine.
Fax (38-041) 237 27 63. Tel. (38-041) 234 07 62.
E-mail: listvan@ukr.net

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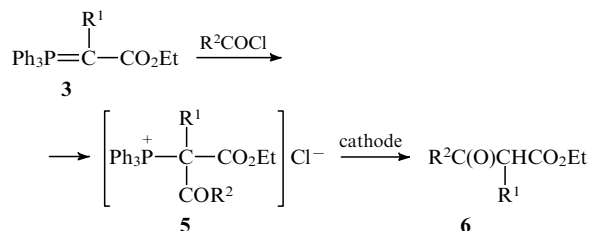
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Reduction of *C*-acylated phosphonium salts **4** with sodium borohydride occurs *via* intermediate betaines, which quickly eliminate triphenylphosphine oxide to give alkenes.¹⁶



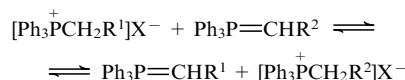
$\text{R}^1 = \text{Me}$; $\text{R}^2 = \text{Me, Ph}$; $\text{R}^3 = \text{Ph, MeC}_6\text{H}_4$.

A similar reaction of acyl chlorides with phosphoranes **3** containing the ester group, followed by cathodic reduction of acylated phosphonium chlorides **5**, provides a method to obtain esters of α -substituted β -oxo acids **6**.¹⁷



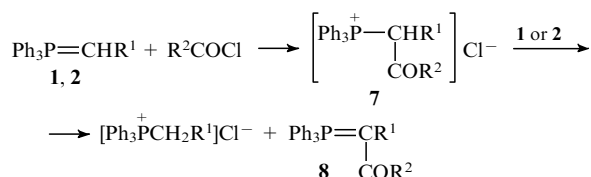
$\text{R}^1 = \text{Me, Pr, C}_5\text{H}_{11}, (\text{CH}_2)_2\text{CO}_2\text{Me, Ph, CH}=\text{CHPh, (CH}_2)_2\text{Ph}$;
 $\text{R}^2 = \text{Et, Bu}$.

Monosubstituted alkylidenephosphoranes **2** containing a hydrogen atom at the ylide carbon are conjugated bases, whereas the corresponding phosphonium salts are acids. The position of equilibrium depends on the nature of substituents R^1 and R^2



and is strongly (often, almost completely) shifted to the right if R^1 is a much stronger electron-withdrawing group than R^2 ; in fact, this is the case in acylation reactions.

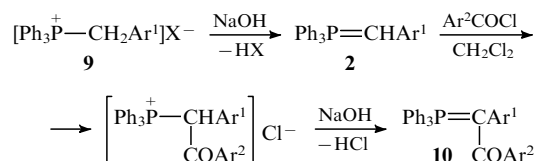
The phosphonium salts **7** initially formed upon acylation of phosphoranes **1** and **2** are rather strong acids due to the effect of the acyl group. They eliminate HCl under the action of the initial phosphorane molecules to give acylated ylides **8** (weaker bases than the original phosphoranes). Thus, transylation occurs:^{18–21} the phosphonium salt and the ylide react to give a new phosphonium salt and a new ylide. This principle is widely employed in the synthesis of α -acylated ylides **8**.^{22–29}



$\text{R}^1 = \text{H, Me, Et, Pr}^n, \text{Pr}^i, \text{Bu}^n, \text{C}_5\text{H}_{11}, \text{Ph, CO}_2\text{Et}$; $\text{R}^2 = \text{Me, Et, Pr}^n, \text{Pr}^i, \text{Bu}^n, \text{Bu}^i, \text{C}_5\text{H}_{11}, \text{C}_6\text{H}_{13}, \text{cyclo-C}_4\text{H}_7, \text{cyclo-C}_6\text{H}_{11}, \text{CH}=\text{CHMe, Ph, 2-MeOC}_6\text{H}_4, \text{2-MeSC}_6\text{H}_4, \text{CH}_2\text{P}(\text{O})(\text{OEt})_2$.

The usual procedure for the acylation of unstable alkylidene- and arylmethylidenephosphoranes **1–3** ($\text{R}^1, \text{R}^2 = \text{Alk, Ar}$) involves the addition of phenyl- or butyllithium to a solution of the appropriate phosphonium salt in an anhydrous solvent, followed by treatment of the resulting phosphorane with the acylating agent in an inert atmosphere. The process can be simplified considerably by using the two-phase system CH_2Cl_2 –50% aqueous NaOH. These conditions were used to acylate benzylidenetriphenylphosphorane and other arylmethyl-

idenephosphoranes (**2**, $\text{R}^1 = \text{Ar}$)^{30–32} formed upon treatment of the corresponding phosphonium salts **9** with NaOH.[†]



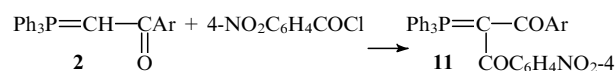
$\text{Ar}^1 = \text{Ph, 4-PhC}_6\text{H}_4, 2,4\text{-Cl}_2\text{C}_6\text{H}_3, 3\text{-FC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-MeO}_2\text{CC}_6\text{H}_4, 2,3,5,6\text{-Cl}_4\text{-4-MeC}_6, 4\text{-PhCOC}_6\text{H}_4, 4\text{-(4-MeC}_6\text{H}_4\text{N}=\text{N)C}_6\text{H}_4, 1\text{-naphthyl, 2-naphthyl, 4-methyl-1-naphthyl, 9-phenanthryl}$;
 $\text{Ar}^2 = \text{Ph, 4-ClC}_6\text{H}_4, 3\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-furyl}$.

The reaction is carried out under conditions of phase-transfer catalysis; the phosphonium salt serves as the carrier of ions from the aqueous phase to the organic phase. This procedure makes acylphosphoranes **10** accessible; the latter are used in syntheses of diarylacetylenes.

This two-phase system can also be used to acylate stable ylides; in this case, there is no need to isolate the free ylide beforehand.³²

The optimum phosphorane-to-acyl chloride ratio in transylation is 2 : 1. Otherwise, the excess acyl chloride can further react with the acylated ylide to give side products.

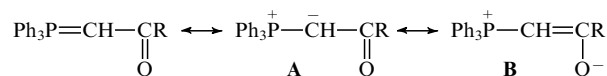
The reactions of aroylmethylidenetriphenylphosphoranes (**2**, $\text{R}^1 = \text{COAr}$) with *p*-nitrobenzoyl chloride in the ratio 2 : 1 resulted in *C*-acylated phosphoranes **11**, which are crystalline products with sharp melting points.³⁴



$\text{Ar} = \text{Ph, 4-ClC}_6\text{H}_4, 4\text{-MeC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-thienyl}$.

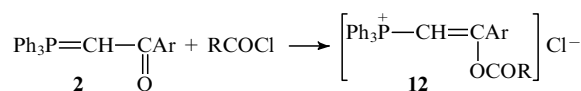
Later, the *C*-acylation of other ylides with similar structures with *p*-nitrobenzoyl chloride as well as cinnamoyl chloride, furoyl chloride and phenylacetyl chloride was described.^{35,36} However, Nesmeyanov *et al.*³⁷ doubted that it was possible to obtain *C*-acylated products from 2-oxoalkylidenephosphoranes; they believed that *O*-acylation was most probable.

In phosphorane molecules containing a carbonyl group bound to the ylide carbon atom, the electron density is shifted from the ylide carbon atom (structure **A**) to the oxygen atom of the carbonyl group to give structure **B**, as confirmed by spectral methods.^{25,38–40}



$\text{R} = \text{Alk, Ar, OAlk}$.

In such a case, the reaction centre of the 2-oxoylide molecule is transferred to the carbonyl oxygen; this is actually observed in acylation and alkylation reactions. For example, it was shown³⁴ that aroylmethylidenetriphenylphosphoranes (**2**, $\text{R}^1 = \text{COAr}$) react with acetyl chloride and benzoyl chloride in accordance with structure **B** to give *O*-acylated salts **12**.

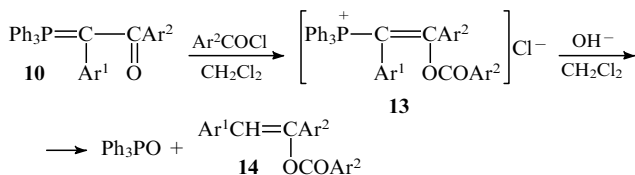


$\text{Ar} = \text{Ph, 4-BrC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-MeC}_6\text{H}_4$; $\text{R} = \text{Me, Ph}$.

[†] Simultaneously, the concentrated alkaline solution acts as a desiccant for dichloromethane.³³

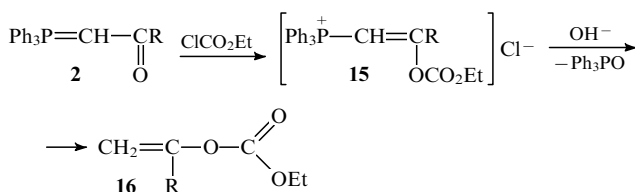
O-Acylation of phosphoranes was also observed in some other studies.^{35, 41–44}

Treatment of phosphorus ylides with a 2.5–3-fold excess of an acyl chloride under conditions of phase-transfer catalysis results in secondary acylation of the initially formed ylide **10**; this is accompanied by the transfer of the reaction centre to the carbonyl oxygen atom. Subsequently, the *O*-acylated phosphonium salt **13** is cleaved by an alkali to give enol esters **14**.^{45, 46}



Ar¹ = Ph, 4-MeC₆H₄, 4-PhC₆H₄, 1-naphthyl, 2-naphthyl, 4-methyl-1-naphthyl; Ar² = Ph, 2-ClC₆H₄, 4-ClC₆H₄, 2-MeC₆H₄, 4-MeC₆H₄.

Chloroformates react with 2-oxoalkylenephosphoranes with the attack also on the oxygen atom under conditions of phase-transfer catalysis giving *O*-acylated phosphonium salts **15**; the latter are cleaved by an alkali into enol carbonates **16**.⁴⁷

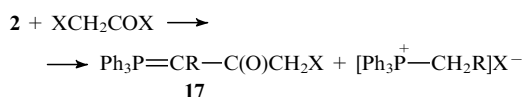


O-Acylated phosphonium salts can be isolated and stored under ordinary conditions, but they are very unstable at elevated temperatures. Probably, *O*-acylated phosphonium salts can serve as acylating agents, with respect to the original phosphorane molecules in particular.

It was shown⁴⁸ that heating of *O*-acylation products results in their slow rearrangement with migration of the acyl residue to the carbon atom, *i.e.*, with formation of *C*-acylation products.

Preparation of *C*-acylated derivatives from 2-oxoalkylenephosphoranes is only possible with acyl chlorides activated by electron-withdrawing groups. In addition to *p*-nitrobenzoyl chlorides, this reaction can be carried out with ethoxalyl chloride, 2-oxoacyl chlorides, 2-furoyl chloride, *etc.*

Halogen-substituted acyl halides (chloroacetyl chloride, bromoacetyl bromide, trichloroacetyl chloride) behave as acylating agents⁴⁹ with respect to alkoxy-carbonyl- and cyanomethylidene-triphenylphosphoranes. The reaction is accompanied by transylidation to give *C*-acylated phosphoranes **17**.

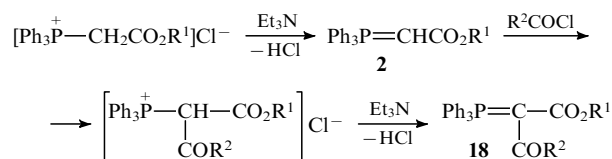


R = CO₂Me, CO₂Et, CN; X = Cl, Br.

The halogen atoms of the α-halogenoketone moiety of the ylides **17** can undergo nucleophilic substitution, although the effect of the phosphoranylidene-methyl group makes them less reactive than in ordinary halogenoketones.

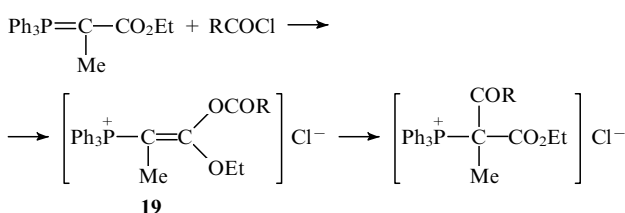
Upon transylidation, half of the starting ylide is present in the reaction mixture as a phosphonium salt. This drawback can be avoided if another base, for example triethylamine, is used to bind the hydrogen halide.^{50–53} Yet another advantage of this method is that preliminary isolation of the starting phosphorane in a free state is unnecessary. One can perform the reaction using an appropriate phosphonium salt and a twofold excess of triethyl-

amine.^{54, 55} Successive transformations of a phosphonium salt gave *C*-acylated ylides **18**.



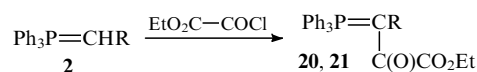
R¹ = Me, Et, Bu, Bn; R² = CHCl₂, CCl₃, CClF₂, CHF₂, CF₃, C₂F₅, CCl₂Me, Ph, 2-MeC₆H₄, 4-MeC₆H₄, 2-MeOC₆H₄, 4-MeOC₆H₄, 4-ClC₆H₄, 2-MeSC₆H₄, C≡CBu, C≡CPh, 2-furyl, 2-thienyl.

It was found⁵⁶ that alkoxy-carbonyl-substituted ylides give unstable *O*-acylated salts **19** at low temperatures, which then undergo spontaneous rearrangement into *C*-acylated phosphonium salts.



R = Me, (CH₂)₂CO₂Me, (CH₂)₂CO₂Bn.

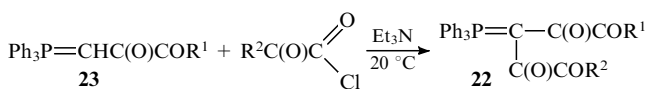
The reaction of acetylmethylidene-triphenylphosphorane (**2**, R = COMe) with ethoxalyl chloride gave ylide **20** with two carbonyl groups and one ester group, whereas the reaction of methoxycarbonylmethylidene-triphenylphosphorane (**2**, R = CO₂Me) gave trioxo ylide **21**, which contains one carbonyl group and two ester groups.⁵⁷



R = COMe (**20**), CO₂Me (**21**).

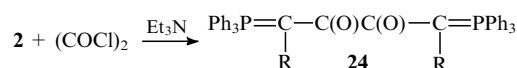
The low yields of phosphoranes **20** and **21** (9% and 33%, respectively) can be explained by the fact that Koz'minykh *et al.*⁵⁷ used an equimolar phosphorane : acyl chloride ratio. Better results were achieved with triethylamine.^{58, 59}

Tetraoxoylides **22** are formed in reactions of dicarbonyl phosphoranes **23** with 2-oxoacyl chlorides.^{60–62}



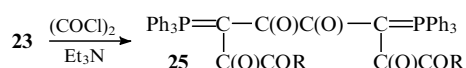
R¹, R² = Me, Ph, OMe, OEt.

The reactions of alkylidenephosphoranes with dicarboxylic acid chlorides result in bisylides. In certain studies,^{61, 63, 64} oxalyl chloride was used for acylation. For example, bisylides **24** were obtained by treatment of phosphoranes **2** with oxalyl chloride in the presence of triethylamine.⁶³ Reactions of alkylidenephosphoranes **2** with other dicarboxylic acid chlorides, as well as reactions of monoacyl chlorides with bisylides containing hydrogen atoms at the ylide carbon atoms, result in similar products.⁶⁴



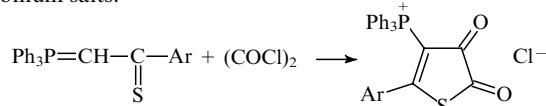
R = Ph, 4-ClC₆H₄, 4-BrC₆H₄, CO₂Me, CO₂Et, CPh.

Furthermore, Aitken and Karodia⁶¹ obtained hexacarbonyl bisylides **25** using the reaction of dicarbonyl phosphoranes **23** with oxalyl chloride.



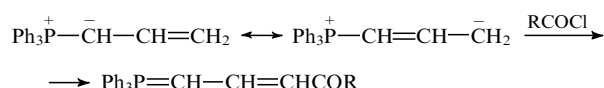
R = Ph, OMe, OEt.

The reactions of oxalyl chloride with alkylidenephosphoranes containing the thiocarbonyl group resulted in heterocyclic phosphonium salts.⁶⁵



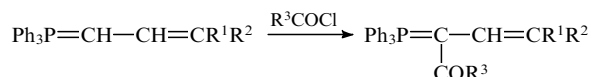
Ar = Ph, 4-MeC₆H₄.

Vinylmethylidenetriphenylphosphorane is acylated at the γ -position; this is accompanied by transylidation.^{66, 67}



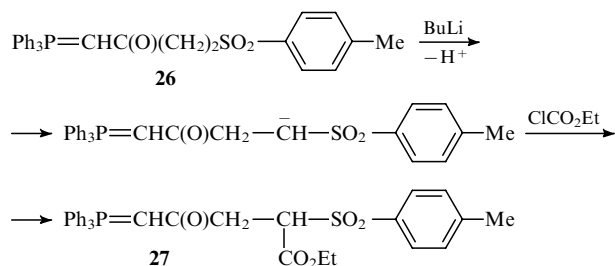
R = Me, Prⁿ, Prⁱ, Buⁿ, OMe.

However, vinylmethylidenephosphoranes containing two γ -substituents only undergo α -acylation.⁶⁸



R¹ = Ph, R² = H; R¹ = R² = Me; R³ = Ph, 4-ClC₆H₄, 4-MeC₆H₄, CH=CHPh.

An unusual example of the acylation of phosphorane **26** containing a sulfonyl group was reported.⁶⁹ Its treatment with butyllithium results in deprotonation from the α -position with respect to the sulfonyl group, giving a carbanionic centre which is stronger than the ylide carbon atom. Subsequent acylation with ethyl chloroformate results in the new phosphorane **27**, which can subsequently be used in the Wittig reaction.

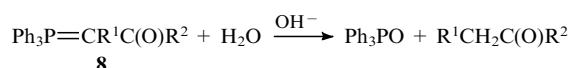


Acylated ylides possess biological activity; in particular, they were found to have antimicrobial properties. A short survey of results of studies on the biological action of acylmethylidenephosphoranes and the corresponding phosphonium salts has been published.⁵⁷

III. Reactions and preparative value of acylated ylides

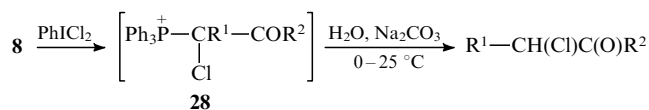
1. Hydrolysis and reduction. Synthesis of ketones and carboxylic acids

Acylphosphoranes **8** can serve as intermediates in the syntheses of other classes of compounds, *e.g.*, ketones, using alkaline hydrolysis,^{15, 18, 70} reductive cleavage in the presence of zinc in acetic acid^{18, 20, 68, 71} or other methods.^{18, 26, 69, 72}



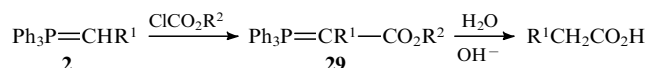
R¹ = H, Me, Pr, Ph; R² = Me, Pr, C₅H₁₁, Ph, CH=CHPh, (CH₂)₂Ph.

Chlorination of phosphoranes **8** with dichloriodobenzene followed by hydrolysis of salts **28** results in α -chloro ketones.²⁶



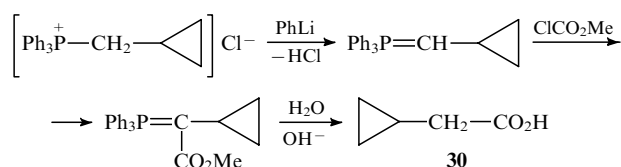
R¹ = Et, Prⁿ, C₅H₁₁, Bn; R² = Me, Prⁱ, cyclo-C₃H₅, cyclo-C₆H₁₁.

The ester group is introduced in alkylidenephosphorane molecules using alkyl chloroformates as acylating agents;^{66, 69, 73} subsequent hydrolysis of the resulting phosphoranes **29** gives carboxylic acids.

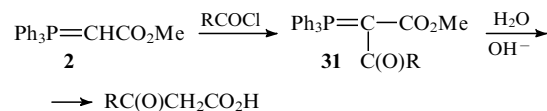


R¹ = H, Me, Et, Pr, cyclo-C₃H₅, cyclo-C₆H₁₁, Ph; R² = Me, Et.

Cyclopropanecarboxylic acid **30** was obtained in 84% yield using this method.⁷³



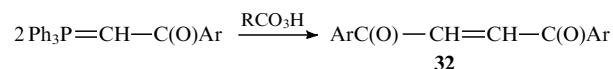
Alkaline hydrolysis of acylated phosphoranes **31** yielded β -oxo acids, while their acid hydrolysis yielded their esters.⁷⁴



R = Me, Pr, C₅H₁₁, C₁₃H₂₇, Ph, 2-furyl.

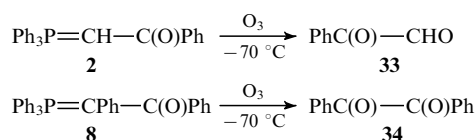
2. Oxidation of acylmethylidenephosphoranes

The oxidation of acylated ylides is yet another example of their preparative usage. Different products are obtained depending on the oxidant. It was shown^{75, 76} that oxidation of stabilised acyl ylides with peroxy acids gives diacyl-substituted ethylenes. The best results were achieved in the synthesis of diaroylethylenes **32**. Presumably, the original phosphorane is partly oxidised into arylglyoxal during the reaction; the latter then undergoes the Wittig reaction with other ylide molecules to give diaroylethylenes.

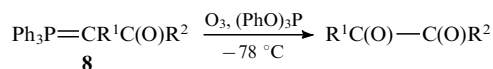


Ar = Ph, 4-BrC₆H₄, 4-MeOC₆H₄, 4-NO₂C₆H₄, 4-MeCONHC₆H₄;
R = Me, C₇H₁₅.

Similar compounds were obtained upon the oxidation of aroylmethylidenetriphenylphosphoranes with selenous acid in dioxane.^{77, 78} Treatment of acyl- and alkoxycarbonylmethylidenephosphoranes with alkene ozonides^{79, 80} results in symmetrical alkenes containing ketone or ester groups. The reaction occurs probably *via* intermediate glyoxals, as was proved⁸¹ by analysing the products obtained upon treatment of aroylmethylidenephosphoranes with ozone at -70°C . Under these conditions, phenylglyoxal (**33**) was obtained from benzoylmethylidenetriphenylphosphorane (**2**, R = C₆H₅) and diketone **34** was obtained from the substituted ylide **8** (R¹ = R² = Ph).

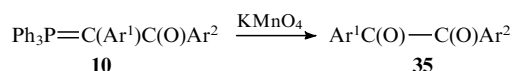


Later, Bestmann *et al.*⁸² showed that it is better to use the ozone–triphenylphosphite adduct for the preparation of diketones from phosphoranes **8**.



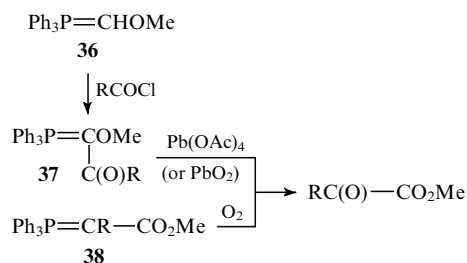
$\text{R}^1 = \text{Me}, \text{Bu}$; $\text{R}^2 = \text{Bu}, \text{C}_5\text{H}_{11}, \text{C}_6\text{H}_{13}, (\text{CH}_2)_8\text{CH}=\text{CH}_2$.

Similar α -diketones were obtained using NaIO_4 ,⁸³ OsO_4 and KMnO_4 ⁸⁴ as oxidants. Potassium permanganate was found to be the most suitable for the oxidation of compounds **10** with aromatic substituents into the corresponding non-symmetrical diketones **35** in a two-phase system.⁸⁵



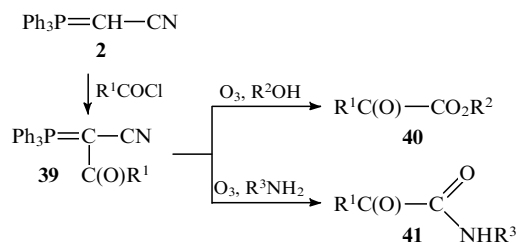
$\text{Ar}^1 = \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 2\text{-NO}_2\text{C}_6\text{H}_4$; $\text{Ar}^2 = \text{Ph}, 2\text{-MeOC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 2\text{-MeSC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 2\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-furyl}, 2\text{-thienyl}$.

Acylation of methoxymethylidenetriphenylphosphorane **36** with acyl chlorides involving transylidation followed by oxidation of the products **37** with lead dioxide or lead tetraacetate was recommended⁸⁶ as a method for the synthesis of α -oxo acid esters. The same esters were obtained by oxidation of phosphoranes **38** with atmospheric oxygen.⁸⁷



$\text{R} = \text{Me}, \text{Pr}^i, \text{Bu}, \text{cyclo-C}_3\text{H}_5, \text{cyclo-C}_4\text{H}_7, \text{Ph}, \text{CH}=\text{CHPh}, \text{C}\equiv\text{CPh}, 3\text{-pyridyl}, 2\text{-(2-furyl)vinyl}$.

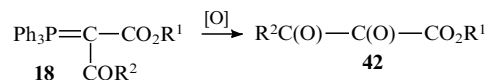
An original method was proposed for the synthesis of esters and amides of α -oxo acids by oxidative cleavage of acyl(cyano)methylidenetriphenylphosphoranes **39** with ozone⁸⁸ or dimethyldioxirane⁸⁹ in the presence of nucleophiles. Thus the oxidation in the presence of alcohols affords esters **40**, whereas in the presence of amines α -oxo amides **41** are formed, including peptides that are active as inhibitors of hydrolytic enzymes.⁸⁸



$\text{R}^1 = \text{Ph}, \text{amino acid and peptide residues}$;
 $\text{R}^2 = \text{H}, \text{Me}, \text{Bn}$; $\text{R}^3 = \text{Bn}, \text{CH}(\text{CH}_2\text{Ph})\text{CO}_2\text{Et}$.

Tricarbonyl compounds, *viz.*, esters of 2,3-dioxo carboxylic acids **42**, were obtained by oxidation of acylated alkylidene-

phosphoranes **18** with ozone,⁹⁰ magnesium monoperoxyphthalate⁹¹ or dimethyldioxirane.⁹²



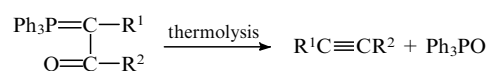
$\text{R}^1 = \text{Me}, \text{Bu}^t, \text{Bn}$; $\text{R}^2 = \text{Me}, (\text{CH}_2)_2\text{Cl}, \text{CH}=\text{CMe}_2, \text{CH}=\text{CHOMe}, (\text{CH}_2)_2\text{CH}=\text{CH}_2, (\text{CH}_2)_2\text{CH}=\text{CMe}_2, \text{CH}_2\text{CH}(\text{Me})\text{CH}_2\text{CH}=\text{CMe}_2, \text{Ph}, \text{CH}=\text{CHPh}, 2\text{-furyl}, 2\text{-thienyl}$.

It is unlikely that nitrogen dioxide tested as an oxidant for alkylidenephosphoranes^{93,94} will find preparative use because even small variations in the phosphorane structure result in different product mixtures.

3. Thermolysis. Synthesis of functionalised acetylenes

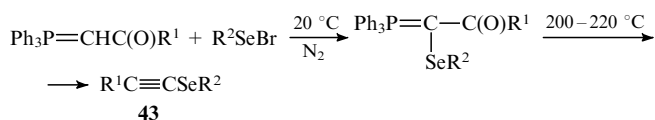
Of other transformations involving acylated ylides, the Wittig reaction occurring at high temperatures is used most widely. In this reaction, the phosphoranylidene group reacts with the carbonyl group of the same molecule in a α -position with respect to the ylide carbon atom so that the phosphorus atom is bound with the oxygen atom of the oxo group, resulting in elimination of triphenylphosphine oxide and formation of a triple $\text{C}\equiv\text{C}$ bond. If the carbonyl group is more remote from the ylide carbon atom, ring closure through the $\text{C}=\text{C}$ bond can occur. The first examples of this reaction were known back in the 1960s.^{41,50,95} The process was carried out at $200\text{--}280^\circ\text{C}$ at reduced pressure with distillation of the resulting products. In the past decade, Aitken *et al.*^{51,52,58,61–64} developed a higher-temperature version of this reaction (500 and even 700°C), *i.e.*, vacuum flash pyrolysis.

If the phosphorane molecule contains one carbonyl group, the reaction gives alkyl(aryl)acetylenes.^{28,29,41,52}



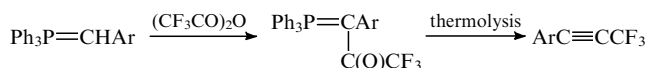
$\text{R}^1, \text{R}^2 = \text{Alk}, \text{Ar}$.

Selenium-substituted acetylenes **43** were obtained using the following scheme:⁹⁶



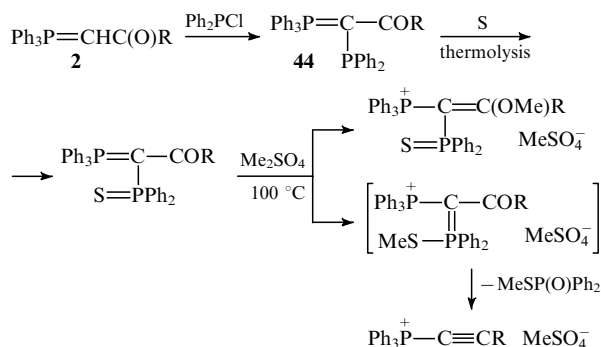
$\text{R}^1 = \text{Me}, \text{CF}_3, \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, 2\text{-thienyl}$; $\text{R}^2 = \text{Ph}, 4\text{-ClC}_6\text{H}_4, 4\text{-Cl-2-NO}_2\text{C}_6\text{H}_3, 3\text{-CF}_3\text{C}_6\text{H}_4$.

Thermolysis of aryl(trifluoroacetyl)methylidenephosphoranes obtained upon acylation of arylmethylidenetriphenylphosphoranes with trifluoroacetic anhydride results in aryl(trifluoromethyl)acetylenes.⁹⁷



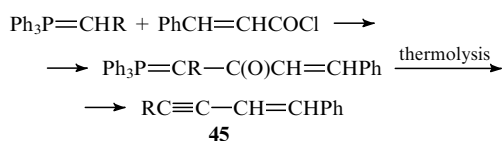
$\text{Ar} = \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4$.

Reactions of diphenylchlorophosphine with alkylidenephosphoranes **2,98** including those containing an oxo group,^{99,100} give ylides **44**. Heating of these compounds with sulfur yields diphenylthiophosphoryl-substituted alkylidenephosphoranes. Methylation of the resulting ylides with dimethyl sulfate occurs both at the oxygen and the sulfur atoms. However, *S*-methylation products are so unstable that they undergo *in situ* thermolysis in mild conditions giving salts of phosphorus-containing acetylene derivatives.¹⁰⁰

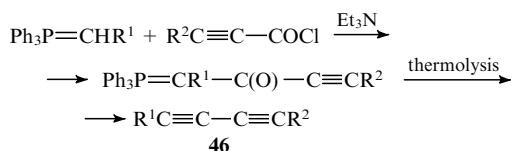


R = Me, Ph.

Acylation of phosphoranes with cinnamoyl chloride followed by thermolysis of the resulting acylides gave conjugated enynes **45**;¹⁰¹ the use of alkynoyl chlorides as acylating agents followed by thermolysis resulted in diacetylenes **46**.^{50, 63}



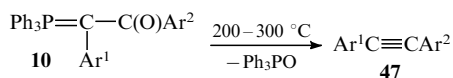
R = H, Me, Et, Prⁿ, Prⁱ, Bu, Ph, 2-MeOC₆H₄, 4-NO₂C₆H₄, 2-thienyl, CO₂Et.



R¹ = Ph, CN, CO₂Et; R² = Bu, Ph.

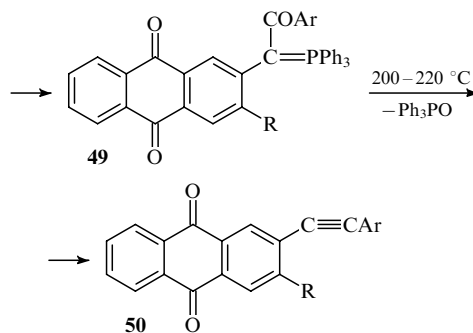
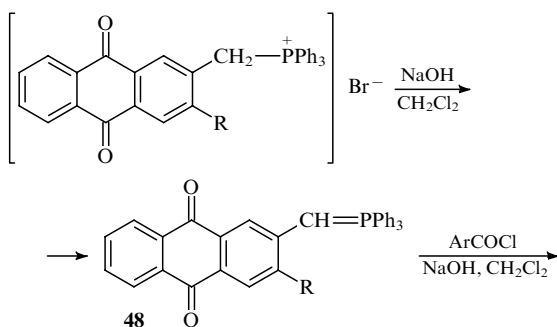
Derivatives **46** were also obtained by high-temperature vacuum flash-pyrolysis of dicarbonyl bisylides **24** containing aromatic substituents. If bisylides **24** incorporate aliphatic substituents, this method fails.⁶³

The thermolysis of phosphoranes is successfully used to synthesise diarylacetylenes. For example, diarylacetylenes **47** with perfluorobenzene rings¹⁰² and with anthracene, phenanthrene, pyrene and chrysene fragments¹⁰³ were obtained by thermolysis of phosphoranes **10** used in the reaction without special purification.



Ar¹, Ar² = Ph, C₆F₅, 1-anthryl, 9-anthryl, 2-phenanthryl, 3-phenanthryl, 9-phenanthryl, 1-pyrenyl, 2-pyrenyl, 6-chrysenyl.

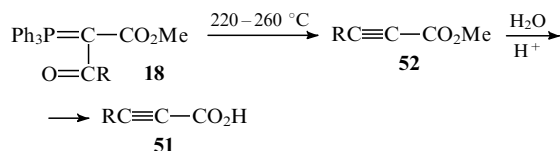
Acylation of anthraquinonylmethylenephosphoranes **48** in a two-phase system followed by thermolysis of the resulting acylides **49** gave diarylacetylenes **50** containing an anthraquinone fragment.¹⁰⁴



R = H, Me, F; Ar = Ph, 4-ClC₆H₄, 4-MeC₆H₄, 3-NO₂C₆H₄, 4-NO₂C₆H₄, 2-furyl.

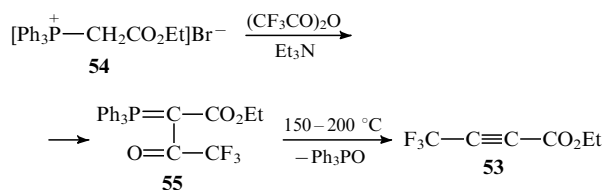
Diarylacetylenes form a considerable group of organic luminophores, although it is not as abundant as that of diarylethylenes.^{103, 105-107}

The thermolysis of acylated phosphoranes is often used to obtain functionalised alkynes: alkynyl ketones,^{42, 50} alkynonitriles,^{41, 50} esters and amides of acetylenecarboxylic acids.^{51, 53, 74, 108-110} A method was suggested⁹⁵ for the synthesis of alkynoic acids **51** by vacuum thermolysis of acylated ylides **18** followed by hydrolysis of the resulting esters **52**.



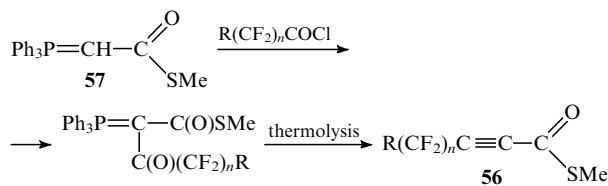
R = Me, Ph, 2-ClC₆H₄, 4-ClC₆H₄, 4-MeC₆H₄, 2-MeOC₆H₄, 3-MeOC₆H₄, 3-NO₂C₆H₄, Bn, CH=CHPh, 1-naphthyl, 2-furyl.

A preparative method for the synthesis of ethyl 4,4,4-trifluorobutynoate **53** from ethoxycarbonylmethyltriphenylphosphonium bromide **54** was developed.⁵⁵ Trifluoroacetic anhydride in the presence of triethylamine was used as the acylating agent. The key step of this reaction involves thermolysis of acylated phosphorane **55** to give compound **53** containing a triple C≡C bond.



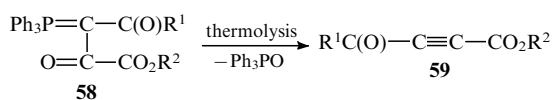
Later, this method was used to obtain esters of other acetylenecarboxylic acids from phosphonium salt **54** and carboxylic acid chlorides.

Thioesters of polyfluorinated carboxylic acids **56** were synthesised by acylation of ylide **57** containing a methylthiocarbonyl group with polyfluorinated acid chlorides followed by heating of the resulting acylides to 190–220 °C *in vacuo*.¹¹¹



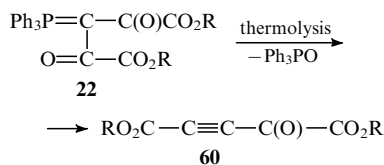
R = CF₃; n = 1, 2, 6; R = Cl; n = 3, 5.

Acetylenedi- and -tricarboxyl compounds were obtained by vacuum flash-pyrolysis. On heating to 500 °C *in vacuo*, phosphoranes **58** give esters of 4-oxoalk-2-ynoic acids **59**.^{58, 59}



$\text{R}^1 = \text{Me}, \text{Ph}, 4\text{-BrC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4, \text{OMe}, \text{OEt};$
 $\text{R}^2 = \text{Me}, \text{Et}.$

Thermolysis of tetracarbonylides **22** resulted in esters of 2-oxopentynedioic acid **60**.^{60, 61}

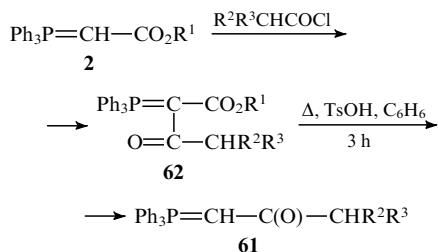


$\text{R} = \text{Me}, \text{Et}.$

However, vacuum flash-pyrolysis of polycarbonyl bisphosphoranes, such as tetraoxobisylides **24** ($\text{R} = \text{COPh}, \text{CO}_2\text{Alk}$) and hexaoxobisylides **25**, result in deeper destruction of the molecules of these compounds.^{61, 63, 64, 112}

If the carbonyl group in the phosphorane molecule is remote from the ylide carbon atom, its thermolysis results in cyclisation and sometimes in heterocyclisation. Some examples of these reactions are documented.^{113–121}

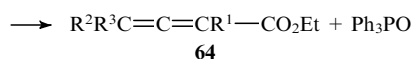
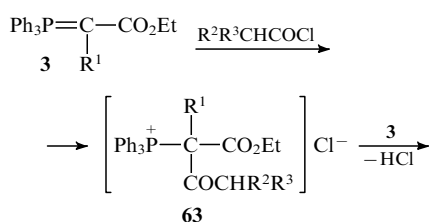
The thermal decomposition of acylated alkoxy carbonylmethylidenephosphoranes **43** or the respective phosphonium salts in acidic media, which involves the loss of the alkoxy carbonyl group and results in acylphosphoranes, can be of value as a preparative method.^{27, 70, 122} The reaction can be used for the synthesis of acylphosphoranes if the corresponding α -halogenoketones are difficult to access. For example, chiral 2-oxoalkylidenephosphoranes **61** were synthesised by acylation of ylides **2** containing an alkoxy carbonyl group with chiral α -substituted acid chlorides followed by decomposition of intermediates **62** by refluxing in benzene in the presence of *p*-toluenesulfonic acid.²⁷



$\text{R}^1 = \text{Me}, \text{Bu}^t; \text{R}^2, \text{R}^3 = \text{F}, \text{Me}, \text{Bu}, \text{cyclo-C}_6\text{H}_{11}\text{CH}_2.$

4. Synthesis of allenic compounds

The synthesis of allenic compounds is yet another interesting and promising example of reactions of alkylidenephosphoranes with acyl chlorides. Bestmann *et al.*^{123, 124} found that the reaction of acyl chlorides with stable phosphorus ylides **3** containing the α -ethoxycarbonyl group results in esters of allenecarboxylic acids. This involves C-acylation of the ylide, the reaction of the resulting phosphonium salts **63** with a second molecule of the original phosphorane **3** with γ -elimination of a proton and simultaneous elimination of triphenylphosphine oxide to give allenecarboxylic esters **64**.



$\text{R}^1 = \text{Me}, \text{Pr}, (\text{CH}_2)_2\text{Ph}; \text{R}^2, \text{R}^3 = \text{H}, \text{Me}, \text{Et}, \text{Pr}, \text{Bu}, \text{C}_5\text{H}_{11}, \text{Ph}, \text{Bn}, \text{CH}_2\text{CO}_2\text{Me}.$

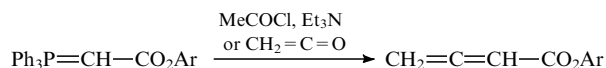
Esters of other allenecarboxylic acids were obtained under the same conditions.¹²⁵ If phosphorane molecules contain hydrogen atoms at the ylide carbon atoms, acylation involves transylidation and allenecarboxylic esters are not formed.

Lang and Hansen^{126, 127} proposed that the reaction be performed in the presence of triethylamine. This also made it possible to obtain allenic derivatives from phosphoranes containing α -hydrogen atoms. In addition, this method allows one to use the corresponding phosphonium salts instead of phosphoranes. The reaction mechanism changes in the presence of triethylamine. Acyl chlorides no longer behave as acylating agents. In the presence of triethylamine, they eliminate HCl to give ketenes, which subsequently undergo the Wittig reaction with phosphoranes.



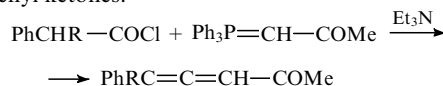
$\text{R}^1, \text{R}^2 = \text{H}, \text{Me}, \text{Et}, \text{Bu}^t, \text{C}_5\text{H}_{11}, \text{Ph}, \text{CO}_2\text{Me}, \text{Cl}.$

This approach was used to synthesise other ethyl¹²⁸ and aryl¹²⁹ allenecarboxylates; the latter were also obtained by independent syntheses from ketene.



$\text{Ar} = \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-Bu}^t\text{C}_6\text{H}_4, 4\text{-Bu}^i\text{C}_6\text{H}_4, 3\text{-MeC}_6\text{H}_4, 2\text{-MeC}_6\text{H}_4, 2\text{-Bu}^n\text{C}_6\text{H}_4, 3,5\text{-Me}_2\text{C}_6\text{H}_3, 2,4\text{-Me}_2\text{C}_6\text{H}_3, 2,3\text{-Me}_2\text{C}_6\text{H}_3, 2,5\text{-Me}_2\text{C}_6\text{H}_3, 2,6\text{-Me}_2\text{C}_6\text{H}_3, 2,3,5\text{-Me}_3\text{C}_6\text{H}_2, 2,4,6\text{-Me}_3\text{C}_6\text{H}_2, 2,3,6\text{-Me}_3\text{C}_6\text{H}_2.$

Phenylacetyl and diphenylacetyl chlorides react with acetyl-methylidenephosphorane in the presence of triethylamine to give allenyl ketones.¹³⁰



$\text{R} = \text{H}, \text{Ph}.$

Silicon-substituted allenes were obtained¹³¹ from phosphoranes and silicon-containing ketenes.

* * *

It should be noted in conclusion that the reaction of phosphorus ylides with acyl chlorides is not the only example of the chemistry of these compounds. Reactions of phosphorus ylides with acyl chlorides are not solely of theoretical interest; they also open new prospects for the synthesis of other classes of compounds that cannot be synthesised by other methods. In particular, it seems promising to synthesise allenic compounds from alkylidenephosphoranes, although this direction has been developed insufficiently yet and there are few publications in this field. Thus, the practical value of alkylidenephosphoranes is not limited to their use as components of the Wittig reaction.

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Lignin. Structural organisation and fractal properties

A P Karmanov, Yu B Monakov

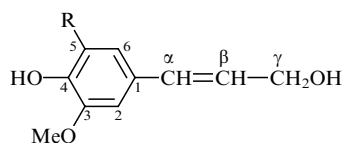
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Abstract. The results of investigations of the topological and supramolecular structures of lignins are considered. The experimental data on the hydrodynamic and conformational properties of dilute solutions of hardwood and softwood lignins are generalised. The relationship between hydrodynamic and fractal properties of lignin macromolecules is analysed and the applicability of various fractal concepts is discussed. Good prospects of using the fractal approach for the study of amorphous polymers with complex topological and supramolecular structures are demonstrated. The bibliography includes 174 references.

I. Introduction

Lignins are polyfunctional biopolymers of plant origin. They are formed upon enzymic dehydrogenation polymerisation of a number of methoxylated derivatives of hydroxycinnamic alcohols (guaiacyl-, syringylpropenol, *etc.*).^{1,2}



R = H (guaiacylpropenol), OMe (syringylpropenol).

Two main classes of these biopolymers are distinguished, namely, the guaiacyl type lignin, typical of conifers, and the guaiacyl-syringyl type lignin, which is formed in deciduous plants. The unique character of lignin as a high-molecular-mass compound is due to the diversity of the structural units (dilignols) that constitute the structure and to diverse types of bonds between them.^{3,4} More than twenty types of dilignols are currently known. The key types of dilignols incorporated in the lignin structure are

shown in Fig. 1. In natural lignins, structural elements with β -O-4-bonds predominate [$C(\beta)-O-C(4)$, ~25%]. This type of dilignol, 1-(4-hydroxy-3-methoxyphenyl)-2-(2'-methoxyphenyloxy)-1,3-propanediol (**1**, β -guaiacyl ether of guaiacylglycerol), is often used as a dimeric compound modelling the natural softwood lignin.

The rules of distribution of various dilignols in the polymer chain are unknown, most likely, they are non-deterministic, which is due to the absence of genetic control during the biosynthesis, at the stage of assembly of the lignin macromolecule.^{1–4} It should, however, be noted that this point of view has lately been criticised. A new concept of lignin biosynthesis based on the view of existence of regio- and stereochemical control of the recombination of monolignols has been proposed.⁵

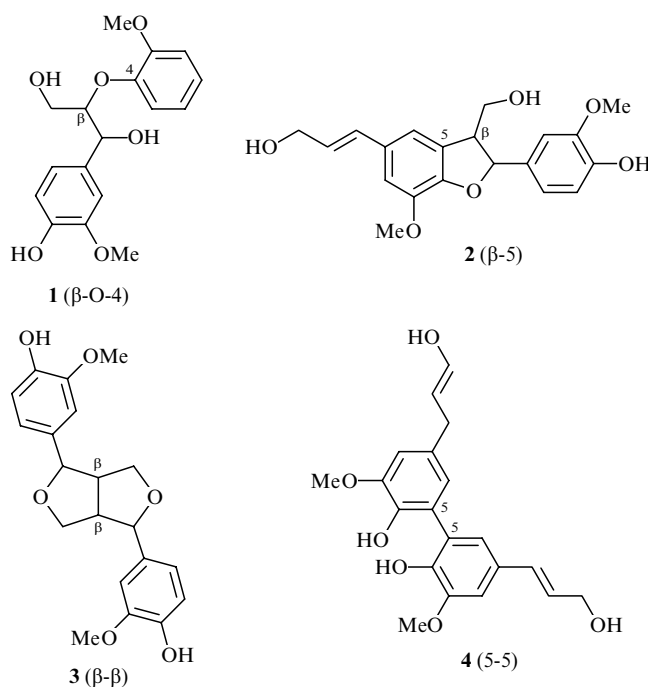


Figure 1. Dimers modelling the microstructural elements of a macromolecule of guaiacyl type lignins: β -O-4-dilignol (**1**); β -5-dilignol (**2**, coumaran structure); β - β -dilignol (**3**, pinoresinol structure); 5-5-dilignol (**4**, biphenyl structure).

A P Karmanov Institute of Chemistry of the Komi Scientific Centre, Urals Branch of the Russian Academy of Sciences, ul. Pervomaiskaya 48, 167610 Syktyvkar, Russian Federation. Fax (7-821) 243 66 77. Tel. (7-821) 243 24 27. E-mail: apk.chemi@ksc.komisc.ru

Yu B Monakov Institute of Organic Chemistry, Ufa Scientific Centre of the Russian Academy of Sciences, prosp. Oktyabrya 71, 450054 Ufa, Russian Federation. Fax (7-347) 235 60 66. Tel. (7-347) 235 61 66. E-mail: monakov@anrb.ru

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The structural organisation of lignin as a biopolymer can be represented as a set of hierarchical levels differing in complexity, namely, the chemical, topological, supramolecular, and ultra-structural ones.⁶ The last-mentioned level is inherent in native lignin. The achievements and problems related to the study of the chemical structure of lignin have been analysed in a review.⁷ In recent years, substantial advances have been made in the study of the topological and supramolecular organisation of lignin. This is largely due to the development of new approaches to the research of polymers based on the use of the concepts of deterministic chaos and synergetics, the fractal theory, and non-linear dynamics.

This review gives an analysis of the data accumulated to date on the hydrodynamic and conformational properties of lignin macromolecules in solutions and on the topological structure and properties of lignin as a fractal object.

The topicality of research into lignin is dictated by the significant role it plays in the chemical processing of wood to produce cellulose, paper or cardboard. The production technology of cellulose-containing materials from one or another plant raw material is determined, first of all, by the structure and properties of the lignin it contains. Fragmentation and subsequent dissolution of softwood lignin, composed mainly of guaiacyl type dilignols, require the most drastic pulping conditions. In this case, alkaline delignification procedures are used, in particular, sulfate and soda pulping. Lignin of hardwood trees or herbaceous plants is delignified rather easily, which is due to its specific structural features, namely, the guaiacyl-syringyl structure. Cellulose is produced from these plant raw materials using a number of organosolvate pulping processes.

Depending on the production method, soluble lignins are classified into technical and slightly decomposed lignins. Technical lignins include alkaline lignins resulting from treatment of wood or stalks of herbaceous plants with sodium hydroxide or a mixture of sodium sulfide and hydroxide (alkaline and sulfate pulping) and lignosulfonates,[†] which are formed as side products upon treatment of the plant raw material with aqueous solutions of oxo compounds of sulfur (the sulfite pulping procedure).⁸ The slightly decomposed lignins can be isolated from plant raw materials under relatively mild conditions.

If the reserves of traditional organic raw materials are exhausted, lignin can become the main source for the production of diverse organic compounds,⁹ which is due to specific features of the chemical structure of lignin and virtual inexhaustibility of the natural plant resources.

II. Conformational properties and topological structure of lignin

Elucidation of the topological structure of lignin macromolecules is one of the most complicated problems of the physical chemistry of lignin. Historically, the views on the topological structure (configuration) of lignin macromolecules have been based on and have varied to follow the views on its chemical structure. Up to the mid-20th century, it was taken for granted that lignin, like cellulose, is a linear polymer. Later, after the publication of studies by Freudenberg and co-workers on lignin biosynthesis *in vitro* and elucidation of the main principles of the growth of polydignols, the views were revised, and, as a consequence, lignin was assigned to the class of branched polymers (see Ref. 1 and references cited therein). Currently, the concept of a network structure of natural lignin proposed by Goring predominates in wood chemistry.^{10–12}

A classical approach to determining the topological structure of polymers includes investigation of the conformational properties of macromolecules in dilute solutions. The conformational properties of macromolecules show themselves, first of all, in the translational and rotational friction processes; therefore, they are

studied using methods of molecular hydrodynamics, in particular, velocity sedimentation, isothermal translational diffusion and capillary viscosimetry. These methods allow one to estimate the size and conformation of the macromolecular coils, which are of crucial significance for determination of the topological structure of polymers. Hydrodynamic methods still remain the experimental basis for virtually all studies of the topological structure of lignin.

Previously,^{1,2} lignosulfonates (LS) have been considered to be the most appropriate lignin specimens for determination of the macromolecular structure of natural lignin, because only the weakest α - and β -ester bonds are hydrolysed during the nucleophilic sulfitation and the degree of side condensation reactions is low. In addition, unlike many other lignin preparations, lignosulfonates are readily soluble in aqueous solutions. Therefore, many studies dealing with the physical chemistry of lignin have been carried out using LS.

Gardon and Mason have studied the hydrodynamic properties of industrial specimens of guaiacyl type LS (silver fir).^{13,14} The measurements of the intrinsic viscosity and the translational diffusion coefficients carried out in brines provided the conclusion that in aqueous solutions, the LS macromolecules occur as the Gaussian impermeable coil conformation. This conclusion was based on analysis of the correlations between the intrinsic viscosity ($[\eta]$), the diffusion coefficient (D), and the molecular mass (M), which were described by Mark–Kuhn–Houwink (MKH) type dependences:

$$[\eta] = K_{\eta} M^a,$$

$$D = K_D M^b,$$

where K_{η} and K_D are empirical constants; a and b are the MKH scaling indices. The a and b values equal to 0.47 and -0.56 , respectively, point to a linear topological structure of LS macromolecules. A similar value for b , equal to -0.57 , has been obtained for a spruce LS specimen in a 0.02 M solution of NaCl.¹⁵ According to another publication,¹⁶ low-molecular-mass LS fractions ($M < 5 \times 10^3$) consist of linear chains, whereas macromolecules with a higher molecular mass have a branched structure.

Studies performed by Goring and co-workers^{11,17} deserve particular attention, because they crucially changed the views on the topological structure of lignins existing at that time. To study the hydrodynamic properties, Goring used LS specimens prepared by laboratory sulfite pulping of spruce wood. It was found that LS has a high polydispersity index [the ratio of the weight-average molecular mass (M_w) to the number-average molecular mass (M_n) reaches 5–7 or even more]. One specimen was fractionated to give nine fractions, whose molecular mass varied from 37.0×10^3 to 1.3×10^6 . According to Goring's opinion, aqueous solutions of LS in a 0.1 M solution of NaCl are molecular disperse systems. The Mark–Kuhn–Houwink scaling indices a and b were found to be 0.32 and -0.33 , respectively, *i.e.*, the hydrodynamic behaviour of the LS macromolecules corresponded to neither the Gaussian impermeable coil nor the Einstein sphere. The set of obtained results led Goring to the conclusion¹¹ that LS macromolecules, like those of other soluble lignins, represent fragments of the three-dimensional network of natural lignin *in situ*. The destruction of the three-dimensional network of natural lignin during its isolation from the plant tissue yields microgel particles of an arbitrary shape, whose hydrodynamic behaviour corresponds to the properties of slightly swollen spherical particles. The intrinsic viscosity of LS is fairly low, which is due to the small hydrodynamic radius of cross-linked particles. After the publication of Goring's studies, the concept of the cross-linked structure of natural lignin has gained wide acceptance among researchers; however, no convincing evidence supporting this hypothesis has been obtained so far.

A similar study, but using industrial lignosulfonates has been carried out by Afanas'ev *et al.*^{18–20} These publications present the results of measurements of the hydrodynamic characteristics of

[†] Lignosulfonates belong to the class of polyelectrolytes, due to the presence of strong acidic groups CO_2H and SO_3H in the chain.

Table 1. Hydrodynamic and molecular characteristics of liginosulfonates in a water–salt buffer solution (pH 6.85).²⁰

$[\eta]$ /cm ³ g ⁻¹	$10^7 D_0$ /cm ² s ⁻¹	dn/dc (see ^a)	$10^{-3} M_w$	M_w/M_n
5.4	0.10	0.200	82.0	1.8
4.7	0.13	0.204	38.0	1.7
4.1	0.15	0.220	23.0	1.8
3.8	0.20	0.220	14.0	1.6
3.7	0.21	0.220	12.0	1.8
3.2	0.24	0.239	8.0	1.4
3.0	0.27	0.250	6.0	1.6

^a Increment of the refractive index.

spruce LS in aqueous and aqueous salt solutions at various pH values (Table 1 presents experimental values for some hydrodynamic parameters of LS obtained at pH 6.85). The researchers demonstrated the satisfiability of the scale invariance principle over a broad range of molecular masses — from 6×10^3 to 82×10^3 . Analysis of the viscosimetry ($a = 0.22$) and diffusion ($b = -0.44$) data led to the conclusion²⁰ that the LS macromolecule is a chaotically branched chain rather than a microgel particle.

Due to the inconsistency of experimental data on the hydrodynamic properties of LS in solutions, the problem of the conformation of LS macromolecules remains debatable. Goring and co-workers¹² believe that LS exists in aqueous solutions as dense globular particles similar to Einstein spheres. However, in this case, the scaling indices a and b should be equal to 0 and -0.33 , respectively, which contradicts the experimental data. The viscosimetric properties of samples and the scaling indices $a > 0.2$ imply that the shape asymmetry of the macromolecular coil changes with the growth in the molecular mass and that the macromolecule can be modelled by an ellipsoid of revolution. Rebinder²¹ believed that LS molecules exist in solutions as spheroids with fairly large aspect ratios.

Among other reasons, the diversity and inconsistency of the data on the conformations of LS (Table 2) are related to the chemical structure of this polymer, which refers to the class of polyacids (polyanions). The presence of ionogenic groups (carboxy and sulfo groups) capable of a variety of interactions results in LS acquiring some properties atypical of natural lignin. Thus dilution of solutions of liginosulfonates to concentrations of $(1-0.5) \times 10^{-2}$ g cm⁻³ usually entails an increase in the reduced viscosity (η_{sp}/c), instead of the expected decrease, which is due to electrostatic effects.²⁸ The addition of monomeric electrolytes which shield electrostatic interactions in the chain does not always produce linear dependences of the reduced viscosity on the LS concentration (Fig. 2).²⁹

The conformational characteristics of LS are dictated by the degree of ionisation of acid groups, which depends on the nature and properties of the solvent, the type of low-molecular-weight additives, the ion strength of the solution, and so on. The solution temperature and pH are also important factors influencing the hydrodynamic properties of LS. In the pH region of 5.5–7.5, the hydrodynamic size of LS molecules dramatically increases as a result of polyelectrolyte swelling; the efficiency of ionisation depends on the molecular masses of fractions according to a complex pattern.²⁰ Evidently, this is due to the inhomogeneity of fractions as regards the number and the nature of acidic, first of all, sulfur-containing groups. The degree of sulfonation of the fractions for field LS specimens varies over a wide range, namely, from 0.5 to 0.96. Therefore, it is clear that the chemical inhomogeneity of LS has an ambiguous influence on the results of hydrodynamic measurements and the conclusions drawn.

An essential factor complicating the research and interpretation of the results of hydrodynamic measurements for liginosulfonates is the aggregation of macromolecules (even in dilute

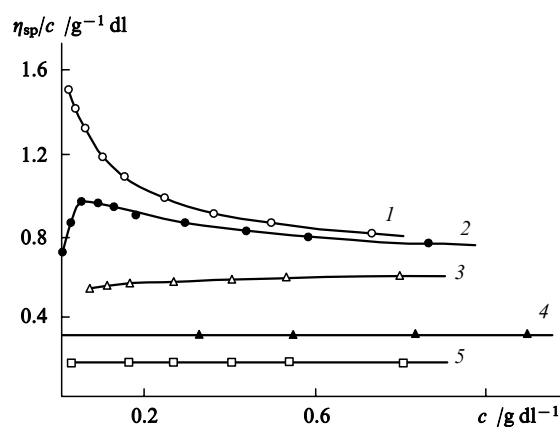
Table 2. Mark–Kuhn–Houwink parameters for samples of technical lignins isolated from wood.

Lignin specimen	Type of wood	Solvent	MKH parameters			Ref.
			a	b	c^a	
Ligno-sulfonate	silver fir	H ₂ O–NaCl (2 M)	0.47	—	—	14
	"	H ₂ O–NaCl (0.5 M)	—	–0.56	—	13
	spruce	H ₂ O–NaCl (0.1 M)	0.32	–0.33	—	17
	"	H ₂ O–NaCl (0.02 M)	—	–0.57	—	15
	"	H ₂ O–BaCl ₂ (0.02 M)	0.19	–0.38	—	22
	"	buffer solution (pH 6.85)	0.22	–0.44	—	20
Lignosulfonate amine	hardwood	methanol	0.54	—	—	23
	softwood	methanol	0.13	—	—	23
Alkaline lignin	spruce	H ₂ O–NaCl (0.1 M)	0.32	—	0.52	10
	"	dioxane	0.12	—	—	1
	poplar	dioxane	0.29	—	—	24
Sulfate lignin	hardwood	DMSO	0.69	—	—	25
	softwood	DMSO	0.14	—	—	26
	spruce	DMSO	0.15	—	—	27

^a c is the scaling index in the Mark–Kuhn–Houwink dependence of the sedimentation coefficient on the polymer molecular mass: $S = K_S M^c$.

solutions). According to a publication,³⁰ the molecular mass of softwood LS measured by the translational diffusion method decreases 6-fold on passing from a 0.1 N aqueous solution of KCl to anhydrous ethanol and decreases 12.5-fold on passing to methanol.

Associates of macromolecules have also been detected in dilute (in particular, aqueous) solutions of LS by velocity sedimentation techniques.^{18,20} The hydrodynamic radius of the aggregates determined by these methods is equal to

**Figure 2.** Reduced viscosity of liginosulfonates η_{sp}/c vs. concentration upon dilution of solutions of liginosulfonates with brines having different molar concentrations.²⁹ NaCl concentration in brine /mol litre⁻¹: (1) 0.00001, (2) 0.001, (3) 0.01, (4) 0.1, (5) 1.

150–200 nm. Raising the solution temperature to 60 °C induces partial decomposition resulting in a more than twofold decrease in the hydrodynamic radius of the aggregates. It should be noted that the formation of ion associates is a typical feature of not only LS but also other polyelectrolytes.³¹

Lignosulfonates are known to be surfactants. The chains of phenylpropane units form hydrophobic fragments of the macromolecules, while highly acidic sulfo groups constitute the hydrophilic shell. It cannot be ruled out that the hydrophilic properties of LS play a significant role in the structural organisation of the macromolecular coil and, correspondingly, influence the hydrodynamic properties of this polymer in aqueous solutions.

Sokolov and co-workers^{27,32,33} have carried out a series of studies dealing with the polymeric properties of alkaline lignins. It was found that both sulfate and alkaline lignins have high polydispersity indices ($M_w/M_n \approx 3-10$). The molecular mass of sulfate lignins varies from 1×10^3 to 34×10^3 . As a rule, alkaline lignins isolated from hardwood have a lower molecular mass than softwood lignins. According to Sokolov,²⁷ the intrinsic viscosity of fractions of sulfate lignin from spruce wood in DMSO varied from 7.4 ($M_w = 1.3 \times 10^3$) to $13.3 \text{ cm}^3 \text{ g}^{-1}$ ($M_w = 38.7 \times 10^3$). The dependence of $\log[\eta]$ on $\log M_w$ is linear (the slope ratio, equal to the scaling index a , is 0.15), *i.e.*, macromolecules of the sulfate lignin are impermeable coils with a high degree of globularity; in the researcher's opinion, they can be modelled by rigid spheres impermeable to the solvent.

This conclusion is at variance with the results obtained by Mayer,²⁵ who gives a higher value of the viscosimetric parameter for sulfate lignin, $a = 0.69$ (see Table 2). This value corresponds to the conformation of a swollen impermeable coil for a linear macromolecule. It should be noted that this study was performed with hardwood lignin. The differing origin of lignin appears to be the most likely reason for the divergence of results obtained in the studies cited above.^{25,27}

Thus, analysis of early publications dealing with the macromolecular structure of lignin attests to a substantial inhomogeneity of sulfate lignins, which is due to specific features of pulping processes.¹⁻³ A brief survey of publications devoted to technical lignins leads to the conclusion that the use of these polymers for elucidating the topological structure of natural lignin does not give unambiguous results. This is due to the substantial transformation of lignin during isolation from the plant tissue.

More successful studies (as regards gaining information on the structural organisation of natural lignins) have been carried out with another group of specimens, which belong to the class of slightly decomposed lignins. The greatest number of publications deal with the hydrodynamic and conformational properties of dioxane lignins (DL) and milled wood lignins (MWL). These lignins can be isolated from plant tissue under relatively mild conditions, which restricts the undesirable oxidation and condensation processes or modification of the chemical and topological structure of macromolecules. The MWL macromolecules do not contain highly acidic functional groups (see Ref. 24) and this eliminates the influence of the solvent, solution pH, *etc.* on the conformations of the specimens in solutions. Therefore, standard hydrodynamic methods of investigation provide fairly reliable information on the conformational characteristics of slightly decomposed lignins. Analysis of published data^{1,2,5} shows that the M_w value for non-fractionated MWL preparations usually does not exceed 30×10^3 for the polydispersity index $M_w/M_n > 1.5$ (the molecular masses of DL are usually higher and the molecular-mass distributions are broader than those of MWL).

The molecular-mass distribution parameters are substantially dependent on the botanical and anatomical origin of lignin as a living natural object. In particular, lignins isolated from different types of wood or even from different parts (the stem, the roots, branches or leaves) of the same plant can differ appreciably in both the chemical structure⁵ and the physicochemical properties including the molecular-mass distribution. Detailed studies of

macromolecular, in particular, hydrodynamic and conformational, properties of lignins of different taxonomic origins are virtually absent. The necessity of performing such works has not been evident until recently, as it has been generally believed that, irrespective of the origin, natural lignins (and celluloses) are biopolymers with the same topological structure for any plant. However, in recent years, we have obtained new data concerning the macromolecular and conformational properties of slightly decomposed lignins of various botanical origins. This allowed us to hypothesise that the topological structure of natural lignins is polyvariant.

Before proceeding to the analysis of experimental data obtained for different lignin specimens, one should note some specific features of these polymers, which are to be taken into account when interpreting the hydrodynamic results. The first one is relatively low molecular masses of all known types of soluble lignins; therefore, some fractions are classified as oligomers. According to a number of publications (see, for example, Refs 31, 34 and 35), the oligomer molecules, unlike the molecules of high-molecular-mass polymers, are characterised by conformational inhomogeneity (depending on the degree of polymerisation) and an enhanced significance of the terminal functional groups. The excluded volume effects[‡] for oligomer fractions can also depend on the degree of polymerisation.³¹ These features can, in principle, violate the scaling relationships and bring about certain difficulties in the research of even slightly decomposed lignins.

The macromolecular properties of methanol lignin isolated from poplar wood have been studied.²⁴ Plotting the dependence of the intrinsic viscosity on the molecular mass showed that the coefficients a present in the MKH equation differ markedly for high and low molecular masses of methanol lignin. For oligomeric fractions, the a value exceeds 0.4 (in a good solvent), while for polymeric fractions, it decreases to 0.3. This regularity also holds in a Θ -solvent, although the values of the coefficients somewhat decrease (by 10%).

An increase in the a values with a decrease in the lignin molecular mass has been noted in several other studies.³⁶⁻³⁸ Pavlov *et al.*³⁹ showed that in the low-molecular-mass region [$M = (0.8-5.8) \times 10^3$], the slope of the dependences of $[\eta]$ and D on the molecular mass of MWL fractions increases, the a and b values approaching 0.5 and -0.5 , respectively. However, most often, experimental data indicate a straight-line dependence $\log[\eta] - \log M$.

It should be noted that the change in the scaling on passing from one region of characteristic sizes to another is usual for any polymer, which is due, first of all, to conformational transitions.^{31,40} Features of the topological structure of some polymers can hamper their transitions from one conformational state to another. In these cases, the region of a universal hydrodynamic behaviour of the molecule is extended. In any case, the macromolecules of soluble slightly decomposed lignins obey the scale invariance principle over a rather wide range of molecular masses $(3-5) \times 10^3 - 100 \times 10^3$,⁴¹ which justifies the application of traditional approaches to the analysis of conformations of these macromolecules, despite the unique features of the chemical structure of lignins.⁴²

The influence of the terminal functional groups on the conformational properties of slightly decomposed lignins is expected to be insignificant, taking into account their chemical structure (the absence of highly acidic functional groups).^{2,5} However, some researchers adhere to a different opinion, based on the fact that the Flory linear swelling coefficient for low-molecular-mass fractions of dioxane lignin ($M_w < 3 \times 10^3$) in a good solvent barely differs from unity.⁴¹ The authors believe that

‡ The excluded volume effect is related to the fact that two polymer chain units should necessarily occupy two physically different sites in space; this effect influences the conformation of the polymer chain in solution.

Table 3. Hydrodynamic characteristics of fractions of milled wood lignins from pine (*Pinus silvestris*) in DMSO.³⁹

Fraction	$[\eta]$ /cm ³ g ⁻¹	$10^7 D$ /cm ² s ⁻¹	$10^{13} S$ /s	$10^{-3} M_{SD}$	$10^{-3} M_{D\eta}$	$10^{10} A_0$ /erg mol ^{-1/3} K ⁻¹	k_X
1	15.5	2.6	1.7	78	57	4.08	1.1
2	8.1	4.4	0.9	24	23	3.78	2.1
3	8.0	3.5	0.7	24	45	2.99	1.9
4	7.8	6.15	0.5	10.4	8.6	3.93	1.2
5	7.2	7.2	0.4	6.7	5.8	3.87	1.9
6	6.3	7.5	0.3	4.8	5.8	3.45	1.0
7	5.9	7.0	—	—	7.7	—	1.0
8	3.5	15.6	—	—	1.2	—	0.6
9	3.4	15.3	—	—	1.3	—	0.7
10	2.7	15.4	—	—	1.6	—	2.2
11	4.3	16.2	—	—	0.9	—	4.3
12	2.0	21.3	—	—	0.8	—	5.3

this is due to the interaction of the polymer functional groups, resulting in the formation of densely packed weakly solvated coils. The influence of other factors caused by the low molecular mass of the polymers cannot be ruled out either. This influence shows itself as a divergence of the experimental scaling indices obtained by different researchers under analogous conditions. For example it has been noted³⁷ that the Stockmayer–Fixman dependence of $[\eta] \times M^{-0.5}$ on $M^{0.5}$ at $M \rightarrow 0$ found for dioxane lignin isolated from pine wood deviates from a straight line towards higher $[\eta] \times M^{-0.5}$ values, whereas in another publication,²⁴ an almost perfect straight line was obtained.

The greatest number of publications are devoted to softwood lignins, which belong to guaiacyl type lignins. Some of these studies have been considered in a review.⁴³ Detailed investigation of lignins from milled pine wood in DMSO has been reported.³⁹ A sample of this lignin was thoroughly separated into 12 fractions for which velocity sedimentation (S), translational diffusion (D) and intrinsic viscosity ($[\eta]$) coefficients were determined (Table 3).

Attention is drawn by high values and a substantial scatter of the Huggins coefficients (k_H) over the fractions. Earlier studies usually did not report or discuss the k_H values because the interpretation and the physical meaning of the Huggins constant have been and still remain obscure. It is known that typical polymers with a linear topology of macromolecules in good solvents are characterised by $k_H \approx 0.2–0.3$.⁴⁴ Guaiacyl lignins differ from guaiacyl-syringyl lignins or linear polymers by great fluctuations of the Huggins parameter (in some cases, by more than an order of magnitude). In our opinion,⁴⁵ this is due to the specific fractal structure of the macromolecules of softwood lignins. The relationship between the Huggins parameter and the fractal dimension of macromolecules for a number of flexible- and semirigid-chain polymers in dilute solutions has been analysed by Kozlov *et al.*⁴⁶

Turning back to the discussion of the results obtained by Pavlov *et al.*,³⁹ it should be mentioned that the dependences of the hydrodynamic characteristics S , D and $[\eta]$ on M_{SD} and $M_{D\eta}$ were approximated by straight lines with a linear correlation coefficient of not less than 0.91. Shkaeva⁴⁷ has obtained an unexpectedly

high viscosimetric Mark–Kuhn–Houwink parameter for a pine wood lignin ($M_w = 27 \times 10^3$) ($a = 0.79$), which corresponds to the conformation of an impermeable swollen coil for linear polymers in a good solvent. Apparently, this result requires further investigations by sedimentation and diffusion techniques. The Mark–Kuhn–Houwink parameters determined for guaiacyl lignins by different investigators^{37, 39, 43, 48–51} are summarised in Table 4.

These results show that the softwood guaiacyl lignins are distinguished by low intrinsic viscosity and low magnitudes of the Mark–Kuhn–Houwink parameter a , which is indicative of compact shape of the lignin macromolecules, related, in all probability, to their branching. The lowest parameter a found is 0.10;¹¹ however, most often, publications give a value of ~ 0.25 or somewhat higher (see, for example, Refs 48–50). This value coincides with the theoretical value for chaotically branched macromolecules.³¹ The parameters b for a variety of softwood lignin specimens in various solvents found from translational diffusion data fall in a rather narrow range, $b = -(0.3–0.4)$.⁴³

A number of publications report the values for the Tsvetkov–Klenin hydrodynamic invariant (A_0),^{39, 50–52} normally calculated using the equation

$$A_0 = (R[D]^2[S][\eta])^{1/3},$$

where R is the universal gas constant; $[D] = D\eta_0/T$, $[S] = S\eta_0/(1 - \bar{v}\rho_0)$ ($\bar{v}$ is the specific partial volume of the polymer, ρ_0 is the density of the solvent).

For impermeable spherical particles, the theoretical A_0 value is $\sim 2.9 \times 10^{-10}$ erg mol^{-1/3} K⁻¹ (see Ref. 53). For synthetic flexible-chain and moderately rigid-chain polymers, A_0 is normally higher, being equal to $(3.2 \pm 0.2) \times 10^{-10}$ erg mol^{-1/3} K⁻¹. For the milled pine wood lignin, the average value of the Tsvetkov–Klenin hydrodynamic invariant amounts to 3.7×10^{-10} erg mol^{-1/3} K⁻¹ (the range is from 2.99 to 4.08, see Table 3).³⁹ Other researchers reported lower A_0 values for this lignin. For lignin of milled spruce wood, the A_0 values were, on average, 2.95×10^{-10} erg mol^{-1/3} K⁻¹ (see Ref. 51). The following values of the hydrodynamic invariant A_0 have been obtained:⁵⁰ the average value for the pine wood DL is

Table 4. Mark–Kuhn–Houwink parameters for guaiacyl (softwood) lignins in various solvents.

Specimen	Type of wood	Solvent	$10^{-3} M$	MHK parameters			$10^2 K_\eta$	$10^5 K_D$	$10^{16} K_S$	Ref.
				a	b	c				
Milled wood lignin	pine tree (<i>Pinus silvestris</i>)	DMSO	4.8–78.0	0.28	–0.41	0.60	0.56	2.5	1.9	39
	"	DMF	3.0–14.6	0.26	–0.43	0.57	0.64	6.5	8.3	37
	spruce (<i>Picea sp.</i>)	pyridine	1.9–24.4	0.12	–0.39	0.61	2.6	3.9	3.9	51
Dioxane lignin	pine tree (<i>Pinus silvestris</i>)	dioxane	4.3–25.0	0.24	–0.35	0.65	0.65	2.2	2.2	48, 49
	"	DMSO	2.1–100	0.25	–0.40	—	1.27	1.9	—	50
	spruce (<i>Picea sp.</i>)	dioxane	1.6–9.8	0.25	—	0.56	—	—	—	43

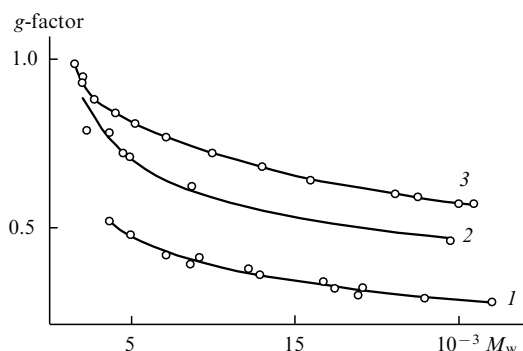


Figure 3. Branching g -factor vs. molecular mass for fractions of softwood lignins.

(1) spruce wood DL;⁵⁴ (2) pine wood DL-1; (3) pine wood DL-2.⁵⁵

$2.9 \times 10^{-10} \text{ erg mol}^{-1/3} \text{ K}^{-1}$ and that for MWL in DMF is $3.0 \times 10^{-10} \text{ erg mol}^{-1/3} \text{ K}^{-1}$. It is noteworthy that published data concerning the experimental determination of A_0 are rather scanty and are actually limited to the above examples.

Generally, analysis of the experimental data on hydrodynamic and conformational properties of slightly decomposed lignins isolated from softwood shows that the macromolecules of these lignins are characterised by high diffusional mobility and low intrinsic viscosity. These features, in combination with data on the Mark–Kuhn–Houwink scaling parameters, the hydrodynamic invariant, and the Huggins parameters, attest to a branched structure of the macromolecules of softwood lignins. Obviously, these lignins refer to the class of chaotically branched polymers.

The degree of branching of a macromolecule can be characterised by the so-called g -factor. The magnitude of the g -factor is determined by the ratio of the radii of gyration of the branched (R_b^2) and linear (R_l^2) chains with identical molecular masses and thermodynamic flexibilities

$$g = \frac{R_b^2}{R_l^2}.$$

Analysis of the resulting g -factors shows^{20, 33, 43, 54, 55} that this value depends on the molecular mass of lignin (Fig. 3). The g -factor decreases from 1 (for the lowest-molecular-mass fractions) to 0.3–0.5 (for the fractions with $M > 25 \times 10^3$). A similar pattern of dependence of g on M is observed for synthetic chaotically branched polymers.³¹ Running a few steps forward, we would like to note that an absolutely different pattern of dependence has been found for hardwood lignins, in particular, the g -factor increases with an increase in the lignin molecular mass.

In recent years, guaiacyl-syringyl type lignins have aroused enhanced interest in researchers;^{56, 57} this is related to solution of

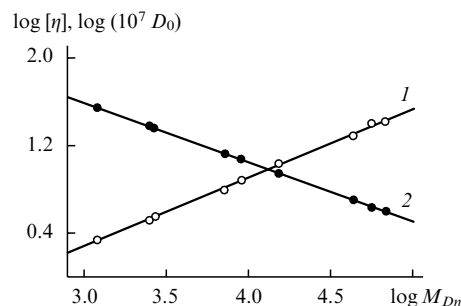


Figure 4. Mark–Kuhn–Houwink dependences plotted for a milled birch wood lignin.⁵⁸

(1) $\log[\eta]$ vs. $\log M_{D\eta}$; (2) $\log D_0$ vs. $\log M_{D\eta}$.

purely applied problems associated with the involvement of new types of plant raw materials, *i.e.*, annual plants and hardwood, instead of softwood, in the manufacture of cellulose materials. It was found that the polymeric properties of lignins isolated from angiosperms differ appreciably from the properties of lignins isolated from gymnospermous plants, which is related to specific features of biosynthesis and, as a consequence, to differences in the topological structures of macromolecules.

Table 5 contains the hydrodynamic characteristics that we determined for a lignin specimen from milled aspen wood.⁵⁸ Comparison of the experimental data demonstrates that the aspen wood lignin has a higher intrinsic viscosity and much lower values of the Tsvetkov–Klenin hydrodynamic invariant compared to those of softwood lignins. Study of a series of samples of guaiacyl-syringyl lignins isolated from birch and aspen wood has shown^{58–61} that hydrodynamic characteristics of these lignins follow linear dependences on their molecular masses (Fig. 4). As shown by calculations, the control relations

$$(1 - c) = |b| = \frac{a + 1}{3}, \quad (1)$$

$$K_\eta^{1/3} K_D = \frac{A_0 T}{\eta_0}, \quad (2)$$

$$K_\eta^{1/3} K_S = \frac{A_0(1 - \bar{v}\rho_0)}{\eta_0 R}, \quad (3)$$

hold for these lignin samples within the bounds confined by the root-mean-square errors of scaling indices. This indicates that the equivalence principle is obeyed in the translational and rotational friction processes. Therefore, it was concluded that, irrespective of the size, the lignin macromolecules are topologically similar, and, hence, the scale invariance principle, fundamental for polymers, holds. Table 6 presents the Mark–Kuhn–Houwink parameters, which allow one to determine the conformation of the macro-

Table 5. Hydrodynamic characteristics of fractions of lignins from milled aspen (*Populus tremula*) in DMF.⁵⁸

Fraction	$[\eta] / \text{cm}^3 \text{ g}^{-1}$	$10^7 D_0 / \text{cm}^2 \text{ s}^{-1}$	$10^{13} S_0 / \text{s}$	$10^{-3} M_{SD}$	$10^{-3} M_{D\eta}$	$10^{10} A_0 / \text{erg mol}^{-1/3} \text{ K}^{-1}$	k_X
1	34.3	3.0	3.57	90.7	98.9	2.5	0.24
2	16.1	5.5	2.11	29.2	34.2	2.4	0.58
3	10.1	8.6	1.89	16.7	14.3	2.7	0.24
4	6.9	12.5	1.52	9.3	6.8	2.8	0.75
5	6.1	13.2	1.03	5.9	6.5	2.5	0.36
6	5.9	14.0	0.88	4.8	5.6	2.4	0.24
7	4.2	19.2	—	—	3.3	—	0.63
8	3.7	20.1	—	—	3.2	—	1.67
9	3.5	22.4	—	—	2.5	—	1.15
10	3.1	24.2	—	—	2.1	—	1.37
Initial specimen	9.3	9.6	—	—	11.9	—	0.88

Table 6. Mark–Kuhn–Houwink parameters for guaiacyl-syringyl (hardwood) lignins in DMF.

Lignin specimen	Type of wood	$10^{-3} M$	MHK parameters			$10^2 K_\eta$	$10^5 K_D$	$10^{16} K_S$	Ref.
			a	b	c				
MWL	birch (<i>Betula verrucosa</i>)	6.1–64.5	0.61	−0.53	0.47	2.78	15.5	19.4	58
MWL	"	6.3–21.5	0.69	−0.50	0.50	1.86	9.2	12.7	61
DL	"	4.0–49.8	0.57	−0.45	0.55	4.0	21.0	8.5	60
MWL	aspen (<i>Populus tremula</i>)	4.8–90.7	0.62	−0.55	0.45	2.70	15.9	20.9	58
DL	"	6.9–22.5	0.61	—	0.47	3.6	—	20.9	61
ML ^a	poplar (<i>Populus trichocarpa</i>)	1.5–73.7	0.41	—	—	—	—	—	24

^a Methanol lignin, 2-methoxyethanol as the solvent.

molecule. For a number of specimens of guaiacyl-syringyl lignins, the scaling indices a , b and c are equal to 0.6 ± 0.1 , -0.5 ± 0.05 and 0.5 ± 0.05 . These are usual values for linear flexible-chain polymers. Upon analysis of the scaling indices, one can infer that the macromolecules of hardwood lignins in dilute solutions ($c[\eta] \leq 1$) acquire the conformation of a swollen impermeable coil. This demonstrates that hardwood lignins belong to a universal class of polymers with a linear macrochain topology. However, the intrinsic viscosities of these specimens are much lower than those for typical linear flexible-chain polymers with the same molecular mass. The average values for the Flory–Mandelkern hydrodynamic invariants $[\Phi^{1/3}P^{-1}] = (1.7-2.3) \times 10^6$ are lower than the theoretical values for linear Gaussian macromolecules (2.7×10^6) and correspond to the hydrodynamic invariants for branched polymers. Noteworthy is the fact⁶⁰ that in the case of DL, the pattern of dependence of the hydrodynamic invariant $\Phi^{1/3}P^{-1}$ on the molecular mass is similar to that found for regularly branched polymers, in particular, lactodendrimers (Fig. 5), but differs from the pattern of dependence typical of chaotically branched polymers.

Analysis of the published data dealing with the properties of guaiacyl-syringyl lignins shows that the hydrodynamic behaviour of the macromolecules of lignins isolated from the secondary xylem of deciduous trees differs from the behaviours of both flexible- and rigid-chain linear polymers and also from the behaviour of typical chaotically branched polymers, although some criteria are satisfied. In our opinion, soluble hardwood lignins should be attributed to the class of star polymers. The linear structure of the branches of star macromolecules ensures the maintenance of scaling parameters typical of a linear topology; however, the presence of the branching unit — the star centre — decreases appreciably the hydrodynamic dimensions of the macromolecule. This results in abnormally low intrinsic viscosity and

in a decrease in the Flory–Mandelkern and Tsvetkov–Klenin hydrodynamic invariants, which are sensitive to the degree of branching.

This assumption is supported by the results of simulation of the growth of polydisperse polymer stars with linear branches within the framework of the self-avoiding random walk (SARW) model.⁶² According to this model, one-centre star tri- and tetra-functional macromolecules form impermeable coils with a Mark–Kuhn–Houwink diffusional parameter b close to -0.5 and a fractal dimension d_f equal to 2.⁸ It is pertinent to recall that Flory⁶³ has shown theoretically that the viscosimetric parameters a for star and linear macromolecules coincide. Later, this result was confirmed experimentally⁶⁴ in relation to polystyrenes. A star-like polymer structure in a good solvent should have, in conformity with the logic of the excluded volume effect, the fractal dimension of $5/3 < d_f < 2$. Experimental results reported by Belyaev *et al.*⁵⁹ confirm the validity of assignment of the macromolecules of guaiacyl syringyl-lignins to the star type.

III. Lignin macromolecule as a fractal object

The use of classical physicochemical methods of polymer science for the study of dilute solutions of lignin made it possible to elucidate the key hydrodynamic characteristics of its macromolecules, namely, intrinsic viscosity, diffusion and sedimentation coefficients, scaling indices and hydrodynamic invariants. The properties and structure of lignin were found to depend on not only the method used to isolate it from the plant tissue but also on the taxonomic origin. Analysis of the hydrodynamic characteristics of guaiacyl-syringyl lignins showed that the macromolecules of hardwood lignins have a star-like structure, their conformational properties being determined by the linear topology of branches. The hydrodynamic behaviour of guaiacyl lignins differs substantially from the behaviour of polymers with a linear topology of macromolecules.

Despite the long-term studies and a rather vast amount of experimental data on the hydrodynamic properties of lignins of different origin, the task of establishing the topological structure of the macromolecules of natural lignins still remains unsolved. There are grounds for suggesting that traditional approaches and methods are inadequate for obtaining exhaustive information on the structure of macromolecules of natural lignins. The discovery of deterministic chaos, dynamic self-organisation and strange attractor phenomena in the lignin biosynthesis^{65–67} indicates that solving the problem of structure organisation of lignin generally and its topological structure specifically requires resorting to new approaches.

It has been found in recent decades that the structure of a substance formed under conditions far from thermodynamic

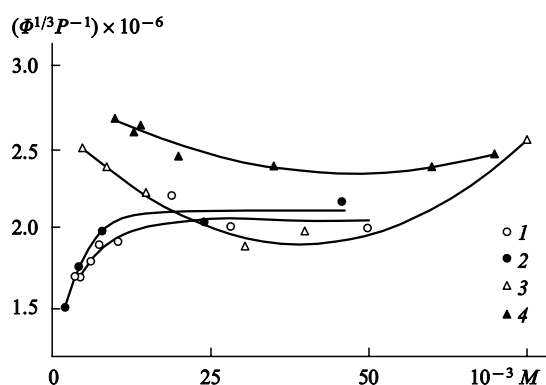


Figure 5. Flory–Mandelkern hydrodynamic invariant vs. the molecular mass of polymer fractions with different topological structures. Polymer: (1) birch wood DL,⁶⁰ (2) dendrimer,⁵³ (3) pine MWL,⁵⁰ (4) chaotically branched polyphenylquinoxaline.⁶⁰

§ The fractal dimension of a macromolecular coil in solution is determined by two types of interaction, namely, the interaction of the coil elements with each other and polymer interaction with the solvent.

equilibrium can be described in terms of the mathematical body of fractal geometry and synergetics.^{68–70} The synthesis of polymers, including natural ones, takes place most often under such non-equilibrium conditions. This ultimately results in the formation of fractal structures at one or another level of the polymer structural organisation. It has been stated⁷¹ that any polymer that does not exist in the crystalline state should necessarily have a fractal structure over some scale range. This opinion is confirmed by numerous experimental data.^{46, 72, 73} This is why synergetics and fractal analysis are used more and more extensively to study polymers with complex topological structure, for example, cross-linked polymers and chaotically branched polymers.

In 1986, the possibility of describing the supramolecular structure of lignin within the bounds of the fractal concept was hypothesised for the first time.⁷⁴ By the end of the 20th century, the fractal theory had gained wide application in natural sciences, including polymer science. Below we consider the main properties of fractal objects of differing nature and discuss the experimental data on the fractal properties of lignin.

1. Structure and fractal properties of polymers

Examples demonstrating the scope and prospects of the application of fractal concepts to description of the macromolecular properties of polymers are documented.^{75–80} The key properties of the polymer fractals include self-similarity, fractional dimensions, size dependence of the density, and restricted (regarding the size) domain of existence.^{75, 77} Polymers possess statistical self-similarity but over some limited scale range.⁷¹

A macromolecule is often considered as a fractal cluster assembled from monomer units.⁸¹ The mass M and the density ρ of such a macromolecule are described by the following relation:

$$M = m_0 \left(\frac{R}{a_0} \right)^{d_f},$$

$$\rho = \rho_0 \left(\frac{R}{a_0} \right)^{D-d_f},$$

where m_0 , a_0 and ρ_0 are the mass, the size and the density of a monomer unit; R is the size of the macromolecule; d_f is the mass fractal dimension; D is the dimension of the Euclidean space.

Important characteristics of a macromolecular coil include the radius of gyration R_g and the hydrodynamic radius R_H , which are derived from the results of viscosimetric or diffusion measurements. These parameters depend on the molecular mass (M) and the way it is distributed in space (the latter characteristic is taken into account by the index ν , which is equal to 0.5 for the Θ -state)

$$R_g \sim M^\nu, R_H \sim M^\nu. \quad (4)$$

The fractal dimension of a single macromolecule is determined by both the topological structure (configuration) and the conformational state. For example, a linear macromolecule can possess different fractal properties depending on the number and the size of monomer units, quality of the solvent, temperature and the concentration of macromolecules, *i.e.*, on those factors that dictate the conformation of the macromolecule.

Baranov *et al.*⁸² considered the fractal properties of various conformational states of a linear macromolecule in 3D space (Table 7).

The fractal dimension of a macromolecule is determined by the relation $d_f = 1/\nu$ (see Ref. 83); thus, the fractal dimension of a

macromolecular coil in a Θ -solvent is 2. In a good solvent, $\nu = 3/5$ and, correspondingly, $d_f = 1.67$.

For the globular state, $\nu = 1/3$ and $d_f = 3$, *i.e.*, the globular conformation is not fractal. A globule is characterised by a distribution of the ‘everywhere dense’ type (this does not mean, however, that globular structures are absolutely compact, because the macromolecule bulk contains some amount of the solvent). For a rod-like conformation of the macromolecules, the topological dimension coincides with the fractal dimension and $d_f = 1$; in this conformation, the macromolecule is not a fractal either. Finally, for a permeable coil, $\nu = 2/3$ and $d_f = 3/2$. In this case, the macromolecule is a fractal.

Thus, the fractal properties of linear polymers are determined by their conformational characteristics and a macromolecule can be a fractal object only in three cases: when it acquires the conformation of a Θ -coil, a permeable coil, or a coil in a good solvent. The main criteria of fractality, namely, a fractional dimension and the scale invariance principle, are satisfied for these conformations. The configuration of macromolecules of natural lignin is not linear, as was shown in Section II; therefore, it is pertinent to consider theoretical models that allow one to study the fractal properties of branched structures.

a. Models of the percolation cluster and ‘lattice animals’ clusters

The model of percolation cluster (percolation theory) proposed by Broadbent and Hammersley⁸⁴ is a mathematical model that allows one to study the regularities of the formation of branched polymeric structures. This model is underlain by a lattice composed of a number of points and bonds. Bonding of the lattice points to each other forms a cluster (a branched macromolecule), which is a fractal characterised by a quite definite fractal dimension dependent on the lattice structure and dimension, the growth mechanism and the p value (p is the probability that a lattice point belongs to the cluster). The percolation cluster model is characterised by universal behaviour of various parameters near the percolation threshold when $p = p_c$ (transition from a finite cluster to an infinite cluster after a critical concentration of points has been attained).[¶] The fractal dimension of an infinite critical cluster depends on the lattice dimension and is equal to 1.89 for two-dimensional and 2.5 for three-dimensional lattices.⁸⁵ The structure of percolation clusters above the transition point ($p > p_c$) is characterised as uniformly bound, and $d_f = D$, where D is the dimension of the Euclidean space.

When $p < p_c$, there exist a set of clusters that correspond to a universal class of ‘lattice animals’. These simulate the statistical behaviour of branched polymers in solutions and represent an ensemble of clusters for which any configuration of a specified size is equally probable. Clusters that refer to the type of ‘lattice animals’ have the following fractal dimensions:⁸⁶ $d_f = 1.55 \pm 0.05$ for the two-dimensional case and 2.00 ± 0.05 for the three-dimensional case. A study of the influence of the mechanism of growth of branched macromolecules on their topological structure and fractal characteristics has been reported.⁸⁷ It was found that the applicability of the ‘lattice animals’ cluster model is limited to particular classes of branched polymers.

b. Models of particle–cluster and cluster–cluster type diffusion-limited aggregation

The model of diffusion-limited aggregation of the particle–cluster type (DLA P–C) is the best known kinetic model of irreversible growth of fractal clusters. This model has been developed by Witten and Sander⁸⁸ and has been used subsequently to study the growth of colloid particles of differing nature, electrolysis and polymerisation processes, hydrodynamic structures of the ‘viscous finger’ type, *etc.* All these processes and structures are subject to the same mathematical description under certain conditions.

¶ The formation of an infinite cluster is a phase transition.

Table 7. Characteristics of a linear macromolecule as a fractal object.⁸²

Conformation	ν	a	d_f
Θ -coil	1/2	1/2	2
Swollen coil	3/5	4/5	5/3
Permeable coil	2/3	1	3/2

The DLA P–C model has been considered in detail in the books.^{76,80}

If the Brownian (random) motion of particles involved in the Witten–Sander model is replaced by rectilinear motion, the resulting cluster will represent a compact aggregate with a dimension d_f equal to the dimension of the fractal lattice (the Wald–Sutherland model).⁸⁹ Compact clusters are also produced in other aggregation models of the particle–cluster type, namely, in the ‘rain’ model and in the Eden model.⁹⁰

The model of diffusion-limited aggregation of the cluster–cluster type (DLA C–C) is the most plausible model of the growth of aerosol particles.^{91,92} It was also used to study dehydropolymerisation of monolignols.⁷⁴

The fractal dimension of the clusters assembled from monodisperse particles is equal to 1.78 ± 0.05 . The polydispersity of particles barely changes the fractal dimension of the cluster. The influence of the growth conditions of clusters (diffusion velocity, the probability of addition upon collision, process reversibility) on their structural characteristics has been studied.⁹³ A decrease in the probability of addition was found to entail the formation of denser aggregates, the fractal dimension of the clusters being increased to 2.0 ± 0.06 .

c. Fractal dimensions

The conformational state of a macromolecule in solution is determined by the solvent quality, the solution temperature, the polymer concentration, *etc.* A change in the polymerisation conditions may entail conformational transitions accompanied by a change in scaling indices, the Mark–Kuhn–Houwink parameters and the critical index ν . The nature of transitions between these states can be different. Some transitions correspond to the ‘disorder–disorder’ or ‘fractal- $d_f^i \leftrightarrow$ fractal- d_f^j ’ transitions.⁸² Determination of fractal dimensions using the scaling indices from data of hydrodynamic measurements allows one to establish reliably the macromolecule conformation. However, it is evident that macromolecules possess not only conformational fractal properties but also configurational fractal properties caused by mutual arrangement of topological elements — knots, side branches, subchains, cross-links, rings, *etc.* Therefore, the use of only Hausdorff type dimensions, applied most often to describe fractal objects, is, apparently, inadequate for unambiguous description of the structural organisation of a polymer molecule because these dimensions do not allow one to have an idea of its configuration.⁷¹ According to Mandelbrot,⁹⁴ more accurate description of a complex structure requires the use of a larger number of fractal dimensions.

The connectivity of the structure elements, *i.e.*, the configuration of a macromolecule, can be estimated using the so-called spectral (or fracton) dimension d_s , proposed⁹⁵ to characterise the natural vibrations of fractals. The fracton dimension can be determined from the equation describing the vibrations of a random network, which differs from the equation describing the random walk of a particle across a fractal lattice (with the dimension d_w) only by the order of the derivative.⁸⁵ The d_s value can be found from the relation

$$d_s = \frac{2d_f}{d_w},$$

where $d_w = 2 + \delta$ (δ is the scaling index of abnormal diffusion). For macromolecules with any configuration other than linear, $\delta > 0$.

The fractal and fracton dimensions calculated within the bounds of various cluster models are presented in Table 8.

A specific feature of the fracton dimension is independence of its value of the way of insertion of a fractal object into the Euclidean space. In other words, the fracton dimension, unlike the fractal dimension of the Hausdorff type, does not depend on the conformational state of the macromolecule and is dictated

Table 8. Fractal (d_f), fracton (d_s) and chemical (d_l) dimensions for branched structures in terms of different cluster models.

Model	D	d_s		d_f		d_l	
		value	Ref.	value	Ref.	value	Ref.
Percolation cluster model	2	1.33	85	1.9	95	1.64	96
	3	1.33	85	2.5	95	1.83	96
DLA P–C	2	1.20	97	1.71	98	1.71	90
	3	1.2–1.4	99	2.50	98	2.50	90
DLA C–C	2	≤ 1.2	100	1.45	101	1.22	102
	3	≤ 1.26	100	1.80	93	1.42	102
Model of the ‘lattice animals’ clusters	2	1.55	86	1.12	86	1.33	90
	3	2.0	86	1.19	86	1.45	90

only by its topological structure. The fracton dimension of a linear macromolecule is equal to unity.

Along with the fracton dimension d_s , the topology of a macromolecular cluster can be characterised by the chemical dimension (connectivity parameter) d_l which takes into account the arrangement of all chemical bonds occurring between cluster particles. The chemical fractal dimension of the cluster is determined by the expression¹⁰³

$$N \sim l^{d_l},$$

where N is the number of cluster species (monomer units if a polymer fractal is considered); l is the so-called chemical distance, *i.e.*, the shortest distance between two knots of the macromolecule. The chemical dimension reflects the internal connectivity in the polymeric fractal; therefore, in some cases, it is called the internal dimension. It follows from the connectivity position that $d_l \geq 1$. For a linear polymer chain, the chemical dimension is equal to unity. For a chaotically branched structure formed by the Witten–Sander model (the DLA P–C model), the chemical and fractal dimensions coincide ($d_l = d_f$). As opposed to this, structures formed by the DLA C–C mechanism are less branched, which is manifested as a decrease in the chemical (internal) dimension with respect to the fractal dimension (see Table 8).

d. Multifractal formalism

The models considered above describe objects as monofractals. Biopolymers are usually distinguished by a complicated structural hierarchy with numerous structural sublevels, and each of these can be characterised by particular order parameters. In addition, even at one level of structural organisation, fractal ensembles that reflect the structure of a real compound often require that a spectrum of dimensions rather than a single dimension be used. The differences between them serve as a measure of the degree of inhomogeneity of the object under consideration. This circumstance stipulated the necessity of introducing the concept of the multifractal. A multifractal can be presented as a combination (superposition) of monofractals with different fractal dimensions.

Olemskoi and Flat¹⁰⁴ considered the formalism permitting one to derive the regularities of structure formation from the set of monofractals. The applicability of the multifractal formalism to investigations of structural organisation of objects and physical processes is associated with considering the Renyi dimensions D_q .^{72,75,105} The Renyi dimensions are determined from the equation

$$D_q = - \frac{\lim_{\varepsilon \rightarrow 0} K_q(\varepsilon)}{\ln \varepsilon},$$

where ε is the size of a cell into which the phase space was split; $K_q(\varepsilon)$ are generalised entropies calculated from the equation

$$K_q(\varepsilon) = \frac{\ln \sum P_i(\varepsilon)}{1 - q}$$

$[P_i(\varepsilon)]$ is the probability that a particle gets into an i th cell; $q = 0, 1, 2, \dots, n$.

By definition, D_0 ($q = 0$) is a self-similarity dimension, D_1 ($q = 1$) is the information dimension and D_2 ($q = 2$) is the correlation integral index. For homogeneous sets that obey the relation $P_i(\varepsilon) \sim \varepsilon^D$, the Renyi dimensions of different orders coincide. Apparently, the multifractal formalism concept can prove fairly useful in the study of cross-linked polymers and processes (including chemical ones) accompanied by the formation of temporal fractals.

2. Fractal properties of lignin macromolecules

Due to the progress in the development of fractal theory, it became possible to begin the search for new approaches to the investigation of plant biopolymers with intricate structures, first of all, lignin. It has been demonstrated^{106,107} that the fractal theory can be used to characterise lignin and its biosynthetic analogues, *i.e.*, dehydropolymers. Dehydropolymerisation of monomer precursors of lignin *in vitro* is initiated by the peroxidase–hydrogen peroxide enzymic complex. Freudenberg and co-workers developed two methods for laboratory biosynthesis of lignin, namely bulk and end-wise polymerisation (see references cited in Ref. 1). According to Sarkanen,¹ bulk and end-wise dehydropolymers differ from each other in both the chemical and topological structures. Analysis of the conditions of synthesis of various biosynthetic lignins and comparison of them with the growth conditions of fractal clusters made it possible to hypothesise that the bulk and end-wise polymers correspond to definite universal classes of fractal objects.

The end-wise polymerisation is performed by 100-h continuous feeding of a highly dilute solution of the monomer into a large volume of a fairly dilute (10^{-7} mol litre $^{-1}$) solution of enzymic complex. The monomer diffusion is considered to be the rate-determining step of the polymerisation of monomeric lignin precursor. Under these conditions, the macromolecule grows through successive addition of the monomer phenoxyl radicals to those few macromolecules that have formed at the initial stages of reaction. Comparison of the end-wise protocol with the known theoretical models of fractal growth led Ozol-Kalnin⁷⁴ to the conclusion that end-wise polymers belong to the class of Witten–Sander fractal clusters (the DLA P–C model).

In the case of bulk polymerisation, unlike end-wise polymerisation, a rather concentrated solution of the monomer is injected in the reaction area as one portion. Under these conditions, in the opinion of Ozol-Kalnin and co-workers,^{74,90} numerous polymerisation centres appear immediately and the macromolecules grow according to the DLA C–C model.

In order to verify this hypothesis, we synthesised bulk and end-wise dehydropolymers on the basis of a guaiacyl type monomer precursor, namely, ferulic acid ($C_{10}H_{10}O_4$).¹⁰⁸ The fractal dimension of the macromolecule was determined from the data of hydrodynamic measurements in dilute solutions of dehydropolymers in thermodynamically good solvents (DMSO, dioxane). It was found that the hydrodynamic radius of the macromolecule satisfies scaling relation (4). The fractal dimension $d_f = 1/\nu$ (according to translational diffusion data) for the bulk polymer was found to be 2.35 and that for the end-wise polymer was 1.51. The velocity sedimentation coefficients and the intrinsic viscosity also showed a scaling dependence on the molecular mass of the dehydropolymers. This made it possible to calculate the fractal dimension by two more independent methods. The data¹⁰⁸ indicate that bulk lignin corresponds to the DLA P–C model, while end-wise lignin, to the DLA C–C model, as regards their fractal dimensions (see Table 8).

It is noteworthy that the applicability of the DLA C–C model to the description of fractal properties of end-wise lignin gives rise to certain doubts. The fracton and chemical dimensions of clusters

in the DLA C–C model are greater than 1, which implies branching, whereas the Mark–Kuhn–Houwink parameters of the end-wise lignin ($a = 0.8$, $b = -0.58$, $c = 0.45$) and the Flory–Mandelkern hydrodynamic invariant ($\Phi^{1/3}P^{-1} = 2.7 \times 10^{-6}$) obtained in the study cited¹⁰⁸ attest to a linear structure. It is more likely that the fractal properties of this polymer correspond to its conformational state in a good solvent.

One achievement of fractal geometry is elucidation of the relationship between the statistical and fractal properties of polymer chains.⁷⁶ It was shown¹⁰⁹ that the equilibrium statistics of linear polymers is adequately modelled by SARW paths, which demonstrate the fractal properties. The key factors that determine the analogy between the descriptions of a macromolecule and the path of a randomly walking particle are the chain structure and the excluded volume effect.

The conformational characteristics of a linear macromolecule depend on only two parameters, the number of units in the chain (N) and the size of the monomer unit (a_0). Thus, according to the Flory theory, the size of the macromolecule (R) is described by the following scaling relation

$$R \sim a_0 N^{\nu_F},$$

where ν_F is the critical index in the Flory theory, which depends on the dimension of the Euclidean space D :¹¹⁰ $\nu_F = 3/(d+2)$ for $D < 4$ and $\nu_F = 1/2$ for $D > 4$.

According to the SARW model, the average squared distance between the start and the end of the path whose length is N steps obeys the equation

$$\langle R^2(N) \rangle \sim AN^{2\nu_c},$$

where A is a coefficient depending on the lattice dimension and the length of the walk path; ν_c is the critical index in the SARW model.

Mimicking of the Brownian (random) walk on lattices with different dimensions gave¹⁰⁹ the following values for the critical index ν_c : $\nu_c = 0.749$ for $D = 2$; $\nu_c = 0.592$ for $D = 3$; $\nu_c = 0.5$ for $D > 4$.

It can be easily seen that the critical indices ν_F (in the Flory theory) and ν_c (in the SARW model) virtually coincide. This suggests⁷⁶ that the asymptotics of the path of the self-avoiding random walk and the polymeric chain in a thermodynamically good solvent belong to one class of universality, the path itself being a fractal whose self-similar dimension d_f can be determined from the relation

$$\nu_F = \nu_c = \frac{1}{d_f}. \quad (5)$$

Thus, the problem of belonging of the macromolecule of end-wise lignin to fractal objects can be solved unambiguously and refers to metrics, *i.e.*, the mode of arrangement of monomer units in space, rather than to topology ($d_t = 1$). Relations (4) and (5) imply the possibility of determining the fractal dimensions of polymers on the basis of experimentally measurable parameters that characterise, in one way or another, the relationship between the degree of polymerisation N or the molecular mass M and the size of the macromolecule. According to Frenkel' and co-workers,⁸²

$$\nu_F = \frac{1+a}{3}.$$

In this case, if the equivalence principle is obeyed in the translational and rotation friction processes, the known equalities (1)–(3) hold between the hydrodynamic scaling indices. Therefore, the fractal dimension d_f of a macromolecule in solution can be estimated by usual molecular hydrodynamics methods.

Analysis of the published data on the hydrodynamic properties of various lignins (Table 9) and comparison of these data with fractal models led to the hypothesis that the supramolecular structure of lignins *in situ* is an infinite network composed of fractal clusters linked to one another.¹¹¹ When lignins are isolated

Table 9. Fractal dimensions of some lignins.⁹⁰

Lignin specimen	Solvent	$d_f = 3/(a+1)$	$d_f = 1/ b $
Hydrotropic lignin	dioxane	2.68	—
Dioxane lignin	pyridine	2.61	2.78
Bjorkman lignin	—	—	2.70
Sulfate lignin	—	—	2.56
Alkaline lignin	0.1 M buffer	2.27	—
Lignosulfonate	methanol	1.95	—
	2 M NaCl	2.27	3.0
	0.02 M NaCl	—	1.79

from the plant tissue, the inhomogeneous fractal network is destroyed and its fragments pass to the solution as fractal clusters. Relying on the hydrodynamic characteristics of dioxane lignins in solutions determined by Pla and Yan,¹¹² Ozol-Kalnina and co-workers¹¹¹ concluded that lignin can be assigned to fractals of the DLA P–C type. The fractal dimension calculated from the scaling relation

$$g = CM_w^{3/d-3/2},$$

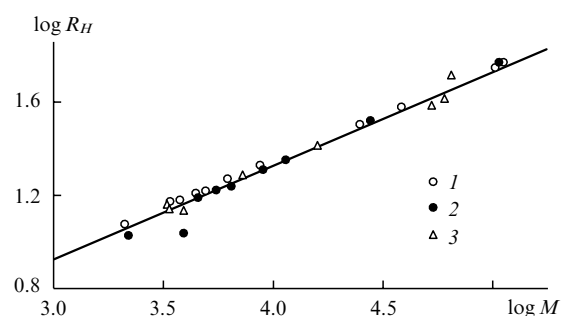
was equal to 2.439 ± 0.007 , which is consistent, in the first approximation, with the dimension of Witten–Sander fractal clusters. However, for other lignin specimens (see Table 9), quite a substantial scatter in the fractal dimensions is observed, which evidently depends on the pre-history and the molecular-mass distribution of the samples under study and on the chosen solvent.

The rather low fractal dimensions of lignosulfonates refer, in the opinion of Ozol-Kalnina *et al.*,¹⁰⁶ to the lignin structure modified upon the chemical reactions that take place during wood cooking rather than to the initial structure of natural lignin. It has also been assumed not without reason^{90, 106} that lignins of various classes of universality can be localised in different structural elements of the cell wall, in particular, the possibility of formation of ‘dense’ Eden type structures with $d_f = d_l = d$ during lignin biosynthesis has not been considered improbable. Thus, the researchers were unable to draw unambiguous conclusions concerning the concordance of the structure of these lignins to particular classes of fractals.

In our opinion, the most reliable data on the fractal properties of lignosulfonates are presented in two publications^{113, 114} dealing with lignin obtained by sulfite pulping of softwood. The molecular mass of these specimens was determined by the non-established equilibrium technique and by laser correlation spectroscopy. The fractal dimensions determined by three independent methods were, on average, 2.44 ± 0.18 .¹¹⁵

The scaling and fractal properties of the macromolecules of MWL isolated from the pine-tree xylem have been studied.¹¹⁶ The investigation of the macromolecular properties of a number of fractions of this lignin in dilute DMSO solutions confirmed that the main criteria of fractality, namely, the scale invariance principle [in the range of molecular masses $(0.5–64) \times 10^3$] and a fractional dimension, are met. The fractal structure of the macromolecule is manifested in the pattern of mass distribution in space being given by relation (4); this allows one to find the fractal dimension d_f from the plot $\log R_H - \log M$ constructed for each lignin fraction using experimental data (Fig. 6). In the case of MWL, the d_f value proved to be 2.32. The fractal dimensions of MWL specimens calculated from the velocity sedimentation coefficients and intrinsic viscosity were 2.32 and 2.40; thus, they can be classified as fractal objects of the DLA P–C type.

A similar conclusion has been drawn in a study of hydrodynamic and scaling properties of another MWL specimen isolated from pine wood (see Table 4). In this case, the polymer was separated into 9 fractions in the range of molecular masses of $(1.7–14.6) \times 10^3$, for which the scaling principle was found to hold. The results of studies of the molecular hydrodynamics by

**Figure 6.** $\log R_H$ vs. $\log M$ for pine wood lignin specimens.¹¹⁶

Specimen: (1) MWL in DMSO, (2) DL in DMSO, (3) DL in dioxane.

different methods proved to be almost identical; the fractal dimension was 2.32 ± 0.02 .

The macromolecules of the Pepper lignin (DL-1–DL-4) (Table 10) are also typical fractal objects with a fractional dimension in any of the studied solvents including dioxane, DMF and DMSO. The self-similar properties are obeyed in the range of molecular masses $(3.0–100) \times 10^3$ (Fig. 7).

Thus, the fractal dimensions of slightly decomposed lignins isolated from softwood are mainly in the range of 2.3–2.8, the isolation procedure having little influence on the fractal properties of the specimens. The data reported in the literature indicate that macromolecules of softwood lignins refer to the versatile class of DLA P–C type fractals.

The numerical values of the fractal dimension d_f characterise the growth of the fractal cluster, in this case, the dehydropolymerisation of monolignols. It is of prime interest to study the effects of different factors (for example, the degree of branching, intramolecular cyclisation) on the microstructure of the cluster and to elucidate the relationships between these factors and the fractal dimension, which is known to be a global property of the cluster.

Table 10. Fractal dimension (d_f) of lignin specimens isolated from various types of plants (according to sedimentation and diffusion analysis and viscosimetry).^{55, 60, 61, 108, 116, 117}

Specimen	Plant	Solvent	d_f determined by		
			viscosimetry	sedimentation analysis	diffusion analysis
DL-1	pine wood (<i>Pinus silvestris</i>)	dioxane	2.54	—	2.56
DL-2	"	dioxane	2.36	—	2.32
MWL	"	DMSO	2.40	2.32	2.32
DL-3	"	DMSO	2.54	—	2.50
DL-4	"	dioxane	2.42	2.86	2.86
LS	spruce (<i>Picea sp.</i>)	buffer solution	2.46	—	2.27
MWL	birch (<i>Betula verrucosa</i>)	DMF	1.86	1.89	1.89
DL	"	DMF	1.91	2.2	1.75
MWL	aspen (<i>Populus tremula</i>)	DMF	1.85	1.82	1.82
DL	"	DMF	2.0	—	1.89
DL	parsnip (<i>Heracleum sosnovsk.</i>)	DMF	1.66	2.3	1.64
DL	mountain ash (<i>Sorbus aucuparia</i>)	DMF	1.8	1.92	1.85

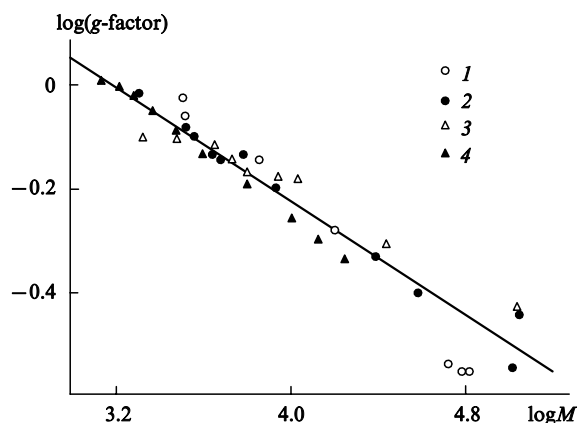


Figure 7. Branching g -factors vs. molecular mass of lignin.¹¹⁶ Specimen: (1) MWL, (2) DL-1, (3) DL-2, (4) DL-3 (the digits mean the numbers of fractions).

It has been proposed⁵⁵ to simulate various versions of dehydropolymerisation using a modified model[†] of the growth of fractal aggregates of the DLA P–C type.

Unlike the classical Witten–Sander model of diffusion-limited aggregation, this model has been supplemented by the parameter P describing the probability of addition of a monomer unit to the growing aggregate upon collision. The probability of addition simulates the chemical reactivity and indicates which process (diffusion or chemical reaction) predominates in the irreversible formation of bonds. The free path of particles in the walk on a lattice, the probability P and the space geometry were shown to influence the formation of the microstructure of the fractal macromolecules constructed in terms of this model.

It has been proposed¹¹¹ that, depending on the conditions, one can observe the formation of either a ‘fractal forest’ or a separate ‘tree with bushes’, which corresponds to the growth of a branched lignin macromolecule in a cell wall in the narrow space between the cellulose fibrils. Since the growth of branches is restricted by the walls, the resulting cluster will possess a much lower effective branching than that produced in the case of unrestricted growth in all directions. The hydrodynamic behaviour of such a macromolecule, especially if it contains a rather large number of rings, will differ substantially from the behaviour of fractal macromolecules of the Witten–Sander type. The possibility of formation of ‘bushes’ within the bounds of the fractal growth procedure implies that the presence of the so-called sol fraction in natural lignin (Brauns lignin) cannot serve as evidence supporting the assumption of the network structure of lignin.

An important topological feature of network and branched polymers is the presence of intramolecular rings. It was found that chaotically branched fractal clusters formed in terms of the modified diffusion-limited aggregation model also contain cyclic structures. According to the publication,¹¹⁷ the procedure of counting intramolecular rings is reduced to counting the number of particles n that close the rings during the growth of the fractal cluster. Figure 8 shows the dependence of the degree of intramolecular cyclisation Y on the probability of addition of a particle to the growing aggregate for several free paths L . The Y value is defined as the ratio of the number of particles n closing the rings to the total number of particles N in this cluster. It should be borne in mind that the Y value defined in this way gives, most likely, a somewhat underestimated degree of cyclisation, because the

[†] Some other models of this type were also proposed earlier,⁷⁸ since the basic Witten–Sander concept is characterised by exceptional versatility and is applicable to investigation of diverse physical phenomena and processes.

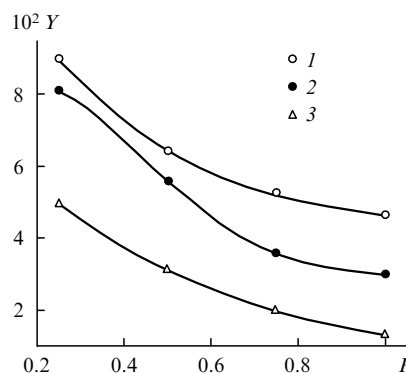


Figure 8. Degree of cyclisation (Y) vs. probability of the addition (P) of a particle to the growing cluster for different free paths L .¹¹⁷ Free path L : (1) 1000, (2) 100, (3) 5.

addition of one particle to the cluster can give rise to two or more (for a lattice with an arbitrary dimension) rings. The number of intramolecular rings depends on various factors including the addition probability P , the free path of particles L and the lattice dimension. The smallest number of rings is found in the clusters formed at $L = 1$ and $P = 1$, i.e., within the framework of the classical DLA P–C model.

It should be noted that accumulation of cyclic structures during the growth of the fractal aggregate obeys the Hurst statistics with an R/S index equal to 0.8 (Fig. 9). This means that simulation of the polymer structure by the diffusion-restricted aggregation technique can give information not only on the structure but also on the dynamics of fractal processes. This aspect is discussed in Section III.3.

In a study of structural features of the fractal cluster,¹¹⁸ the mechanism of surface diffusion of monomer particles was taken into account. It was shown that the combination of Brownian and surface diffusions with variation of the free walk length allows one to model the growth of aggregates of various universal classes. The fractal properties of the clusters were studied by analysing the generating function (measure) of the cluster[‡] within the multifractal approach.

Study of the physicochemical properties of guaiacyl-syringyl lignins has shown^{60,61} that the macromolecules of hardwood

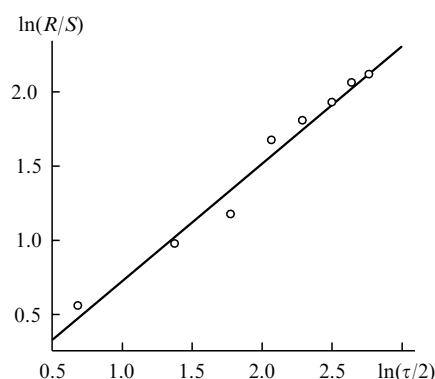


Figure 9. Accumulation of intramolecular cyclic structures during the growth of the Witten–Sander type fractal cluster⁶² according to the Hurst equation: $R/S = (A\tau)^H$ (R is the range of the accumulated deviation from the average value, S is the standard deviation equal to the square root of the variance, τ is the time span, A is constant, in this particular case, $A = 1/2$).

[‡] Generating functions are used in the probability theory to simulate random processes.

lignins, like those of softwood lignins, are structures with a fractional dimension. The d_f values for the macromolecules of hardwood lignins found by different methods are presented in Table 10.

The dimension of the macromolecule d_f is often determined from the slope of the straight line $\log M = f(\log R_\eta)$, where R_η is the hydrodynamic radius calculated from the equation

$$[\eta] = \frac{10\pi N_a R_\eta^3}{3M},$$

(N_a is the Avogadro number).

On average, the fractal dimensions of hardwood lignins ($d_f = 1.84 - 1.98$) are much lower than those for softwood lignins ($d_f = 2.3 - 2.8$). Whereas the fractal dimensions of softwood lignins¹¹⁶ are consistent with the d_f values for the three-dimensional fractal clusters formed in the Witten–Sander model, the d_f values of hardwood lignins are close to the fractal dimensions of the clusters formed in terms of the SARW models.

Lignins of herbaceous plants have been least studied. Table 11 contains the fractal dimensions of lignins for a monocotyledonous plant family of Gramineae determined from the results of investigation of the hydrodynamic properties of these lignins in dilute solutions in DMF (good solvent).⁶¹ The d_f values of dioxane lignins isolated from the herb stalks occur in the range from 1.5 to 1.8. Judging by these data, the macromolecules of herbaceous and hardwood lignins should be attributed to different universal classes (according to the chemotaxonomic classification generally accepted in lignin chemistry, these lignins belong to the same type of guaiacyl-syringyl lignins).

Table 11. Fractal dimension (d_f) of the macromolecules of dioxane lignins of herbaceous plants of the Gramineae family according to sedimentation and diffusion analyses and viscosimetry (DMF as the solvent).⁶¹

Plant	d_f determined by		
	viscosimetry	sedimentation analysis	diffusion analysis
Rye (<i>Secale sp.</i>)	1.80	1.72	1.50
Oats (<i>Avena sativa</i>)	1.72	1.69	1.69
Barley (<i>Hordeum sp.</i>)	1.77	1.64	1.69
Wheat (<i>Triticum sp.</i>)	1.73	1.64	1.68

It follows from analysis of the macromolecular properties of birch and aspen lignins that the macromolecules are star-like. The simulation of growth of polydisperse polymer stars with linear branches within the framework of the SARW model has shown⁶² that one-centre star-like tri- and tetrafunctional macromolecules form impermeable Gaussian coils with Mark–Kuhn–Houwink parameters (a , b , c) close to 0.5 and a fractal dimension of ~ 2 (2.02–2.04). It is noteworthy that these values do not coincide with the values obtained in terms of the SARW model for linear chains ($a = 0.78$, $d_f = 1.67$). Although the results of the theoretical simulation of star polymers remain debatable, they are still consistent with the known statement^{63,64} that the Mark–Kuhn–Houwink parameter a (and, hence, d_f) for these polymers does not depend on the quality of the solvent. Since the d_f values of the hardwood lignins studied differ insignificantly from the value 2.0, which was found for the clusters formed according to the model of ‘lattice animals’, ultimate determination of the fractal structure of the macromolecules of guaiacyl-syringyl lignins requires further investigations.

Further progress in solving the problem of the fractal structure of lignin is apparently related to estimation of the fracton

dimension d_s , which describes the connectivity, *i.e.*, characterises directly the topological structure of the macromolecule.^{71,72} Determination of the fracton dimension is based on the study of the spectra of natural vibrations of fractals. The notion of fractons, *i.e.*, localised vibrational states in fractal materials, was introduced in the study of wave phenomena in fractal materials.⁹⁵ The function describing the density of frequency distribution of fractons is a power function,⁷² because the scaling principle is obeyed for fractal objects. The mathematical power is determined by the fracton (spectral) dimension, which functions as a space dimension in the low-frequency asymptote of the density of vibrational states.

Using the fracton theory, one can determine the vibrational spectrum of a fractal object and estimate its fracton dimension. The properties of fractons can be studied only in the region of fractal behaviour of real materials. For polymers, the characteristic sizes do not exceed the optical wavelength in the visible spectrum. Therefore, Raman light scattering and inelastic neutron scattering are the key spectral methods used to study fractons. However, these methods have not yet found wide application in the study of polymers. At present, the fracton dimensions have been determined only for proteins,⁷¹ poly(methyl methacrylate)¹¹⁹ and epoxy polymers.¹²⁰ It should be noted that both theoretical and experimental methods for determination of the fracton dimension are at an early stage of development.^{104,121} Probably, this accounts for the inconsistency of obtained results.⁷¹ As regards lignins, their fracton spectra have not yet been studied; however, in view of the complexity of the topological structure of lignins, the necessity of such studies is beyond doubt.

3. Fractal properties of lignin biosynthesis

To continue the discussion of the fractal properties of lignins, one should note that the results of investigations outlined above are based on representing lignins as fractal objects arising in some aggregation processes. However, the concept of fractals has been markedly extended in recent years. Fractal structures of not only objects but also processes have been considered.^{122,123} It was found that many chemical systems can be represented as complex dynamic systems of a finite dimension with a chaotic behaviour.^{124–126} The mathematical image of the dynamic (deterministic) chaos is represented by the so-called strange attractor, which is characterised by the fractal structure of its paths in the phase space.^{127–130}

In chemistry, the Belousov–Zhabotinskii system is the best known example of a complex system involving any conceivable type of complex dynamic behaviour.^{68,131} Studies of the Belousov–Zhabotinskii reaction revealed diverse chaos and self-organisation phenomena giving rise to periodic space–time structures.

Dynamic self-organisation phenomena have been discovered in the enzymic dehydrogenation polymerisation of monolignols during lignin biosynthesis *in vitro*.^{132,133} Conduction of monolignol dehydropolymerisation under one-dimensional diffusion conditions has been shown¹³⁴ to result in space–time dissipative structures.

Chaotic and periodic oscillations of chemiluminescence intensity have been detected^{135,136} in a study of lignin oxidation processes in alkaline media.

Karmanov *et al.*⁶⁵ reported the first attempt to study the dynamics of dehydropolymerisation of monomeric lignin precursors in relation to ferulic acid; they demonstrated the possibility of existence of the dynamic mode of the ‘strange attractor’ type. The process was monitored by the redox method in the ‘two-dimensional’ variant of the lignin biosynthesis *in vitro*. The redox potentials were determined from the ratio of oxidised and reduced forms of the substrate and the initiator of the polymerisation. This method for determination of redox potentials has been used previously in the study of chemical transformations of the reduced nicotinamide adenine dinucleotide (NADH), ascorbic acid and other compounds.¹³⁷ It should be noted that the redox method does not possess sensitivity with respect to any of the compounds

involved in the reaction. Nevertheless, it yields a function of state of the reaction system, which is directly related to the reactant concentrations. The dynamics of the system which undergoes dehydrogenation and thus evolves with time is obtained as a time series of redox potentials, which constitutes a database suitable for analysis and identification of the dynamic behaviour of the system by means of non-linear dynamics methods.

Thus, by obtaining a chronologically ordered series of redox potentials, one can elucidate characteristic features of the process dynamics, identify the presence or absence of nontrivial phenomena (symmetry violation effect, correlations at the macroscopic scales, *etc.*), which can be indicative of the occurrence of dynamic self-organisation processes.

The formation of chaotic modes of dehydropolymerisation has been observed in a study of the dynamics of the coniferyl alcohol–hydrogen peroxide–horse-radish peroxidase system.⁶⁶ The dynamic modes implemented during lignin biosynthesis *in vitro* were identified using the strategy of time series analysis based on the deterministic chaos concept.^{68–69} This concept is underlain by methods of non-linear dynamics of non-equilibrium systems and the theory of fractal ensembles.^{68, 75} It was found that chaotic oscillations can differ in their properties; this leads unambiguously to differences in the structure and properties of the corresponding attractors.¹²²

The dynamics of polymerisation of monomer precursors of lignin was studied in several stages. The first stage was the construction of a geometrical image (attractor) of the process in multidimensional phase spaces; this was followed by analysis of multidimensional pseudo-phase paths with identification of the boundaries of the scaling region and the scaling indices (dimensions) and analysis by the attractor topology with estimation of its correlation dimension; subsequently, the dimension of the space of embedding was determined. The research showed^{66, 67} that the time dependences of redox potentials during polymerisation of guaiacyl monolignols obey all the main criteria of deterministic chaos, namely, the ‘continuous spectrum’ criterion and scaling and fractional dimension of the phase paths.

The ‘continuous spectrum’ criterion (the fast Fourier transform spectrum, FFT) discerns chaotic and periodic spectra, as the former are responsible for a continuous FFT spectrum, while the latter, for a discrete spectrum.

The criterion of a fractional dimension of the phase paths allows one to distinguish between deterministic chaos and structureless chaos. The dimension of the phase path for a process accompanied by dynamic self-organisation is known¹³⁸ to be strictly smaller than two (for a two-dimensional case) or strictly smaller than three (for a three-dimensional space). This is due to restriction of the phase space. It can be stated with confidence that polymerisation of monolignols shows an ordered (structured) dynamic behaviour. Structureless chaos is characterised by a distribution of the ‘everywhere dense’ type; therefore, the phase path dimension coincides with the space of embedding dimension.

The next stage of investigation of the polymerisation of coniferyl alcohol included quantitative evaluation of the phase paths of the process; usually, they are constructed using the Packard time delay method.¹³⁹ Figure 10 shows the two-dimensional pseudo-phase portrait of the dynamics of enzymic polymerisation of coniferyl alcohol in the horse-radish peroxidase–hydrogen peroxide system constructed using this method.

The features of the distribution of points in the phase paths in space (point sets, as the path is a set of N points) were estimated and the path convergence to some attractor $C(r)$ was established using the Heaviside integral correlation function¹⁴⁰

$$C(r) = \frac{1}{N^2} \sum_{i,j=1}^N \Theta(r - |x_i - x_j|), \quad (6)$$

where N is the number of points in the path; $\Theta(r)$ is the Heaviside function; r is the specified distance across which the points are counted; x_i is a point in the phase path with the coordinates $[h(x)$,

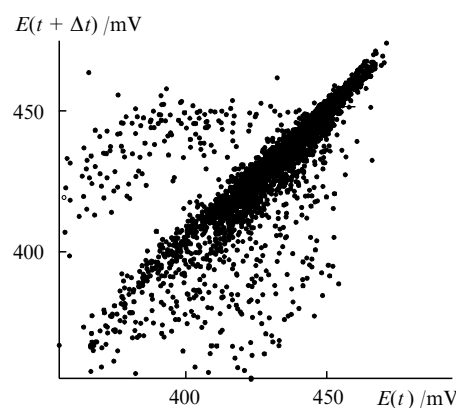


Figure 10. Pseudo-phase portrait of the dynamics of the enzymic polymerisation of coniferyl alcohol in the horse-radish peroxidase–hydrogen peroxide system. $E(t)$ and $E(t + \Delta t)$ are the redox potentials at instants t and $t + \Delta t$, respectively.

$h(x + \Delta x)$, $h(x + 2\Delta x)$, ..., $h(x + (D - 1)\Delta x)$; $|x_i - x_j|$ is the distance from an i th point to a j th point. The function $\Theta(r) = 1$ if $r > 0$ and $\Theta(r) = 0$ if $r \leq 0$.

It was found that the Heaviside function is an invariant measure for the systems under study, because in this case, the scaling principle is obeyed. The correlation dimension of the attractor d was determined from the equation $\log C(r) = d \log r$.¹⁴¹ For polymerisation of coniferyl alcohol, the d index was found to be 1.93 (for another monomeric precursor, ferulic acid, $d = 1.7 - 1.8$). Since all the criteria of deterministic chaos are fulfilled, it was concluded that the dynamic behaviour of the coniferyl alcohol–hydrogen peroxide–peroxidase and ferulic acid–hydrogen peroxide–peroxidase systems has a certain internal order — a structure with fractal properties. The researchers believe that the last-mentioned circumstance^{66, 67} implies that under the chosen conditions, the time evolution of the chemical systems under study is a stable dynamic state called strange attractor.

It is noteworthy that there is a certain relationship between characteristics of the attractor of the dehydrogenation system and the topological structure of the macromolecule of the reaction product (dehydropolymer). It was found that the Mark–Kuhn–Houwink scaling indices calculated from dynamic data are in satisfactory agreement with the results of hydrodynamic measurements.¹⁴² In particular, the parameter a for ferulic acid and coniferyl alcohol is in the range $0.17 < a < 0.38$. These values of scaling indices are normal for the macromolecules of biosynthetic analogues of softwood lignin and correspond to fractal clusters of the Witten–Sander type.

Karmanov and Matveev¹⁴³ have studied the dynamic features of lignin biosynthesis using a different approach based on the self-organised criticality theory.¹⁴⁴ A system functioning in the self-organised criticality mode is known to generate so-called flicker-noise vibrations. The main feature of systems with flicker noise is the fact that their power spectrum is described by the dependence¹⁴⁵

$$A(f) \sim \frac{1}{f^v},$$

where A is the spectral density of the autocorrelator of the dynamic variable, f is frequency, v is the mathematical power. The power spectrum ($1/f$ spectrum) is a function that shows how the energy is distributed over frequencies.

It was shown¹⁴³ that simulation of polymerisation of coniferyl alcohol is subject to a dependence characteristic of the flicker noise (Fig. 11) with $v = 0.8$ (the usual value for a typical flicker noise is $v = 0.8 - 1.3$, see Ref. 146).

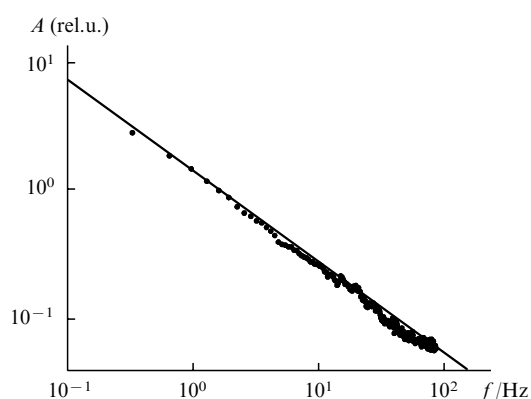


Figure 11. Power spectrum ($1/f$ spectrum) of oscillations of the redox potential during lignin biosynthesis *in vitro* in the coniferyl alcohol–hydrogen peroxide–horse-radish peroxidase system.¹⁴³

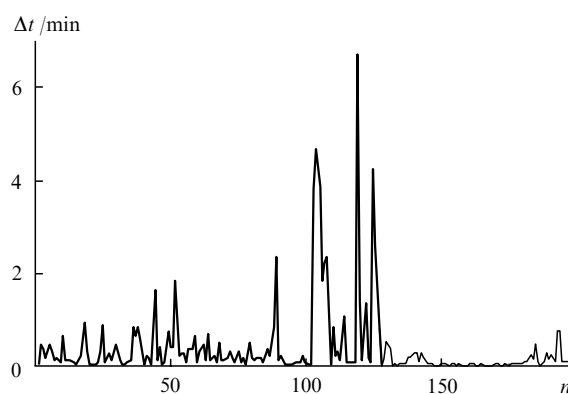


Figure 12. Duration of the laminar phase (Δt) in the dehydropolymerisation of coniferyl alcohol as a function of chronologically ordered fluctuations of redox potentials (n is the ordinal number of the fluctuations).

Yet another feature of the system functioning in the self-organised criticality mode is generation of temporal fractals. Figure 12 shows the dependence of the duration of the laminar phase (Δt is the time delay between fluctuations with numbers $n-1$ and n) of dehydropolymerisation of coniferyl alcohol in the hydrogen peroxide–horse-radish peroxidase system on the function of chronologically ordered fluctuations of redox potentials. Mathematical analysis of this dependence leads to the conclusion that fluctuations of the redox potentials are mutually time-correlated, *i.e.*, in this case, an ordered temporal structure of the fractal type exists. This fact was confirmed by identification of the scale invariance and a fractional dimension of the pseudo-phase portrait of the process dynamics. This proves that the concept of self-organised criticality describes adequately the dynamics of the generation–recombination process of phenoxyl radicals, giving rise to the macromolecules of biosynthetic lignin.

Timashev and co-workers¹⁴⁷ have performed a theoretical investigation of the formation and recombination of radicals. It was shown that the number of free radicals in the steady-state stage of the process fluctuates around some constant value. The Fourier transform spectrum of the temporal series of the number of radicals has a flicker noise characteristic; hence, the process dynamics fits in the self-organised criticality concept. The total dimensions of the attractor of lignin biosynthesis *in vitro* estimated according to the deterministic chaos theory and the self-organised criticality theory are markedly different (Table 12); this means that the dynamics of lignin biosynthesis needs to be further investigated.

The presence of fractal structure in the processes of monolignol polymerisation is confirmed by determination of the H value in the Hurst equation (see the caption to Fig. 9), which is a

Table 12. Characteristics of the chaotic attractor of the lignin biosynthesis *in vitro*.

Dimension of the enveloping space	Correlation dimension d	
	DCT ^a	SOC ^b
2	1.9	1.8
3	2.8	1.9
∞	3.2	2.5

^a The calculation was carried out using the deterministic chaos theory (DCT).⁶⁶

^b The calculation was carried out using the self-organised criticality theory (SOC).¹⁴³

statistical characteristic of the structure calculated using the equation

$$\frac{R}{S} = \left(\frac{\tau}{2}\right)^H.$$

Analysis of the parameters of the Hurst equation (Table 13) confirms that the processes involved in lignin biosynthesis possess a fractal structure.[§]

[§] Systems with deterministic chaos, *i.e.*, those having a fractal ordering, are characterised by $0.5 < H < 1$. For random processes, the Hurst value H is 0.5.

Table 13. Hurst equation parameters for processes related to lignin biosynthesis.

Investigation object	The range of H values	The average H value	Standard deviation	A	Ref.
Lignin biosynthesis <i>in vitro</i> ^a	0.67–0.96	0.85	—	0.88	66
Lignin biosynthesis <i>in vitro</i> ^b	—	0.87	0.01	—	66
Dynamics of cell membrane lignification	0.63–0.95	0.9	0.2	0.9	142, 148
Dynamics of variation of k_X vs. M for fractions of DL and MWL specimens	—	0.79	0.05	–0.08	45
Dynamics of variation of k_X vs. M for fractions of dehydropolymer specimens	—	0.82	0.07	0.01	45
Dynamics of accumulation of intramolecular rings in fractal clusters	—	0.85	0.14	–0.08	75
Annual rings of spruce	0.56–0.94	0.79	0.08	—	55
Random processes	—	0.5	0.01	1–1.5	75

^a Ferulic acid as the monomer. ^b Coniferyl alcohol as the monomer.

IV. Supramolecular structure of lignin

The supramolecular structure of polymers is known to define the mutual arrangement of macrochains and their aggregates. The relevant quantitative characteristics include the size and shape of aggregates and the degree of ordering stipulated by the level of intramolecular interactions. The methods used most often to study the supramolecular structure include X-ray diffraction, electron diffraction and electron microscopy.

Studies dealing with the supramolecular structure of lignins are few. Evidently, the reason is that lignins, which are amorphous polymers, do not usually contain any ordered supramolecular structures such as crystallites, spherulites, *etc.* One more reason is the low efficiency of classical structural methods in the study of amorphous objects.

The wide-angle X-ray scattering provides little information when applied to amorphous polymers. Only in especially favourable cases is it possible to reveal the diffraction effects caused by chemical periodicity of the chain and mutual orientation of the chains. Since lignins are biopolymers with irregular chemical structure, a large set of primary microstructure elements and a rather complex topological structure, the X-ray diffraction pattern obtained for lignins (irrespective of the pre-history of specimens) is expected to represent an amorphous halo. Indeed, this was the case in an X-ray diffraction study of milled spruce wood lignin.¹⁴⁹ Therefore, the results obtained by Pilipchuk *et al.*,¹⁵⁰ who investigated milled wood lignin by electron diffraction, were surprising. These researchers used 2% solutions of lignin in dioxane and acetone and monitored the changes that took place in solutions and films during evaporation of the solvent. After evaporation of dioxane from the solution for 20 h, specific patterns typical of polycrystalline samples were observed on the lignin film thus formed. Further research confirmed the presence of ordering in the structure of films obtained from the dioxane solution; they gave rise to electron diffraction patterns typical of crystalline substances with a long-range order. The pictures of these films obtained by means of an electron microscope showed the presence of symmetrical aggregates consisting mainly of spherical particles of virtually identical sizes. Presumably, during the formation of dioxane films under the experimental conditions, dynamic self-organisation processes take place to give ordered dissipative structures. However, new research is needed to confirm these results. Unlike films obtained from the dioxane solution, the films formed from the acetone solution were fully amorphous.

Most often, the supramolecular structure of lignin is studied using various modifications of electron microscopy. The purpose of a series of studies was to identify individual macromolecules in the photomicrographs obtained by transmission electron microscopy. According to Fengel *et al.*,² lignin of milled spruce wood and ethanol lignin form spherical particles (globules 10 to 100 nm in diameter), the particle shape being independent of the sample preparation procedure. It cannot be ruled out that the smallest of the visible particles are single macromolecules; however, they might also be aggregates, as globules tend to form associates.

Study of lignosulfonates revealed the presence of globular structures 20 to 50 nm in diameter and larger aggregates of an irregular shape. Unlike lignosulfonates, sulfate lignin of pine wood forms substantially smaller particles.² However, in another study,¹⁵¹ the formation of much larger globular particles of sulfate lignin, with a size of 40–100 nm, has been detected. Taking into account that the molecular mass of this lignin did not exceed 1×10^4 , one can suggest that these particles are aggregates composed of several macromolecules. In the presence of electrolytes, sulfate lignin coagulates to give coarse aggregates of an irregular shape. It is clear that to observe separate macromolecules by electron microscopy, new, more rigorous methods for sample preparation need to be worked out. In this connection, noteworthy is the study by Lebedev,¹⁵² who proposed to solve this problem using vacuum atomisation of highly dilute solutions of polymers in mixtures of a solvent and a precipitating agent.

Another group of studies is concerned with the supramolecular organisation of lignins by scanning electron microscopy (SEM). Andersons *et al.*,¹⁵³ who studied the spruce MWL, found spherical domains with a size ranging from 0.5 to several micrometers after evaporation of DMSO. It should be noted that the morphology of lignin films depends on a whole series of factors, in particular, the presence of carbohydrates and the nature of the solvent and the support. If the film is prepared by dispersing a dioxane solution of lignin in an aqueous solution of hemicelluloses, no spherical domains are detected after solvent evaporation and removal of hemicelluloses from the film. In a study of biosynthetic lignin¹⁵⁴ obtained by the end-wise method on the basis of ferulic acid ($M_w = 3 \times 10^4$), spherical particles with a size of 3–5 μm were detected. Study of the dynamics of formation of the supramolecular particles during polymerisation of coniferyl alcohol, ferulic acid, eugenol and isoeugenol has shown¹⁵⁵ that the growth of macromolecules of the dehydropolymer proceeds through the formation of intermediate supramolecular particles with a size of 0.2 to 1.45 μm . In the presence of hemicelluloses, the size of these particles does not exceed 0.3 μm .

The structure of lignins in a scale range of 0.1–10 μm is mainly determined by exogenous factors including temperature and the thermodynamic quality of the solvent used to form the film. It has been found¹⁵⁶ that evaporation of a good solvent gives rise to two types of globular structures in the films of dioxane lignin from pine wood. The diameter of particles of one type does not exceed 1 μm , while that for the other particle type, $\sim 5 \mu\text{m}$. When a poor solvent is evaporated, the loose arrangement of particles, typical of the former case, is replaced by a rather dense packing of the polymer with a structure indiscernible by the SEM method. Mechanical drawing of the specimen plasticised by a good solvent induces the formation of pseudo-fibrils, which are aggregates stretched along the drawing direction of the globule. The formation of oblong aggregates from primary globules of the polymer (polyether acrylate) and their adjustment to one another have also been described in other studies.^{157, 158}

The supramolecular structure of two types of dehydropolymers based on coniferyl alcohol synthesised by enzymic and photochemical methods has been studied.^{159–161} The polymer prepared by the traditional method using peroxidase is composed, as shown by raster-tunnel microscopy, of virtually perfect globular microparticles with a rather narrow size distribution with a maximum at about 500 nm. The globular supramolecular structures tend to form regular macrostructures shaped like triangles, hexagons or helices. Apparently, the geometry of the macrostructures is determined by the nature of the substrate. The most perfect structures were formed on the graphite surface. The photochemical procedure also yields globular supramolecular microparticles. However, in this case, no ordered aggregates are formed (irrespective of the substrate type).

A number of publications^{162–164} are devoted to the supramolecular structure of natural lignin, *i.e.*, lignin of the cell walls of the tree xylem. The most weighty results concerning the structural organisation of natural lignin were obtained using transmission electron microscopy combined with the lignin skeleton method. It was found¹⁶² that lignin of the secondary cell wall has a loose network-like structure formed by globular particles bunched into aggregates of different shapes and sizes. In the central layer, the average size of the supramolecular aggregates is equal to 38 nm. In the outer layers of the secondary cell walls, lignin is present as oblong particles ~ 45 nm wide arranged at right angles to the cell axis. In the primary shell of the pine wood tracheids, lignin occurs as a dense finely grained material,¹⁶³ whereas lignin of the central layer consists of oblong particles oriented along the cellulose microfibrils. The results of investigations suggest the formation of lignin with an ordered structure in cell walls, which is related to the formation of various supramolecular structures during lignin biosynthesis, including fibril-like particles, lamellae and globular structures.

Bogomolov and co-workers¹⁶⁴ studied supramolecular structures formed in the pine wood lignin skeletons before and after partial delignification. The research revealed the presence of (i) structureless lignin in all morphological elements of the cell wall and blind pits; (ii) lamellar lignin in the primary shell, blind pits and the inner layers that line the tracheid cavity; (iii) oblong particles of the type of bars in the secondary shell. The researchers noted different behaviours of these supramolecular structures during alkaline delignification. Conversely, according to other researchers,^{2,165} lignin in the wood is totally amorphous and nonstructured, the shape of lignin particles being determined by the shape of spaces between cellulose microfibrils that are filled during lignification of plant cells.

The inconsistency of the results may be due to specific features of the methods used to obtain lignin skeletons. As a rule, this is done by hydrolysis of wood by various acids (sulfuric, hydrochloric or hydrofluoric), the duration of acid treatment needed to dissolve cellulose and hemicelluloses reaching 3–4 months. During the treatment, the acid concentration is gradually increased and, at the final stages, it is brought to 70%–80%. In the opinion of some researchers,^{2,7,12} high acid concentrations can be responsible for modification of the native structure of lignin.

A promising method for the preparation of lignin specimens is periodate oxidation¹⁶⁶ based on the ability of periodic acid to selectively oxidise and dissolve the polysaccharide components of cell walls. The periodate method for the preparation of lignin skeletons is favourably distinguished from other procedures by mild treatment conditions [neutral pH, low concentration of the reactant (0.08 M), relatively short period (7 days)], which minimise undesirable changes in the structural organisation of the initial lignin.

This method has been successfully used to confirm⁵⁵ the globular morphology of lignin in the central layer of the secondary cell wall of the pine wood tracheid. Meanwhile, the outer layers of the cell membrane were found to contain substantial amounts of oblong and fibril-like supramolecular structures. It was found that globular lignin of the central layer, unlike other lignin forms, is readily soluble in acetic acid after cryochemical treatment of the plant material; however, the reasons for the different behaviours of these lignins remain obscure: this may be due either to structural inhomogeneity or to unequal accessibilities of layers in the cell membrane.

Many researchers have mentioned the clearly disordered pattern of the supramolecular organisation and distribution of lignin in all layers of the cell wall including the intercellular layer—the median plate. This circumstance implies the need for extending the range of physicochemical techniques used to study lignin. A study by Raman spectroscopy has shown¹⁶⁷ that the arrangement of the chains of lignin macromolecules in the cell membranes of spruce wood obeys a certain order. The anisotropy of the paramagnetic properties of the natural lignin of spruce wood pointing to predominant orientation of lignin macrochains along the plant cell axis has been detected by EPR spectroscopy.¹⁶⁸ A γ -photon scattering study of the structural organisation of the plant tissue¹⁶⁹ has shown the presence of fractal order in the packing of polymer chains of both cellulose and lignin.

Solution-free diagnostics of the topological structure of polymers based on thermomechanical analysis is a new method in the study of the supramolecular structure of polymers.^{170,171} The data obtained for hydrolytic lignins led Ol'khov *et al.*¹⁷² to the conclusion that lignins contain partly amorphous and partly crystalline supramolecular structures in which the amorphous blocks have a pseudo-network structure with branching points of a physical nature, these roles being played by crystallites. The degree of crystallinity was found to be dictated by the pre-history of lignin specimens.

Yet another procedure proposed¹⁷³ for investigating the supramolecular structure of lignin is a combination of electron microscopy and densitometric analysis of photomicrographs of the lignin skeletons of pine wood tracheids. The mathematical

processing of densitograms has revealed a certain order in the lignin distribution along the radial direction of the wood cell, which had a self-similarity fractal dimension equal to 1.5.⁵⁵ More recent studies¹³³ indicate that this value is somewhat underestimated. A further development of this method^{142,148} has been the use of non-linear dynamics, fractal geometry and synergetics methods for the analysis of the images obtained by electron microscopy. The following procedure was proposed for the analysis of the electron-microscopy images of lignin polymers. First, so-called spatial series characterising the concentrations of lignin in the radial and tangential directions of a plant cell were constructed and then pseudo-phase portraits were obtained by the Packard method. Second, the integral correlation functions were calculated. Third, the dimensions of the pseudo-phase paths in the spaces with different dimensions were found. The realisation of this algorithm allows one to distinguish between chaotic and ordered structural organisations of the polymer and to establish the order parameters if the system proves to be ordered.

The research showed that the correlation function $C(r)$ of the electron-microscopic images of lignin polymers under analysis is an invariant measure and the distribution function of the ensemble of points in the pseudo-phase space, which reflects the mutual positions of the supramolecular microparticles in the secondary cell wall, is a power function, $C(r) \sim r^{-d}$ (d is a fractional number, $2 < d < 3$). In the researchers' opinion, this implies¹⁴⁸ that the supramolecular organisation of the cell membrane lignin should be described as being scale invariant, *i.e.*, natural lignin has an ordered structure on a scale of 0.01–10 μm .

Table 14 presents some order parameters for the supramolecular structure of lignin, namely, fractal (correlation) dimensions d and the Hurst indices H . A similar fractal type ordering has been established for the supramolecular structure of a number of polyamide acids and polyamides,^{71,174} whose fractal dimension varies in the range of 1.70–1.91 depending on the thermal pre-history of the specimens.

Table 14. Order parameters of the lignins of pine and poplar wood cell membranes.¹⁴⁸

Plant	Specimen	Hurst parameter H	Correlation dimension d for	
			$D = 2$	$D = \infty$
Pine (<i>Pinus silvestris</i>)	xylem	0.88	1.85	5.17
	tracheid			
	xylem tracheid after sulfate pulping	0.90	1.90	5.05
Poplar (<i>Populus nigra</i>)	fibre of the xylem	0.74	1.75	—
	libroform			

The results of studies of the supramolecular structure of lignin indicate that lignification of cell membranes is accompanied by dynamic self-organisation processes, giving rise to self-organised structure of the fractal type. It should also be noted that quantitative analysis of the photomicrographs of cell membranes revealed a power size distribution function for the number of supramolecular elements, $N(r) \sim r^{-n}$, which is typical of systems with self-organised criticality.

A topical problem of the wood chemistry is quantitative characteristics of the structural changes of cell membrane lignin during the production of cellulose. A study of the structure of pine wood lignin at different stages of delignification has been reported.¹⁴² The order parameters of the supramolecular structure of lignin before and after sulfate pulping remain virtually the same, indicating that the structural organisation of lignin as a

fractal object is retained during delignification. However, the size of the supramolecular particles varies depending on the degree of wood delignification. These data demonstrate that the chemical processes that accompany the sulfate pulping of wood are not related to any non-linear self-organisation processes.

V. Conclusion

Despite the vast experimental material accumulated in lignin chemistry, the problem of structural organisation of this natural biopolymer still remains topical. The topological structures of lignin macromolecules are studied using traditional methods of polymer chemistry, which are based on the study of conformational characteristics of the macromolecules by molecular hydrodynamics, namely, capillary viscosimetry, velocity sedimentation and translational diffusion. However, analysis of the relevant publications shows that the problem of determining the topological structure of natural lignin remains unsolved in terms of traditional approaches.

In recent years, a new system approach to the study of lignin structure has been proposed. This approach creates the theoretical grounds for further research into not only topological but also chemical and supramolecular structures. The strategy is to elucidate the genesis of the deterministic chaos and to establish the quantitative criteria of the order arising at different levels of lignin structural organisation upon self-organisation during lignin biosynthesis. These experimental and theoretical studies are based on modern concepts of synergetics, non-linear dynamics and fractal theory.

The experimental data on the conformational and fractal properties of macromolecules of natural lignins obtained in this way are inconsistent with the existing view of the network structure of lignin. Study of the topological and supramolecular structure of natural lignins of different taxonomic origins, *i.e.*, softwood, hardwood and herbaceous lignins, demonstrated that macromolecules of guaiacyl (softwood) lignins are chaotically branched fractal structures whose parameters correspond to the universal Witten–Sander class of fractals, while macromolecules of guaiacyl-syringyl (hardwood) lignins are star-like structures whose scaling parameters are determined by the linear topology of branches. This provided grounds for a new concept which defines the topological structure of lignins as polyvariant. It was found that the topological structure of lignins depends on the functional groups of monomer precursors, polymerisation conditions and dynamic self-organisation.

The fractal properties of lignin at both the topological and supramolecular levels are due to non-linear self-organisation and are related to a dynamic mode of a strange attractor type. Reconstruction of chaotic attractors in terms of the non-linear dynamics of non-equilibrium systems within the framework of chemical synergetics provided data on the dimension of enzymic polymerisation of the basic monolignols of the guaiacyl type.

New methods for the study of the supramolecular structure of lignin were developed. Quantitative characteristics for the structural changes of the lignin of cell membranes of plant tissues during the production of cellulose were obtained.

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Molecular models of solvation in polar liquids

G N Chuev, M V Basilevsky

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Abstract. The state-of-the-art theory of solvation in polar liquids is considered. The main molecular models and protocols for the calculation of solvation are presented. The protocols based on advanced electrostatic models of solvation, the use of correlation functions found by solving the integral equations of statistical physics and the numerical modelling of solvation processes using Monte Carlo and molecular dynamics methods are described. Attention is focused on the application of the above models to the thermodynamics of the solvation of ions and hydrophobic and polar molecules. Peculiarities of the modelling of processes related to solvation such as electron transfer, conformational and tautomeric equilibria, and solvatochromic shifts in the electronic spectra of the solvated molecules are discussed. The bibliography includes 325 references.

I. Introduction

The character of interaction of a solute with the solvent during solvation depends on the physicochemical properties of solutions and liquid-phase associates. Vast experimental material on the solvation of various molecular objects has been accumulated to date; numerous data on the effect of the solvent on the structural and spectral parameters of the solute molecules, the kinetics and mechanisms of chemical and biochemical reactions are documented. Suffice it to say that in only one monograph¹ devoted to the solvation effects in organic chemistry, does the number of

references exceed 2500. According to the Institute of Scientific Information (Philadelphia, USA), more than 10 000 papers on the topic 'solvation' are published annually in scientific journals.

Solvation of molecules is accompanied by various physico-chemical processes.^{2,3} A solvation shell is formed around each molecule. The physical properties of the solvent can substantially change — dissociation or association of molecules can take place, and the conformations and the electronic structures of both solvated species and solvent species can be affected. This gives rise to diverse specific solvation effects. On the basis of the enormous body of experimental data, a large number of solvation models have been constructed, which are used for interpretation of different solvation effects.

Starting with the Born model,⁴ theoretical studies of solvation for one-atomic ions have long been based on the continuum model of the medium. In recent years, considerable advances have been made along this line related to the improvement of the existing and development of new protocols for the calculation of solvation effects. The general trend is to take into account the molecular structure of the solvent. Description of the solvent at the molecular level can be implemented either within the bounds of continuum approximations, which are vivid and simple as regards the calculations, or on the basis of a consistent statistical theory (the method of integral equations). A special place belongs to the numerical simulation of the solvation effects by molecular dynamics (MD) or Monte Carlo (MC) techniques, which are used more and more often as the computing machinery develops.

The improvement of the simple continuum solvation schemes proposed previously gives rise to an hierarchy of phenomenological approximations, intermediate between these simplest schemes and true molecular theories of solvation. Particular applications of the theory of solvation make use (not always critically) of the whole range of the available methods of this theory. The purpose of this review is to analyse and describe systematically the results obtained using the molecular models of solvation proposed recently.

The review can be divided conventionally into three parts that include Sections II – V, VI – IX and X – XII, respectively. The first part outlines the general scheme for the calculation of solvation

G N Chuev Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, 142292 Pushchino, Moscow Region, Russian Federation. Fax (7-096) 739 05 53. Tel. (7-096) 773 91 09. E-mail: genchuev@rambler.ru

M V Basilevsky State Scientific Centre of the Russian Federation 'L Ya Karpov Institute of Physical Chemistry', ul. Vorontsovo Pole 10, 105064 Moscow, Russian Federation. Fax (7-095) 975 24 50. Tel. (7-095) 917 39 03. E-mail: basil@cc.nifhi.ac.ru

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and describes the calculation of solvation processes on the basis of upgraded continuum models and integral equations. Since voluminous literature on the MD and MC numerical simulation techniques is available (see, for example, Refs 5–14), we have not discussed here their principles and engineering implementations, but, as an exception, have touched upon the problems of taking into account the electrostatic interactions within the framework of these methods and have briefly considered the calculation of the change in the thermodynamic functions upon solvation — this aspect is especially important for chemical and biological applications. The second part dealing with hydrophobic effects provides a brief description of thermodynamic integration, which is an efficient up-to-date algorithm of such calculations, and considers typical objects to which various methods of solvation theory are applied, depending on the conditions. These objects can be represented by hydrophobic molecules, ions, polar molecules and quantum particles (solvated electrons, bipolarons and positronium). The third part is devoted to the study of processes related to solvation (electron transfer, conformational and tautomeric equilibria and solvatochromic shifts in the electronic spectra). The prospects for using the molecular models of solvation in polar liquids are considered in the Conclusion.

In order to maintain a reasonable relationship between the coverage of information and the logics of narration, we restricted the scope of this review to analysis of the key methods of the solvation theory and did not dwell on detailed discussion of the results obtained.

II. General scheme for the calculation of solvation

The choice of the intermolecular interaction potentials plays a crucial role in the theory of solvation. In most solvation theories, particles of the solute¹⁵ and the solvent (both atoms and molecules) are considered within the framework of classical mechanics. The set of methods and calculation algorithms involved are often referred to as ‘molecular mechanics’ (MM).^{16,17} In this case, it is suggested most often that these potentials can be represented as sums of effective atom–atom pair potentials

$$U(\mathbf{R}^{(N)}) = \sum_{I \neq J}^N u(|\mathbf{R}_I - \mathbf{R}_J|).$$

Here $U(\mathbf{R}^{(N)})$ is the potential energy of the solute–solvent system, N is the total number of atoms in the system, $\mathbf{R}_I$ and $\mathbf{R}_J$ are the radius-vectors of atoms I and J , respectively. The summation covered every possible pair of atoms where both atoms belong to either the solute or a solvent molecule, or one atom belongs to the solute and the other one, to the solvent molecule. The indices I and J imply simultaneously the type and the number of an atom. An advantage of this approach is the possibility of finally reducing the problem to the study of only radial atom–atom potential functions. However, even in this approximation, parametrisation of the interatomic force fields is very complicated. This requires specification of the functional form of each potential containing adjusting parameters, which are selected by comparing the results of trial calculations with the experimental data on the structure and thermodynamic properties of one-atomic and molecular liquids. A number of parametrisation protocols for the intra- and intermolecular force fields (AMBER,¹⁸ CHARMM,¹⁹ OPLS,²⁰ GROMOS,²¹ GROMACS,²² etc.) have been developed. These techniques make use of the partial charges of atoms q_i for parametrisation of the Coulomb interaction and the Lennard-Jones model for parametrisation of the non-Coulomb contribution to atom–atom potentials.

The main phase in the calculation of classical molecular models is determination of the equilibrium ensemble of atomic configurations

$$\bar{\mathbf{R}}^{(N)} = \bar{\mathbf{R}}_1 \bar{\mathbf{R}}_2 \dots \bar{\mathbf{R}}_N$$

in a chosen volume of the medium either by solving dynamic equations (MD method) or using the MC method. In both cases, the final outcome is the calculated atom–atom (AA) correlation function (CF) $g_{AB}(|\mathbf{R}_1 - \mathbf{R}_2|)$, which is related to the conditional probability that one atom A of some molecule will be found at point $\mathbf{R}_1$ provided that atom B of another molecule occurs at point $\mathbf{R}_2$.²³

The presence of chemical bonds gives rise to correlations that are specified by intramolecular correlation functions (IMCF). For rigid molecules, IMCF depends only on the molecular geometry, while for non-rigid molecules, averaging of these functions over all molecular conformations should be carried out. The atom–atom correlation functions (AACF) and the IMCF provide full information on the local microscopic structure of the solution and the solvated complex. All thermodynamic values (Gibbs energy of solvation ΔG , chemical potential μ and so on) can also be calculated from the correlation functions and the intra- and intermolecular interaction potentials.²³

More detailed investigations of real solvation systems require a quantum-mechanical (QM) calculation of electron density distribution $\rho_e(\mathbf{r})$ and many-electron wave function $\Psi(\mathbf{r}^{(n)})$ (n is the number of electrons). However, the quantum-chemical calculations from ‘primary principles’ are very laborious and can now be carried out only for systems consisting of several tens of atoms. For systems comprising hundreds of atoms, semiempirical methods are employed. Therefore, hybrid (QM/MM) methods, i.e., calculation protocols that use simultaneously the equations of quantum and molecular (classical) mechanics, are now actively used to study solvation. All molecules of the solution are divided into two subsystems, namely, the solute (for which the quantum calculations are carried out) and the solvent, which is described on the basis of classical molecular models. Correspondingly, quantum (Q), classical (M) and mixed (QM) contributions to the intermolecular potentials are distinguished. The full Hamiltonian H of the system includes each of these contributions.

$$H = H_Q + H_{QM} + H_M, \quad (1)$$

$$H_Q = \sum_i \frac{\mathbf{P}_i^2}{2m_i} + \sum_{ij} \frac{Z_i Z_j}{|\mathbf{R}_i - \mathbf{R}_j|} + \langle \Psi | H_e | \Psi \rangle,$$

$$H_{QM} = \sum_{iI} \left[\frac{Z_i q_I}{|\mathbf{R}_i - \mathbf{R}_I|} - \left\langle \Psi \left| \frac{q_I}{|\mathbf{r}_i - \mathbf{R}_I|} \right| \Psi \right\rangle + V(|\mathbf{R}_i - \mathbf{R}_I|) \right],$$

$$H_M = \sum_I \frac{\mathbf{P}_I^2}{2m_I} + \sum_{IJ} u(|\mathbf{R}_I - \mathbf{R}_J|).$$

Here, the subscripts i, j, I, J refer to atoms of the quantum and classical subsystems, respectively; $\mathbf{P}_i, \mathbf{P}_I$ and $\mathbf{R}_i, \mathbf{R}_I$ are the impulses and coordinates (radius-vectors) of atoms; Z_i, m_i are the charge and the mass of the solute nuclei, H_e is the electron Hamiltonian (we do not write it out in an explicit form) and the brackets $\langle \Psi | \dots | \Psi \rangle$ mean averaging over the electronic configuration of the solute with coordinates of the electrons $\mathbf{r}_i$. The operator H_{QM} contains both the electrostatic (the first two terms) and non-electrostatic (V) contributions.

The use of Hamiltonian (1) implies the calculation of the many-electron wave function Ψ and the equilibrium configuration $\bar{\mathbf{R}}^{(N)}$ of the solvent molecules. In terms of the method of correlation functions, the problem of solvation can be reduced to the investigation of the effective Hamiltonian H_{ef} , which governs the behaviour of the quantum subsystem in the external field $V_{\text{ef}}(\mathbf{R})$ created by solvent molecules at point $\mathbf{R}_i$,

$$H_{\text{ef}} = H_Q + V_{\text{ef}} = \sum_i \frac{\mathbf{P}_i^2}{2m_i} + \sum_{ij} \frac{Z_i Z_j}{|\mathbf{R}_i - \mathbf{R}_j|} + \langle \Psi | H_e | \Psi \rangle + \sum_{AB} \int g_{AB}(\mathbf{r}) u_{AB}(|\mathbf{r} - \mathbf{R}|) d\mathbf{r}, \quad (2)$$

where $g_{AB}(\mathbf{r})$ is the AACF between atoms of the solvated complex and the solvent and $u_{AB}(\mathbf{r})$ are the corresponding atom–atom potentials. The free Gibbs energy of solvation of the system (per solute species) is given by the equation

$$\Delta G = \langle \Psi | H_{\text{ef}} | \Psi \rangle - \langle \Psi_0 | H_Q | \Psi_0 \rangle + \mu, \quad (3)$$

where $\Psi_0(\mathbf{r}^{(n)})$ and $\Psi(\mathbf{r}^{(n)})$ are many-electron wave functions of the solute in vacuum and in the solvent, respectively, μ is the chemical potential of the solvent, which can be expressed in terms of the CF. Since the AACF is determined by the equilibrium configuration of the solvent molecules, which also depends on the electron density distribution $\rho_e(\mathbf{r})$, self-consistent calculation of Ψ and $g_{AB}(\mathbf{r})$ is required. The calculation procedure is as follows. Some initial approximation is taken for the wave function Ψ and for the spatial configuration of the solute. The next stage is to calculate the charge distribution on the solute atoms, to find the equilibrium configuration $\mathbf{R}^{(N)}$ and $g_{AB}(\mathbf{r})$, to calculate the external field and, finally, to correct Ψ by calculating the electron density distribution in this external field. This procedure should be repeated until full self-consistency is attained. Various modifications of this procedure are related to the choice of methods for calculating $g_{AB}(\mathbf{r})$ (MD, MC or integral equations) and Ψ . The allowance made for electron polarisation of the solvent molecule changes appreciably the whole calculation scheme.

In the general case, the calculation of the equilibrium configuration of the solute + solvent system, like the calculation of the AACF, is labour-consuming; therefore, additional simplifications are used in continuum models. The approximations based on the linear response theory²⁴ allow one to reduce the problem to the calculation of the wave function Ψ in the reactive self-consistent field (SCF) V_{ef} , which depends on the dielectric constant of the liquid and charge distribution in the solute. Thus, using continuum models (CM), one can calculate the energy of solvation and the electron density distribution on the solvated molecule without calculating the correlation functions. Actually, this requires only an additional self-consistent calculation of V_{ef} , which can be naturally included into standard quantum-chemical procedures.²⁵

III. Continuum models

The linear response approximation in the theory of solvation appears to be justified for considering the electrostatic interactions in the system consisting of a solute and the solvent. It is widely used for systems where such interactions predominate, *i.e.*, for charged and highly polar solutes in polar solvents. This approximation forms the basis for the continuum theory. It is formulated as a relationship between the charge distribution on the solute $\rho_Z(\mathbf{r})$, which depends on the charge of the atomic nuclei and the electron density distribution $\rho_e(\mathbf{r})$, *i.e.*,

$$\rho_Z(\mathbf{r}) = \sum_i Z_i \delta(\mathbf{r} - \mathbf{R}_i) - \rho_e(\mathbf{r}),$$

and the field of the medium ‘response’ $V(\mathbf{r})$, *i.e.*, electrostatic field

$$V(\mathbf{r}) = \hat{K} \rho_Z = \int \rho_Z(\mathbf{r}') K(\mathbf{r}, \mathbf{r}') d\mathbf{r}'. \quad (4)$$

Here $\hat{K}$ is the linear integral operator with a symmetric nucleus $K(\mathbf{r}, \mathbf{r}')$ (the Coulomb Green function, which has the following form for the case of electrostatic potential in vacuum: $|\mathbf{r} - \mathbf{r}'|^{-1}$). Within the linear theory, the Helmholtz free energy of solvation is equal to

$$\Delta F = \frac{1}{2} \int \rho_Z(\mathbf{r}) V(\mathbf{r}) d\mathbf{r} = \frac{1}{2} \int \rho_Z(\mathbf{r}') K(\mathbf{r}, \mathbf{r}') \rho_Z(\mathbf{r}) d\mathbf{r}. \quad (5)$$

In the simplest case of a homogeneous medium, the charge distribution $\rho_Z(\mathbf{r})$ is related to the induction field $\mathbf{D}(\mathbf{r})$ by the Poisson equation

$$\nabla \mathbf{D} = 4\pi \rho_Z(\mathbf{r}), \quad (6)$$

and the polarisation $\mathbf{P}(\mathbf{r})$ of the medium is equal to

$$\mathbf{P}(\mathbf{r}) = \frac{1}{4} \pi \left(1 - \frac{1}{\epsilon_0} \right) \mathbf{D}(\mathbf{r}), \quad (7)$$

$$\mathbf{D} = \epsilon_0 \mathbf{E},$$

where ϵ_0 is the static dielectric constant of the solvent, $\mathbf{E}$ is the electric field. A variable polarisation arises in a homogeneous medium as the response field. This simple model has found wide application in early versions of the electron transfer theory.

To describe the solvation effects at an up-to-date level, one should take into account the discrete (atomic) structure of the solvated molecule. There appears a boundary separating the region occupied by the solute (the ‘cavity’ in which the dielectric constant ϵ is taken to be unity) from the surrounding area filled with a continuous medium with $\epsilon = \epsilon_0$. With such boundary conditions, it is inconvenient to use the variables $\mathbf{P}(\mathbf{r})$ and $\mathbf{D}(\mathbf{r})$, and transition to the general relations (4) and (5) is expedient. In this case, the response nucleus $K(\mathbf{r}, \mathbf{r}')$ is defined as the function ϵ_0 . The numerical implementation of this procedure is equivalent to the solution of the Poisson equation with the appropriate boundary conditions, which can be different depending on the particular method used to specify the boundary of the cavity accommodating the solute. Some of these methods are mentioned below.

A more general formulation of electrostatic equations is proposed in non-local electrostatics.^{26,27} For a homogeneous medium, simple relations (6) and (7) are replaced by the relation

$$\mathbf{P}(\mathbf{r}) = \int \mathbf{E}(\mathbf{r}') \chi(\mathbf{r} - \mathbf{r}') d\mathbf{r}'. \quad (8)$$

Here $\chi(\mathbf{r} - \mathbf{r}')$ is the non-local generalised dielectric susceptibility. In the standard phenomenological approach,^{26–29} it is expressed in terms of the dielectric function $\chi(\mathbf{k})$ [Fourier transform of the function $\chi(\mathbf{r})$], which is in turn related to the dielectric susceptibility $\epsilon(\mathbf{k})$ in the following way:

$$\chi(\mathbf{k}) = \frac{1}{4\pi} \left[1 - \frac{1}{\epsilon(\mathbf{k})} \right]. \quad (9)$$

This approach allows one to take into account the structure of the medium in the continuum theory. As an example, we consider the model function $\chi(\mathbf{k})$ for the isotropic case where it depends only on the length of the vector $\mathbf{k}$. In the simplest variant, this model has the form^{24–30}

$$\chi(\mathbf{k}) = \chi_0 + \frac{\chi_1}{1 + k^2 \varsigma^2}. \quad (10)$$

Here χ_0 and χ_1 are constants, the former determining the local, while the latter, the non-local components of the susceptibility; $k = |\mathbf{k}|$; the model parameter ς is the correlation length. After the backward transformation, the Fourier function (10) gives rise to a ‘susceptibility kernel,’ which depends only on the distance between the points $\mathbf{r}$ and $\mathbf{r}'$

$$\chi(|\mathbf{r} - \mathbf{r}'|) = \chi_0 \delta(\mathbf{r} - \mathbf{r}') + \frac{\chi_1}{4\pi \varsigma^2 |\mathbf{r} - \mathbf{r}'|} \exp(-\varsigma^{-1} |\mathbf{r} - \mathbf{r}'|), \quad (11)$$

where δ is the Dirac delta function.

In conformity with relation (8), the response $\mathbf{P}(\mathbf{r})$ decays exponentially with an increase in the distance $|\mathbf{r} - \mathbf{r}'|$, and the dielectric shielding of the solute charge is efficient only at distances not exceeding ς . In the description of the orientational polarisation of the medium, the ς value is of the order of the characteristic size of the solvent particles.

The applicability of local models is restricted by the limited case $\varsigma \lesssim \varsigma_0$, where ς_0 is the characteristic size of the solvated molecule. By introducing multimodal model functions as the sums of Lorentzian functions (10) with different parameters $\varsigma_1, \varsigma_2, \dots$, equation (10) can be generalised to describe the structure of the solvent around the solute in more detail.^{24–28} The non-local models for an inhomogeneous medium are complex and have

been developed only for spherically symmetric systems,^{30–33} although the equations describing them are also known for the general case.^{31–33} In these models, linear relation (4), and, finally, (leaving aside the technical complexity), the response nucleus $K(\mathbf{r}, \mathbf{r}')$ can be expressed in terms of the function $\chi(\mathbf{k})$ or $\varepsilon(\mathbf{k})$.

This type of approach can be extended to time-dependent effects by introducing the functions $\chi(\mathbf{k}, \omega)$ or $\varepsilon(\mathbf{k}, \omega)$ that depend on the frequency ω . In the absence of spatial dispersion, they are reduced to the functions $\chi(\omega)$ and $\varepsilon(\omega)$, which are complex values.³⁴ For example,

$$\varepsilon(\omega) = \varepsilon_1(\omega) + \varepsilon_2(\omega),$$

where the terms ε_1 (real) and ε_2 (imaginary) are even and odd functions of ω , respectively. The transition to time functions is performed by the Fourier inversion.

Relation (4) also holds for molecular theories if the applicability conditions of the linear response are met. Then the nucleus $K(\mathbf{r}, \mathbf{r}')$ can be calculated within the framework of one or another microscopic model. In the classical limit, the Kirkwood formula holds,^{34,35} which expresses the nucleus of the integral operator $\hat{K}$ in terms of the correlation function $\langle \Delta V(\mathbf{r}) \Delta V(\mathbf{r}') \rangle_{\rho_Z T}$ of fluctuations of the microscopic electric field

$$K(\mathbf{r}, \mathbf{r}') = -\beta \langle \Delta V(\mathbf{r}) \Delta V(\mathbf{r}') \rangle_{\rho_Z T}, \quad (12)$$

where $\beta = (k_B T)^{-1}$, k_B is the Boltzmann constant; averaging involves an ensemble with fixed charge density distribution ρ_Z and temperature T . Relation (12) allows one to perform MC or MD simulation of the nucleus $K(\mathbf{r}, \mathbf{r}')$ on the basis of calculations of the correlation function $\langle \Delta V(\mathbf{r}) \Delta V(\mathbf{r}') \rangle$. Finally, it becomes possible to transfer the approaches developed in the continuum theory to molecular models.

Of all the existing computation schemes, the continuum theory most simply, although roughly, takes into account the solvation effects. Owing to the simplicity of the numerical procedure, continuum models have been widely distributed and underlie a large number of applied computer programs. Here, we only briefly touch on different versions of continuum models, because voluminous literature devoted to this topic is available.^{36–43}

Continuum models can be classified in terms of the procedure of calculation of the reactive self-consistent field V_{ef} acting upon the solute [see Eqn (2)]; in terms of the method of inclusion of the short-range contribution V_s ; or in terms of the numerical procedure used to calculate the wave functions Ψ . In addition, in the calculations that are meant to provide the semiquantitative agreement with the experiment, the cavity accommodating the solute should have a complex shape 'adjusted' to the real solute structure; hence, a procedure for finding this cavity is also required.

Quantum-chemical calculations for the solvated complex use most often *ab initio* computations based on the Hartree–Fock (HF) approximation supplemented by some scheme for taking into account the electron correlations.^{44–49} In many publications, the Ψ functions are calculated in terms of the density functional theory (DFT).^{50–53}

Comparison of the data obtained by different methods shows a substantial scatter of the results (Table 1), which is, however, due not only to the calculation scheme chosen but also to the use of different parameters for the interatomic interaction potentials. The results of both HF and DFT calculations are in almost equally satisfactory agreement with the experimental data.

The ways of taking into account the short-range contribution V_s depend on the way of parametrisation of the van der Waals interactions. Most often, the Solvent Accessible Surface (SAS) approximation is used according to which the contribution of short-range forces to ΔG (ΔG_s) is proportional to the solute surface area accessible to the solvent molecules. If the SAS has a complex shape, it is considered as consisting of separate S_i fragments, which correspond to the solute atoms, and ΔG_s is calculated as the sum over the fragments⁶⁰

Table 1. Experimental and calculated [by DFT, MM, HF, SMx (Solvation Model) and CM methods] values of free energy ΔG (kcal mol^{−1}) for the hydration of amines and amides.

Solute	Experiment (see ⁵⁴)	Calculation by the method					
		DFT (see ⁵³)	MM (see ⁵⁵)	HF (see ⁵⁶)	SMx (see ⁵⁷)	MM (see ⁵⁸)	CM (see ⁵⁹)
NH ₃	−4.3	−4.8	−4.0	−5.1	−4.3	−4.2	−6.3
CH ₃ NH ₂	−4.6	−3.0	−3.7	3.5	—	−3.5	−4.5
(CH ₃) ₂ NH	−4.3	—	−1.2	—	−4.3	−1.9	−2.7
(CH ₃) ₃ N	−3.2	—	−0.6	—	−2.6	0.4	−1.2
Acetamide	−9.7	−9.0	−11.9	−9.2	—	—	−9.8
NMA ^a	−10.1	—	−9.3	—	—	—	−7.8
NNDMA ^b	−8.5	—	−7.3	—	—	—	−6.3

^a NMA is *N*-methylacetamide; ^b NNDMA is *N,N*-dimethylacetamide.

$$\Delta G_s = \sum_i A_i S_i, \quad (13)$$

where A_i is a coefficient expressed in the surface tension units. According to the Generalised Born Surface Area (GBSA) model,^{61,62} it is assumed that the A_i value is determined only by the type of atom. In more advanced SMx models,^{63,64} it depends additionally on the type and length of the bonds and (implicitly) on the charge of the i th atom. Attempts have been made to parametrise the separate contributions related to the repulsion of atoms and to their attraction due to dispersion interactions. The complexity of such calculations is obvious, due to the fact that these contributions have opposite signs and partially neutralise each other. In some cases, these contributions are expressed *via* one- and two-electron integrals for the corresponding atomic orbitals and are included in the calculation scheme as a component of the self-consistent field acting on the solute.⁶⁵ The repulsion contribution contains a temperature-dependent 'non-potential' component, namely, the cavitation energy (see Section VI). Other methods for the parametrisation of ΔG_s also exist. Comparative analysis of the existing methods showed⁶⁶ that, with appropriate thoroughness, they all provide similar estimates of ΔG_s .

A number of modifications of continuum models exist, depending on the procedure of calculation of the self-consistent field, which is dictated by the method used to solve the Poisson equation for the electrostatic potential V_{ef} created by the charge distribution $\rho_Z(\mathbf{R})$

$$\nabla \varepsilon(\mathbf{R}) \nabla V_{\text{ef}}(\mathbf{R}) = -4\pi \rho_Z(\mathbf{R}). \quad (14)$$

This equation corresponds to the most general case where the dielectric constant of the (inhomogeneous) medium $\varepsilon(\mathbf{R})$ depends (unlike ε_0) on the spatial coordinates $\mathbf{R}$. Equation (14) can be numerically solved by using various finite-difference schemes or the finite-element method. This way of solving the equation is, however, labour-consuming, because elucidating the details of field distribution $V_{\text{ef}}(\mathbf{R})$ requires the use of a three-dimensional network with a large number of points.⁶⁷ In some cases, poor convergence is observed during the solution. Despite these drawbacks, this approach has quite a lot of supporters, especially among researchers engaged in molecular biology,⁵⁹ which is due to the availability of the relevant program packages for the solution of the Poisson–Boltzmann⁶⁸ and Poisson⁶⁹ equations.

Most often, the cavities of the solute excluded volume are considered, the dielectric constant being a stepwise function

$$\varepsilon(\mathbf{R}) = 1$$

inside the cavity and

$$\varepsilon(\mathbf{R}) = \varepsilon_0$$

outside the cavity. Then for a spherical cavity with the radius a , the solution of Eqn (14) can be written as a multipole expansion into spherical harmonics $Y_l^m(\psi, \theta)$ ^{38, 70}

$$V_{\text{ef}}(R > a) = \sum_{l=0}^{\infty} \frac{2l+1}{l+(l+1)\epsilon} \frac{1}{R^{l+1}} \sum_{m=-l}^l B_{lm} Y_l^m(\psi, \theta),$$

$$V_{\text{ef}}(R \leq a) = V_0(\mathbf{R}) + V_{\sigma}(\mathbf{R}) = \sum_{l=0}^{\infty} \frac{1}{R^{l+1}} \sum_{m=-l}^l B_{lm} Y_l^m(\psi, \theta) + \sum_{l=0}^{\infty} \frac{(l+1)(\epsilon-1)}{l+(l+1)\epsilon} \frac{1}{a^{2l+1}} \sum_{m=-l}^l B_{lm} Y_l^m(\psi, \theta), \quad (15)$$

where $R = |\mathbf{R}|$, B_{lm} are the expansion coefficients. In relation (15), the contributions $V_0(\mathbf{R})$ and $V_{\sigma}(\mathbf{R})$ represent the potential created by the charge distribution on the solute in vacuum and the response field created by the induced charge of the surface of the sphere, respectively. In the case of a solute with an arbitrary shape, one can use a multicentred multipole expansion.³⁸ In this case, the whole surface of the solute is first split into spherical fragments for which expansion (15) is performed, while the self-consistent field $V_{\text{ef}}(\mathbf{R})$ is calculated as a superposition of the contributions of all centres. An essential drawback of this approach is poor convergence of series (15); as a consequence, it is difficult to control the number of terms of the series needed to ensure the specified precision. For small molecules, an accuracy of not less than 93% is attained at $l_{\text{max}} = 8$ (see Ref. 71), whereas for large molecules, l_{max} increases linearly with an increase in the distance from the expansion centres. The case where only the terms with $l_{\text{max}} = 0$ are considered corresponds to the Born approximation⁴ and $l_{\text{max}} = 1$, to the Onsager approximation.⁷² The two last-mentioned protocols are embodied in a large number of computer programs. The former underlies the GBSA model (generalised Born model taking into account the accessible surface),⁶⁰ which is actively used for 'classical' calculations of the solvation energy of biomacromolecules⁷³ or the energy of binding of a ligand to a protein.⁷⁴ Yet another example is represented by SMx models⁶² where this approximation is used for the quantum-chemical calculation of solvation. Note that the results of calculations in terms of these models are highly sensitive to the choice of the a radius.

An alternative method for solving the Poisson equation is the popular Polarised Continuum Model (PCM).^{75–78} According to this model, the solute is immersed in a cavity with a complex shape which is constructed as a combination of (overlapping) spheres drawn around each of the solute atoms. The radii of the spheres are expressed in terms of the van der Waals radii of atoms by introducing a scaling multiplier, which is a method parameter. Equation (14) with the function $\epsilon(\mathbf{R})$, which acquires different constant values inside and outside the cavity, is reduced to the integral relation

$$V_{\sigma}(\mathbf{R}) = V_{\text{ef}}(\mathbf{R}) - V_0(\mathbf{R}) = \int_S \frac{\sigma(\mathbf{R}')}{|\mathbf{R} - \mathbf{R}'|} d\mathbf{R}'. \quad (16)$$

Here, S is the surface area of the boundary of the cavity around the solute over which the corresponding surface integral is calculated.

It follows from electrostatics equations that the surface charge $\sigma(\mathbf{R}')$ on the boundary of the cavity is related to the field strength $E(\mathbf{R}')$ by the relation

$$\sigma(\mathbf{R}') = \frac{1 - \epsilon_0}{4\pi\epsilon_0} \mathbf{n}(\mathbf{R}') E(\mathbf{R}') = \frac{\epsilon_0 - 1}{4\pi\epsilon_0} \mathbf{n}(\mathbf{R}') \nabla [V_0(\mathbf{R}') - V_{\sigma}(\mathbf{R}')], \quad (17)$$

where $\mathbf{n}(\mathbf{R}')$ is the unit vector of the inward normal to the surface S . Equations (16) and (17) taken in combination provide the

possibility of obtaining a closed-loop iterative scheme for the calculation of $\sigma(\mathbf{R}')$ and $V_{\sigma}(\mathbf{R}')$.

The key integral equation of the PCM determines the surface charge $\sigma(\mathbf{R})$ (see Ref. 79)

$$\sigma(\mathbf{R}) = \frac{1 - \epsilon_0}{4\pi\epsilon_0} \left[\int_V a(\mathbf{R}, \mathbf{R}') \rho_z(\mathbf{R}') d\mathbf{R}' + \int_S a(\mathbf{R}, \mathbf{R}') \sigma(\mathbf{R}') d^2\mathbf{R}' + 2\pi\sigma(\mathbf{R}) \right], \quad (18)$$

$$a(\mathbf{R}, \mathbf{R}') = \frac{\partial}{\partial \mathbf{n}(\mathbf{R})} \left(\frac{1}{|\mathbf{R} - \mathbf{R}'|} \right),$$

where a is the normal derivative of the Coulomb potential.

The right-hand part of Eqn (18) is the sum of volume and surface integrals.

Iterative algorithms are used most often to solve Eqns (16) and (17) for $V_{\sigma}(\mathbf{R})$ and $\sigma(\mathbf{R}')$ or the equivalent equation (18) for $\sigma(\mathbf{R})$. The function $\sigma(\mathbf{R})$ is approximated by the network of its values on small segments of the surface S . In some existing alternative (non-iterative) calculation schemes, the set of the $\sigma(\mathbf{R})$ values on the segments of the cavity surrounding the solute is considered as a vector and the Eqns (16), (17) and (18) that determine it are reduced to a high-dimension matrix equation (see the review³⁶ and the references cited therein).

The PCM model is represented by a large number of versions whose comparative analysis has been reported.³⁷ A recent version⁸⁰ makes it possible to carry out the calculation of solvation in liquid crystals and salt solutions. A simplified modification of the PCM is the Conductor-Like Screening Model (COSMO),⁸¹ which assumes that highly polar liquids such as water ($\epsilon_0 = 80$) can be regarded as conductors ($\epsilon_0 = \infty$). The corresponding equation for the charge surface density obtained in terms of this model is solved by the matrix method mentioned above. This scheme is considered to be attractive for calculating the solvation of large biomacromolecules.⁸²

To conclude the Section, let us turn back to the problem of applicability of the linear response theory to the description of solvation. The linear approximation is basic for the use of continuum models; its adequacy was verified by comparing the results of calculations in terms of these models with the results of MD or MC calculations.^{83–85} Comparison showed a substantial deviation of the response from linearity. The deviation is smaller for charged solvated molecules than for polar molecules; in addition, the non-linearity of the real response increases with a decrease in the solute charge. Before the publications,^{83–85} it was believed that non-linear effects should arise in strong electric fields (dielectric saturation). Calculations^{84, 85} revealed an absolutely different effect of purely molecular nature generated in weak fields. It was found that linearity of the dielectric response is violated due to solvent structuring in the near environment of the solute caused by short-range van der Waals interactions. As the strength of the external electric field increases, a 'phase transition' takes place and the linearity is restored. However, studies were carried out only for aqueous solutions, and it is unknown whether this effect is significant for non-aqueous systems.

Apparently, continuum models cannot provide a calculation accuracy above 80% for either free or potential energy, or for the electrostatic potential, irrespective of the way of parametrisation of the non-electrostatic contribution or the shape of the solute cavity. One more shortcoming of the continuum models is that they do not allow one to estimate temperature dependences of the energy of solvation or to study the change in the local structure of the solution near the solute. Nevertheless, due to the relative simplicity of the calculation of ΔG and the possibility of estimating the changes in the electronic structure of the solute, the continuum models appear rather attractive for applications, especially in the field of biochemistry and molecular biology.

IV. Method of integral equations

The MC or MD calculation of the correlation functions is associated with a great amount of computation. By using the CF formalism, it is possible to reduce the problem to a simpler investigation of Ornstein–Zernike type equations.^{23,86,87} These equations relate the atom–atom radial distribution function $g(r)$ to the ‘direct’ correlation function $c(r)$, which plays an important role in the statistical mechanics and determines the two-particle spatial correlations (medium density) caused by the interatomic potential $u(r)$ so that $c(r \rightarrow \infty) \rightarrow -\beta u(r)$. In the case of an infinitely dilute solution where a monoatomic solute in a monoatomic liquid is considered, the equation for the $h_{AB}(r) = g_{AB}(r) - 1$ (see [†]) is written in the form

$$\gamma_{AB}(R) = h_{AB}(R) - c_{AB}(R) = \rho \iint c_{AB}(r) h_{BB}(|r - R|) dr, \quad (19)$$

where ρ is the average solution density, $h_{BB}(r)$ is the full correlation function of the pure solvent. The integral equation (19) connects two functions, h and c , and, hence, it can be supplemented by the ‘closure’ condition. This condition can be obtained as the dependence of the function c_{AB} on the ‘bridge’ functional B

$$c_{AB} = \exp[-\beta u_{AB} + \gamma_{AB} + B(\gamma_{AB})] - \gamma_{AB} - 1.$$

No exact expression for the bridge functional has yet been found; however, a large number of approximate expressions have been obtained for simple liquids by the diagram expansion method;^{88,89} the applicability of such expressions is limited to the $u(r)$ type of interaction. For example, the hyperchain (HC) approximation (HCA) with $B[\gamma(r)] = 0$ is used for long-range interactions and $B[\gamma(r)] = \ln[1 + \gamma(r)] - \gamma(r)$ corresponds to the Percus–Yevick (PY) approximation, which is used for short-range potentials.

In the case of molecular solutions, unlike simple liquids, it is impossible to relate unambiguously the behaviour of the atom–atom potential to the type of closure; therefore, the closure conditions for the atom–atom functions are not rigorously deduced but are also expressed in the HC or PY approximation. This idea has been developed extensively in the Reference Interaction Site Model (RISM) theory,⁹⁰ in which the CF are related by the integral relations

$$\rho H_{AB}(R) = \sum_{CD} W_{AC}(r) C_{CD}(r - r_1) X_{DB}(|r_1 - R|) dr dr_1. \quad (20)$$

Here ρ is the average density of the solvent; H and C are matrices whose elements are the h_{AB} and c_{AB} functions for atoms of different types, respectively; C and D are additional subscripts for the solute and solvent atoms, respectively; W_{AC} is the ‘structural matrix’ composed of the solute correlation functions w_{AC} , and

$$X_{DB}(r) = W_{DB}(r) + \rho H_{DB}(r) \quad (21)$$

is the generalised susceptibility of the pure solvent. Here, matrices are introduced instead of three scalar integral equations for the solute–solute, solute–solvent and solvent–solvent correlation functions. The X_{DB} matrix can be calculated by the MC or MD methods or using integral equations. Like the structural matrix for the complex solute W_{AD} , this matrix specifies the input structural data for Eqn (20). As regards the mathematical statement, the equations of the RISM theory are similar to Eqn (19) and differ only by the presence of an additional weighting factor W caused by intramolecular bonds. The large number of discrepancies

[†] The function h is the full CF. From the standpoint of a mathematician, this function is more convenient, as $h(r \rightarrow \infty) \rightarrow 0$ and the integrals that include $h(r)$ are finite, while $g(r \rightarrow \infty) \rightarrow 1$. In addition to these CF, the ‘indirect’ CF is also used: $\gamma \equiv h - c$.

between the asymptotic estimates of various physical properties and the conclusions drawn in terms of the RISM models are due to the approximate character of this analogy.^{86,91} In particular, for polar liquids, the RISM model substantially underestimates the dielectric constant and, for example, for water, it does not predict adequately thermodynamic and structural properties.⁹² More rigorous approaches also exist;⁹³ however, these are seldom used to study solvation due to the complexity of numerical implementation.⁹⁴

As noted above, all the thermodynamic characteristics of solvation can be found in terms of the AACF. The form of the relevant relations depends on the type of closure. The simplest relations are obtained in the case of the HC approximation where the excess chemical potential μ in the limit of an infinitely dilute solution is determined from the equation⁹⁵

$$\beta\mu = \rho \sum_{AB} \int \left[\frac{1}{2} h_{AB}^2(r) - c_{AB}(r) - \frac{1}{2} \sum_{CD} \int c_{AC}(r) X_{CD}(|r_1 - R|) c_{DB}(r)(|r - r_1|) dr dr_1 \right] \quad (22)$$

By using standard thermodynamic relations, one can also calculate the energy E , the enthalpy H and the entropy Γ of solvation⁹⁶

$$\begin{aligned} E &= \left. \frac{\partial(\beta\mu)}{\partial\beta} \right|_{\rho}, \\ H &= \left. \frac{\partial(\beta\mu)}{\partial\beta} \right|_{\rho}, \\ \Gamma &= \frac{\mu - H}{T}. \end{aligned} \quad (23)$$

The subscripts $|\rho$ and $|\rho$ mean that the derivatives are calculated at a constant density and pressure, respectively.

The RISM equations with allowance for closure, like Eqn (19), are heterogeneous Fredholm integral equations of the second kind in the unknown function $\gamma_{AB}(r)$. The numerical investigation is done using iterative methods. First, some indirect correlation function $\gamma^{in}(r)$ is specified. Then the $c_{AB}(r)$ function is determined using the closure conditions. For the resulting function, the Fourier transform is found and used in the integral equation written in the k space for the calculation of the $\gamma_{AB}(k)$ function. The Fourier inversion is performed for the $\gamma^{out}(k)$ function found, and the process is repeated once again. The procedure of convergence can be accelerated by using various algorithms based on the Newton–Raphson method.^{97,98}

The integral equations can be analytically solved only for a very limited set of potentials and closures.⁹⁹ Despite the small number of such analytical solutions, they are useful for the modelling of structural and thermodynamic properties of solutions on the basis of simplified models. The most important example for polar liquids is represented by the Mean Spherical Approximation (MSA) in which the closure is described in the following form

$$\begin{aligned} h(r < d) &= -1, \\ c(r > d) &= -\beta u(r) \end{aligned} \quad (24)$$

where d is the diameter of the solid sphere.

With this closure, analytical solutions were obtained for solid spheres having an electric charge or a dipole moment.¹⁰⁰ The properties of the MSA allow one to obtain analytical expressions for the free energy of solvation and other thermodynamic values in ion–dipole systems.¹⁰¹ The model can be successfully used to study solvation in water–salt solutions.

In recent years, new calculation schemes have been developed (Three-Dimensional Interaction-Site Model, 3DRISM)^{102–108} in which the structure of the solvent near the solvated molecule is

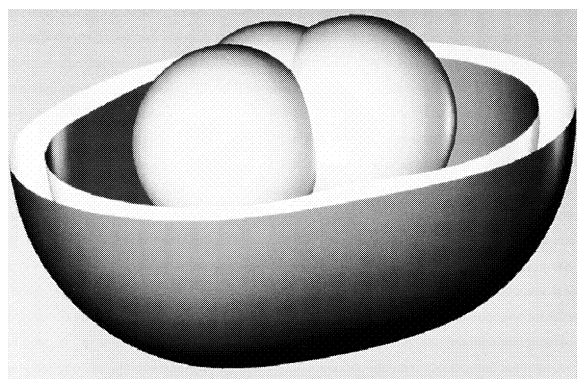


Figure 1. Isovalse surface of the propane–oxygen of the MACF $g(r) = 1.5$ around the propane molecule.¹⁰²

determined by the molecular–atomic correlation functions (MACF) $g_B(r)$. These functions characterise the probability that atom B of the solvent molecule is found at point r , which is specified in the system of coordinates related to the solvated molecule. Figure 1 shows the sectional view of the MACF $g(r)$ isovalse surface for the propane molecule in water.¹⁰² An equation similar to Eqn (20) can be written for MACF,

$$\rho h_B(r) = \sum_A \int c_B(r) X_{AB}(|r - R|) dR, \quad (25)$$

where $c_B(r)$ is the ‘direct’ molecular–atomic CF. For $c_B(r)$, the HCA closure is constructed to relate $c_B(r)$ to $g_B(r)$. In fact, this assumes the additivity of action of the solvated molecule on separate atoms of the solvent molecule. Although $X_{AB}(r)$ is a radial function, the interaction potentials $u_B(r, \Omega)$ and $c_B(r, \Omega)$ depend, in the general case, not only on the distances but also on the orientation Ω with respect to the solvated molecule. The relations involved in the 3DRISM model, unlike the integral equation (20), represent a set of three-dimensional integral equations. The algorithm for the solution of the 3DRISM equation is similar to that described above and differs only by the fact that it requires performing calculations on a three-dimensional network and using the three-dimensional Fourier transform in order to find $\gamma(k_x, k_y, k_z)$.

Yet another modification of the method of integral equations is the study of the molecular correlation functions (MCF) $g_{AB}(r, \Omega)$,^{109, 110} which depend on both the distance between the centres of the molecules and the relative angular orientation of molecules. A ‘molecular’ integral equation similar to Eqn (19) can be written for MCF

$$\begin{aligned} \gamma(r, \Omega) &= h(r, \Omega) - c(r, \Omega) = \\ &= \rho \int h(r - R, \Omega_1) c(R, \Omega - \Omega_1) dR d\Omega_1. \end{aligned} \quad (26)$$

With this type of notation, one can avoid the problems caused by the choice of closure, because the diagram expansion method is naturally extended to the MCF. However, this gives rise to new problems associated with the increase in the dimension of integration in Eqn (26), which leads to a pronounced increase in the number of network points in the numerical approximation of the function $\gamma(r, \Omega)$. As a consequence, it becomes virtually impossible to find an analytical solution to Eqn (26). One way of avoiding the integration by angles is to expand the orientation-dependent CF into a series in eigenfunctions of the rotation operator $D_{\mu\nu}^{mnl}(\Omega_1, \Omega_2, \Omega_R)$. The presence of a particular symmetry group for the solvent particles can reduce significantly the number of expansion terms. In some cases, rather fast convergence of the series ensures a good result even with a relatively small number of terms.¹⁰⁹ Comparison of these results with the results of MC

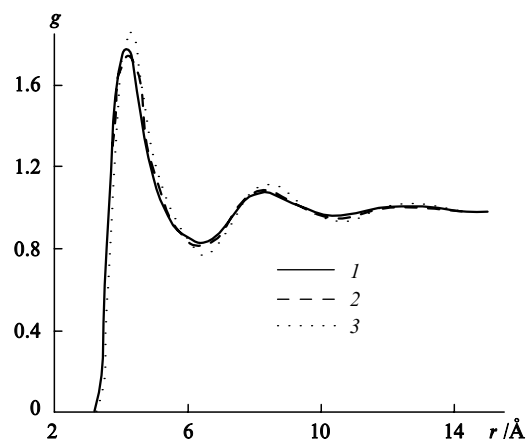


Figure 2. Carbon–methyl correlation functions for acetonitrile;¹⁰⁹ (1) solution of the molecular integral equations, (2) calculation using the RISM equations, (3) MC calculation.

calculations showed close agreement of the data for acetonitrile (Fig. 2). However, the scope of this approach is limited; it can be successfully used only for highly symmetrical solvated complexes.

The main difficulty involved in the use of the method of integral equations is the complexity of its numerical implementation on a computer. In each particular case, it requires designing of special subroutines for different types of closure, potentials, *etc.*; moreover, there is no assurance that the developed algorithm will ensure convergence of the iteration procedure. However, the method of integral equations has also a number of advantages over the MC and MD calculations. For equally complex systems, the amount of calculation is 2 to 3 orders of magnitude smaller in this method than in the two other methods. Since the correlations that are calculated are considered to decay rapidly with an increase in the distance between the particles, the method can be formulated for finite spatial areas. The method does not imply the choice of a periodic spatial cell during the modelling, and the results are not subject to the influence of the boundary conditions. Using modern versions of the method of integral equations, calculations of the solvation can be performed for macromolecules comprising up to 10^3 atoms. Owing to the possibility of re-normalisation of the sought-for correlation functions, this method is also applicable to systems that are difficult to treat in terms of the MC or MD calculations. Examples are systems that incorporate solutes of complex shape or with a large electric charge, electrolyte solutions with low ion strengths, *etc.*

V. Electrostatic interactions in the Monte Carlo and molecular dynamics methods

The complexity of MC and MD calculations of the solvation in polar liquids is due to the fact that calculations are carried out for some limited volume of space (a cell); this may be associated with substantial errors due to the long-range character of the Coulomb forces. The use of periodic boundary conditions requires ‘cutting off’ the Coulomb potentials (usually, at a distance about half of the cell size). This distortion of the potential has only a weak influence on the radial dependence of the CF; however, it can change significantly the behaviour of the orientation correlations. The characteristics of cutting off the Coulomb potentials have been studied rather long ago. The interest in this effect was enhanced after publication of the paper¹¹¹ in which it was shown that this procedure gives rise to a false pattern of interaction of hydrated iron ions. With the cut-off Coulomb potential, likely charged ions were attracted at long distances, whereas calculation by the Ewald method⁸⁵ correctly predicted the asymptotic behaviour of the ions.

The Ewald and reactive field calculations are currently the best methods for taking into account the electrostatic interactions in solvation systems.^{112–114} The Ewald method first developed for the calculation of Coulomb interactions in ion crystals¹¹⁵ is considered to be the most consistent in the calculation of electrostatic potentials. In its modification for periodic molecular systems, the electrostatic energy (U) is expressed through the periodic Ewald pair potential $\varphi(\mathbf{R})$ (see Ref. 85)

$$U = \sum_{I < J} \sum_{\alpha\beta} q_{I\alpha} q_{J\beta} \varphi(|\mathbf{R}_{I\alpha} - \mathbf{R}_{J\beta}|) + \sum_{IJ} \sum_{\alpha < \beta} q_{I\alpha} q_{J\beta} \left[\varphi(|\mathbf{R}_{I\alpha} - \mathbf{R}_{J\beta}|) - \frac{1}{|\mathbf{R}_{I\alpha} - \mathbf{R}_{J\beta}|} \right] + \sum_{I\alpha} \frac{q_{I\alpha}}{2} \lim_{R \rightarrow 0} \left[\varphi(\mathbf{R}) - \frac{1}{R} \right]. \quad (27)$$

The subscripts α and β designate different atoms in different molecules I, J (of the solute or the solvent). The first two terms in this equation correspond to inter- and intramolecular electrostatic contributions to U . The last sum (this term is also called self-action) is a correction, which is necessary because in the point charge limit, the Ewald potential does not reproduce accurately enough the Coulomb potential within an area of the finite size. The sum of partial charges $q_{I\alpha}$ of all atoms disappears for electrically neutral systems. In this case, the use of the Ewald potential is the most justified. For charged solute–solvent systems, the self-action term turns into a constant which can be estimated from the condition

$$\lim_{R \rightarrow 0} \left[\varphi(\mathbf{R}) - \frac{1}{R} \right] = \frac{\zeta}{L},$$

where ζ is a constant equal, for example, to ~ 2.837297 for a cubic cell, L is the linear size of the modelling cell. The appearance of the constant ζ dependent on the modelling conditions is a flaw of the Ewald calculations and the problem related to it is still debated.^{116–121} However, for many applications, it is sufficient to calculate the energy U to within this constant.

The Ewald potential $\varphi(\mathbf{R})$ itself can be written down as a sum of two rapidly converging series

$$\varphi(\mathbf{R}) = \sum_n \frac{\text{erfc}(\eta|\mathbf{R} - n\mathbf{L}|)}{|\mathbf{R} + n\mathbf{L}|} + \sum_k \frac{4\pi}{k^2 L^3} \exp\left[-\frac{k^2}{4\eta^2} + ik\mathbf{R}\right] - \frac{\pi}{L^3 \eta^2}, \quad (28)$$

where η is a shielding parameter which controls the convergence and the relative contributions of the series. However, formally, the Ewald potential does not depend on the selection of this parameter, *i.e.*,

$$\frac{\partial \varphi(\mathbf{R})}{\partial \eta} = 0,$$

while the cell-averaged value of this potential is also equal to zero

$$\int_{L^3} \varphi(\mathbf{R}) d\mathbf{R} = 0.$$

The difference between the Ewald potential and the reactive field potential (see below) is in the way the charge distribution which compensates the total charge of the solvation system is specified. In the case of the Ewald potential, this charge is uniformly distributed over the cell chosen for calculations, whereas in the reactive field method, it lies on a sphere with the radius R_c around the solvated ion under consideration. The calculations^{85, 116–118} showed that in practice, the Ewald potential approximates rather closely the electrostatic interaction.

In the reactive field method, the electrostatic interaction is approximated by using the potential^{112–114}

$$\varphi(R < R_c) = \frac{1}{R} - \frac{1}{R_c} + \frac{(2\epsilon_0 - 1)(R^2 - R_c^2)}{(2\epsilon_0 + 1)R_c^3}, \quad (29)$$

$$\varphi(R > R_c) = 0.$$

The cut-off (at $R > R_c$) Coulomb interaction is modified by adding a surface field borrowed from the continuum theory. Actually, $\varphi(R)$ is the solution of the Poisson equation for the point charge located at the centre of a spherical cell with the size R_c immersed in a dielectric medium with the permeability ϵ_0 and the compensating surface charge on the cell surface. This approximation is used in the MD simulation of an ensemble of solvent molecules surrounding the solute.^{21, 22} In the calculation of the medium response field, the problem of finding the solvation energy is reduced to a hybrid computation (MD/CM) in which some of the molecules of the liquid (inside the chosen cell) are calculated (in the explicit form) by the MD method, while other molecules (outside the cell) are calculated using continuum models. Detailed description of the calculation algorithms on the basis of this hybrid discrete and continuum approach has been reported.¹²² The researchers have found that this protocol allows one to calculate the electrostatic contributions to the free energy of solvation to an accuracy of several kilocalories per mole.

VI. Hydrophobic effects

Noble gases and hydrocarbons are typical examples of hydrophobic solutes. Their poor solubility in water is due to the entropy loss related to the entropy of hydration, which counterbalances or exceeds the benefit in enthalpy.¹²³ The main difference between the hydrophobic and hydrophilic solutes is the fact that the former have no charged or polar groups, which shows itself as the absence of electrostatic contributions to intermolecular potentials.

Study of the hydration of hydrophobic solutes is associated with two problems.¹²⁴ First, adequate simulation of hydrophobic effects requires detailed information on the microstructure and thermodynamic state of water. This information is used as the input data for calculating the hydration. Water has a number of abnormal properties compared to other polar liquids; therefore, in the simulation of hydrophobic solutes, the choice of the molecular model of water and the calculation of its properties should be carried out with special care. The microscopic models of water specially designed for this purpose allow one to calculate rather accurately the thermodynamic parameters of solvation for simple hydrophobic solutes.¹²⁵ Figure 3 shows the temperature dependences of the chemical potential (μ) and its enthalpy (h) and entropy (s) contributions for a methane molecule hydrated under atmospheric pressure. It can be seen that calculated and experimental data agree both qualitatively and quantitatively.

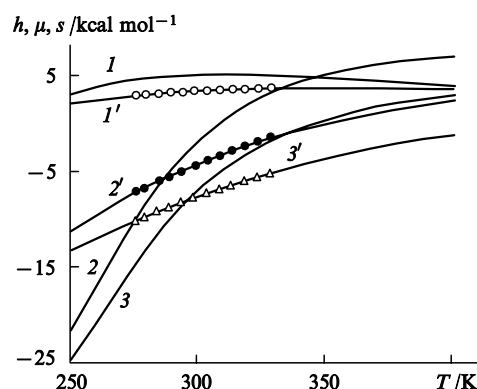


Figure 3. Temperature dependences of the chemical potential (I, I') and its enthalpy ($2, 2'$) and entropy ($3, 3'$) contributions for a methane molecule hydrated under atmospheric pressure; ($I-3$) calculation,¹²⁵ ($I'-3'$) experiment.¹²⁶

The second characteristic feature of hydrophobic solutes is related to geometric factors and excluded volume effects. Depending on the size of the solute, these effects can be manifested in different ways.¹²⁷ For small hydrophobic solutes (such as atoms of noble gases) at low concentrations, the packing effects are associated with reorganisation of water around the solute without rupture of a large number of hydrogen bonds. For mesoscopic hydrophobic solutes (for example, globular proteins), solvation can result in the cleavage of a large number of hydrogen bonds, giving rise to a nonwetting area near the hydrophobic surface of the solute where water occurs in the vapour state.

As an example, we shall consider a spherical model of the solute with a large radius R , which resides in the excluded volume cavity having the same radius. For macroscopically large cavities, Gibbs free energy of solvation is described by the expression^{128, 129}

$$\Delta G \sim \frac{4\pi R^3 p}{3} + 4\pi\sigma R^2, \quad (30)$$

where p and σ are the hydrostatic pressure and the liquid–vapour surface tension coefficient, respectively.

By parametrisation,^{130, 131} this relation can be extrapolated to microscopic cavities which arise upon solvation of molecular species. The first term in relation (30) becomes negligibly small at normal pressures, and the σ value remains the only significant parameter to determine ΔG . In early publications (see, for example, Ref. 128), this parameter has still been interpreted as macroscopic surface tension, although a consistent formulation¹²⁹ interprets σ as a model parameter dependent on the solvent and the cavity size and shape. This approach, called the scaled particle theory, was modified to be applied to non-spherical cavities.^{132, 133} The modern version is based on the density functional theory,¹²⁷ where the free energy of solvation is expressed in terms of generalised water susceptibility $X(r, r')$ [see Eqn (21)]. The free energy of cavity formation in the solvent is called the cavitation energy. It is mainly of the entropy nature. In the absence of electrostatic interactions, the total energy of solvation consists of the cavitation and van der Waals contributions. The latter contribution is due to short-range interactions (which are usually described using Lennard-Jones parametrisation) and is largely an enthalpy effect. The peculiarity of the situation is that the cavitation and van der Waals contributions have opposite signs (Fig. 4). The magnitude of each contribution grows with an increase in the size of the cavity¹³⁴ (often, they are regarded as being proportional to the surface area of the cavity¹³⁵), whereas the overall effect is small ($\sim 2-3$ kcal mol⁻¹) and barely depends on the size of the cavity (at least, for hydrocarbons with a number of carbon atoms ranging from 1 to 6).

Yet another molecular model of the hydrophobic effect is formulated on the basis of the Pratt and Chandler theory¹³⁶ in terms of the integral equation method. This theory reduces determination of ΔG to the calculation of the AACF. It is closely related to the most developed molecular model of hydrophobic solvation, based on the information theory^{124, 137} and is actually a cavitation effect model. With this approach, the free energy of solvation ΔG of a non-polar solid particle is determined in terms of the probability p_0 of formation of a cavity with the corresponding size and shape in the bulk of the liquid

$$\beta\Delta G = -\ln p_0. \quad (31)$$

The probability p_0 can be found by computer simulation^{138–150} or in terms of many-particle correlation functions.¹³⁰ The following simple procedure is also efficient.^{149–152} One should consider the probability distribution $\{p_n\}$ for which the case $n = 0$ corresponds to the probability of formation of an excluded volume cavity [see Eqn (31)]. The p_n values for $n \neq 0$ are interpreted as the probabilities that n solvent (water) molecules are situated in the cavity. The zero, first and second probability moments $\{p_n\}$

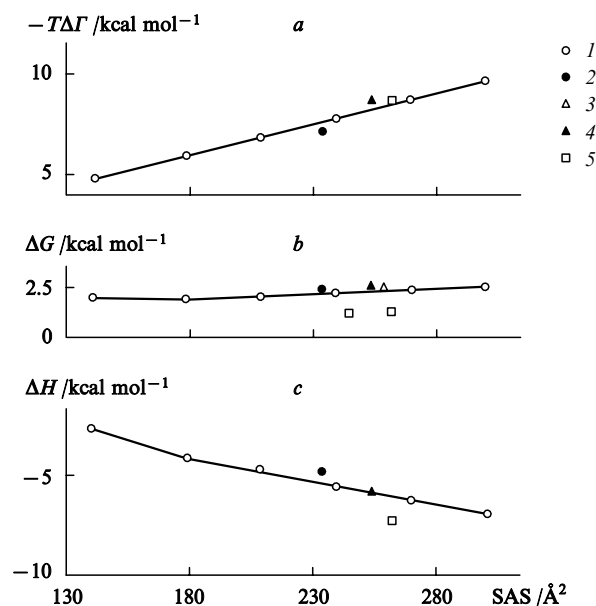


Figure 4. Experimental values of the entropy (a), free energy (b) and enthalpy (c) contributions to the hydration of isobutane (1), 2-methylbutane (2), neopentane (3), cyclopentane (4) and cyclohexane (5); the line shows the approximation of the discrete values by some dependence.¹³⁴

$$\langle 1 \rangle = \sum_n p_n,$$

$$\langle n \rangle = \sum_n n p_n,$$

$$\langle n^2 \rangle = \sum_n n^2 p_n,$$

respectively, can be expressed in terms of values that can be measured experimentally, namely, the density and the generalised susceptibility of water. The distribution $\{p_n\}$ is simulated in the form

$$p_n = p_{0n} \exp(\lambda_0 + \lambda_1 n + \lambda_2 n^2), \quad (32)$$

where p_{0n} is the simplest ‘primer’ distribution, $p_{0n}(n < n_{\max}) = \text{const}$ and $p_{0n}(n > n_{\max}) = 0$, where the maximum number of particles in the cavity $n_{\max}$ is the distribution parameter.¹⁴⁵ The additional parameters, $\lambda_0, \lambda_1, \lambda_2$, are found from the condition of reproducing the three first probability moments $\{p_n\}$, which are specified as noted above. Expression (32) corresponds to the maximum of informational entropy with additional constraints imposed on the moments.¹⁴⁹ By constructing the entropy functional in such a way that the zero, first and second probability moments corresponded to experimental data, Vener *et al.*¹²² have found an expression for the free energy of hydration of noble gas atoms

$$\beta\Delta G \approx \frac{\rho^2 v^2}{\delta n^2}, \quad (33)$$

where ρ is the density of solvent (water) particles, v is the volume of the excluded volume cavity, $\rho v = \langle n \rangle$ is the average number of solvent particles in the cavity, $\delta n^2 = \langle n^2 \rangle - \langle n \rangle^2$ is the variance of the number of particles in the cavity. According to this approximate relation, the temperature dependence of the cavitation energy is determined by two factors, namely, the dependences $\langle n \rangle(T)$ and $\delta n^2(T)$. Relation (33) was confirmed by computer simulation of small-sized solutes;¹²⁴ however, the result is deteriorated with an increase in the size of the excluded volume cavity,¹³⁴ apparently, due to the excessively simplified (‘planar’) form of the function p_{0n} , chosen according to Eqn (32). The MC-

and MD-based simulation shows that, generally, the theory described above reproduces qualitatively the hydrophobic effect but does not provide a quantitative estimate of the temperature dependence of cavitation free energy for solutes of an arbitrary size.

Direct MD and MC calculations of thermodynamic functions are complicated and cumbersome. There are several algorithms efficient for the calculation of free energy, namely, the Umbrella Sampling, Thermodynamic Perturbation, and Thermodynamic Integration methods.^{16, 139–141} The last two methods are used most often; they are useful for the calculation of cavitation effects.^{134, 146} They differ only in procedural points and give the required result after a sequence of consecutive standard MC or MD calculations.

Let us consider, as an example, the use of thermodynamic integration for determining the change $\Delta G = \Delta G_{XY}$ of the free energy of a solvation system

$$G = \beta^{-1} \langle \exp(-\beta U) \rangle$$

caused by its transition from the initial state X to the final state Y upon transfer of a solute particle from the gas phase to the solution. Here U is the potential energy of interactions between the solute and solvent particles and interactions of solvent particles with one another. This value is regarded as a function of the coordinates of solvent particles. Averaging $\langle \dots \rangle$ should be carried out over an equilibrium ensemble of solvent configurations in the presence (Y) and in the absence of the solute (X). To carry out this calculation, an additional parameter λ , equal to zero in the state X and equal to unity in the state Y , is introduced in the potential U . This parameter acquires discrete values $\lambda_i = 0, \lambda_1, \lambda_2, \dots, \lambda_i, \dots, 1$ in the segment $(0, 1)$. Thus the change in the free energy ΔG can be calculated as follows

$$\Delta G = -\frac{1}{\beta} \sum_i \ln \langle \exp\{-\beta[U(\lambda_{i+1}) - U(\lambda_i)]\} \rangle_{\lambda_i} = \int_0^1 \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{\lambda} d\lambda, \quad (34)$$

where $U(\lambda)$ is the potential considered as a function of λ . Analogous relations can be obtained for the enthalpy and entropy contributions to ΔG . The change in the entropy ΔS is determined by the formula

$$-\Delta S = \beta \int_0^1 \left[\left\langle U(\lambda) \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{\lambda} - \langle U(\lambda) \rangle_{\lambda} \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{\lambda} \right] d\lambda. \quad (35)$$

Thus, calculation of thermodynamic values includes a series of MC or MD computations with fixed λ_i followed by numerical integration according to Eqn (34) or (35). The values of the parameter λ can be varied not only by deterministic choice of the intermediate λ_i values but also in a stochastic way during the solution of MD equations^{153, 154} in which the variable λ is included as an additional degree of freedom.

The above-described thermodynamic integration method has been used to study the temperature dependence of the thermodynamic characteristics of the hydration of hydrocarbons.^{143, 144, 155} The functional dependence of the binding energy on the distance between the solute and solvent molecules has also been studied.^{156, 157} Computations performed by various researchers have now been reported^{134, 155, 158} where thermodynamic perturbation and thermodynamic integration procedures have been used for systematic study of the changes in the free energy, the enthalpy and the entropy upon hydration of lower alkanes containing one to six carbon atoms. The results of these calculations were compared with experimental results. However, it was found that the results of MC and MD computations can deviate from experimental thermodynamic data (Table 2), although generally they provide an adequate estimate of the relative changes in ΔG . For hydrophobic molecular solutes, the results of calculations can

Table 2. Experimental and calculated [by 3DRISM, XSOL (Extended Solvation), SMx, SCF and MC methods] values of free energy of hydration ΔG (kcal mol⁻¹) for various solutes.

Solute	Experiment (see ⁵⁴)	Calculation by the method				
		3DRISM (see ¹⁰⁴)	XSOL (see ¹⁵⁹)	SMx (see ¹⁶⁰)	SCF (see ⁵⁰)	MC (see ¹¹)
CH ₄	2.0	2.084	4.5	2.0	—	—
C ₂ H ₆	1.83	1.827	4.1	1.2	—	2.5
n-C ₃ H ₈	1.96	2.024	—	—	—	—
n-C ₄ H ₁₀	2.08	2.136	—	—	—	—
n-C ₅ H ₁₂	2.33	2.292	—	—	—	—
C ₆ H ₆	-0.8	—	-0.7	-1.0	-0.8	-2.9
C ₆ H ₅ CH ₃	-0.8	—	-1.7	-0.9	-0.8	—
CH ₃ OH	-5.1	-3.634	-4.0	-5.4	-5.2	-5.1
C ₂ H ₅ OH	-5.0	-3.375	-5.5	-4.9	-4.5	—
iso-C ₃ H ₇ OH	-4.8	-2.939	-4.0	-3.8	-4.4	—
C ₆ H ₅ OH	-6.6	—	-7.5	-6.6	-5.9	—
H ₂ O	-6.3	—	-7.7	-9.5	-7.3	—
CH ₃ OCH ₃	-1.9	—	-0.5	-2.4	—	-2.6
CH ₃ COCH ₃	-3.8	—	-1.7	-4.3	-4.5	-3.6
CH ₃ CO ₂ H	-6.7	—	-6.7	-6.5	-7.3	-7.7
CH ₃ CO ₂ CH ₃	-3.3	—	-4.1	-4.0	—	-4.6
CH ₃ CN	-3.9	—	0.8	-4.3	—	-5.0
CH ₃ NH ₂	-4.6	—	-4.4	-5.8	-4.3	-6.5
C ₂ H ₅ NH ₂	-4.5	—	-3.2	-4.7	-4.7	—
CH ₃ CONH ₂	-9.7	—	-7.2	-10.3	-11.0	-11.9
(Z)-NMA	-10.1	-6.236	-10.0	-7.8	-8.7	—
(E)-NMA	-10.1	-6.874	-10.4	-7.3	-9.0	—
C ₅ H ₅ N	-4.7	—	-4.5	-5.0	—	-5.1
4-MeC ₅ H ₄ N	-4.9	—	-4.8	-4.9	-5.1	—

be substantially improved by using the 3DRISM procedure and an additional empirical calibration of closure conditions.¹⁰⁴

To conclude the Section, we would like to note that, despite the many years of investigation of hydrophobic effects and the advances made due to the development of molecular models for the hydrophobicity phenomenon,^{124, 127, 129–136} the theory is still far from being completed because in the general case, hydrophobic behaviour is due not only to the type of interaction potentials or the solute geometry, but also to collective effects related to the entropy factor.¹⁶¹

VII. Solvation of ions

Solvation of ions is a trial for various molecular models, as it allows one to reveal the scope and drawbacks of one or another approach. The classical MC and MD models of solvation of monoatomic ions, as well as molecular solutes, make it possible to calculate the microstructure of the solvent around the ion; however, in the case of solvation energy, agreement with the experimental results is less satisfactory. Even accurate MD calculations based on the Ewald potential give deviations of up to 20% of the experimental values.¹⁶² Therefore, in recent years, calculations based on either hybrid and combined protocols (Table 3) or classical polarisation models have been actively carried out. In these procedures, the calculation of the solvation of monoatomic ions is a test routine for verification of the calculation scheme. The quantum corrections usually result in smoother AACF and smaller coordination numbers of the solvated ion (Fig. 5). Quantum calculations also give lower potential barriers for proton or electron transfer. This is clearly seen in relation to the hydrated proton (Fig. 6).

The spherical symmetry of monoatomic ions allows one to derive analytical expressions for the solvation energy within the bounds of different models of the medium. Comparison of these expressions clearly demonstrated the influence of the structure of

Table 3. Experimental and calculated thermodynamic characteristics of hydration (kcal mol^{-1}) of various ions.

Value	Method	Na ⁺	K ⁺	F ⁻	Cl ⁻	Ref.
ΔE	XRISM ^a	0.10	-0.60	2.17	-0.20	163
	experiment	0.25	-0.25	—	-0.27	164
$-\Delta G$	XRISM ^a	80.04	62.01	148.1	86.6	165
	XRISM ^a	77.3,	65.6	—	83.9,	96,
		84.0	—	—	81.9	108
	3DRISM	80.1	—	—	79.5	108
	MC	94.8	64.5	138	88.3	162
	SM5	—	—	106.9	77.3	161
	MD/CM	104.5	75.2	129.1	80.1	122
	QM/MM	—	—	109	81	163
	experiment	89.6,	72.7,	110	80.5,	166,
		96.4	78.9	—	73.9	167
$-E$	XRISM ^a	89.05	71.49	168.8	101.5	164
	XRISM ^a	88.8,	75.8	—	101.1,	96,
		93.7	—	—	96.7	108
	3DRISM	90.2	—	—	93.5	108
$-H$	XRISM ^a	94.1,	75.0	—	105.7,	96,
		93.6	—	—	94.1	108
	3DRISM	95.6	—	—	98.9	108
	experiment	99.9,	80.3,	—	88.2,	166,
		106.6	86.6	—	81.8	167

^a Extended Reference Interaction Site Model.

the solvent on the solvation effects. Let us consider particular examples of the calculation of free energy of solvation of an ion with the charge Q in a spherical cavity with the radius a .

According to Born,⁴ the medium around the cavity is characterised by an invariable dielectric constant, ϵ_0 , while the free energy of solvation is determined by the following relation:

$$\Delta G = -\frac{Q^2}{2a} \left(1 - \frac{1}{\epsilon_0} \right). \quad (36)$$

In this equation, the cavity radius a should be considered as some effective value. Direct use of crystallographic ionic radii gives unsatisfactory results. It has been shown¹⁷⁰ that for ions

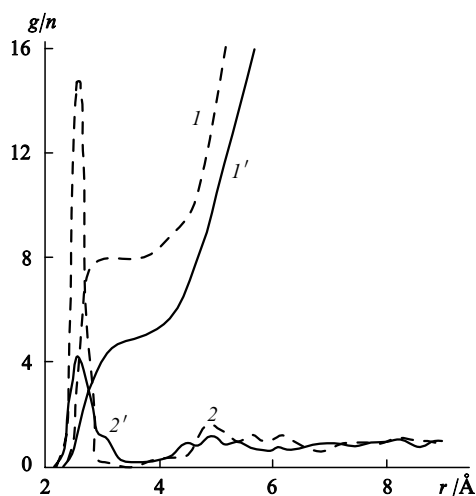


Figure 5. Dependences of the atom-atom (Na-Na) correlation function $g(I, I')$ and the coordination number $n(2, 2')$ on the distance between the centres of the sodium ions solvated in ammonia.¹⁶⁸ The dashed line corresponds to the classical MD calculation and the continuous line shows the QM/MM calculation.

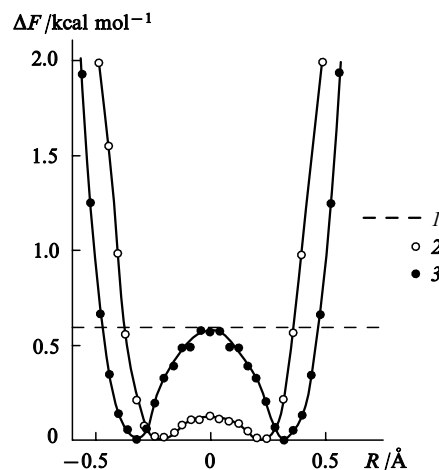


Figure 6. Free energy ΔF of the hydrated proton vs. its coordinate R relative to the midpoint of the O-O bond.¹⁶⁹ (1) energy at 300 K, (2) QM calculation, (3) MD calculation.

with a rather large size, relation (22) is converted into the Born formula with $a = r_{\text{max}}$, where r_{max} is the distance from the ion centre to the first maximum of the radial distribution function $g(r)$. The difference between the values of free energy of hydration of spherical ions found using the Born approximation and by direct solution of the RISM equations for Cl^+ and Cl^- ions is less than 12%.¹⁶⁰ By applying various corrections to formula (36), one can attain a satisfactory agreement between the calculation data and experimental results for a large number of monoatomic ions.^{50, 160, 171} The situation regarding the separation of the enthalpy ΔH and entropy $T\Delta S$ contributions to the Gibbs free energy

$$\Delta G = \Delta H - T\Delta S. \quad (37)$$

is less successful.

Even in complex calculations of the solvation effects, the use of experimental data on the temperature and pressure dependences of the dielectric constant $\epsilon_0(T, P)$ makes it possible to reach quantitative agreement with experimental thermodynamic data (see Table 3).

Direct MD and MC calculations for the free energies of solvation of polyatomic ions with non-spherical shapes have been reported.^{12, 172, 173} Successful implementation of these calculations requires that thorough parametrisation of the Lennard-Jones interaction between atoms of the solute and solvent particles be carried out. Apparently, the dependence of this parametrisation on the partial electric charge on atoms of the ionic solute should also be carried out.¹⁷⁴ However, the problem of selection of appropriate parameters is appreciably complicated by great scatter of experimental data obtained by different researchers for ionic systems.

For qualitative understanding of the solvation effects at the molecular level, it is expedient to continue with the discussion of the solvation models of spherical ions. In doing this, one can see that explicit allowance made for the molecular structure of the solvent changes the theoretical views on the free energy of solvation.

Figure 7 shows the scheme of the concentric two-sphere model of solvation.¹⁷⁵⁻¹⁷⁷ Inside a cavity with the radius a_1 , the dielectric constant is equal to unity, while in the outer region, outside the sphere with the radius a_2 , the dielectric constant is determined by the solvent and is equal to ϵ_0 . The intermediate space between the inner and outer boundaries contains a layer with ϵ_∞ (the optical dielectric constant). For this model, the free energy of solvation is equal to

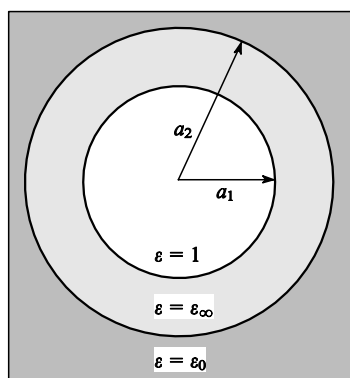


Figure 7. Scheme of the two-sphere model of solvation.

$$\Delta G = -\frac{Q^2}{2} \left[\left(1 - \frac{1}{\varepsilon_\infty} \right) \frac{1}{a_1} + C \frac{1}{a_2} \right], \quad (38)$$

where C is the Pekar factor,

$$C = \frac{1}{\varepsilon_\infty} - \frac{1}{\varepsilon_0}. \quad (39)$$

In the non-local extension of the Born model, the dielectric constant is specified by the function $\varepsilon(k)$. In this case, the following approximate relation holds:^{24–29}

$$\Delta G = -\frac{Q^2}{\pi} \int_0^\infty dk \frac{\sin^2 ka}{k^2 a^2} \left[1 - \frac{1}{\varepsilon(k)} \right], \quad (40)$$

while for the simple Lorentzian model of the dielectric function $\chi(\mathbf{k})$ [see Eqn (10)] with $\chi_0 = (1 - \varepsilon_\infty^{-1})/4\pi$, the following exact expression has been derived:³¹

$$\Delta G = -\frac{Q^2}{2} \left(1 - \frac{1}{\varepsilon_\infty} \right) - \frac{CQ^2}{2} \frac{1 + \sqrt{\varepsilon_0/\varepsilon_\infty} [\coth(a/\zeta) - \zeta/a]}{1 + \sqrt{\varepsilon_0/\varepsilon_\infty} [\coth(a/\zeta) - \zeta/a] + \sqrt{\varepsilon_\infty/\varepsilon_0} (\zeta/a)}. \quad (41)$$

In the MSA theory, according to which the solvent molecules are modelled as hard spheres with dipole moment m , the free energy of solvation is given by^{101, 178}

$$\Delta G = -\left(1 - \frac{1}{\varepsilon_0} \right) \frac{Q^2}{2a + \zeta}, \quad (42)$$

where a is the effective radius of the solute, ζ is the correction to radius a , which depends on the temperature and is expressed in terms of m or ε_0 as the solution of the non-linear Wertheim equation.¹⁷⁹

Relations (38)–(42) clearly demonstrate the influence of the solvent structure. In particular, in the last three models, the expression for the free energy of solvation is reduced to the Born formula (36) in the limit where the characteristic size of the solvent particles (the correlation length in the non-local models or the radius ζ in the MSA model) is much smaller than the radius of the solvated ion. The opposite limit is also of certain interest. Detailed discussion of these asymptotic expressions and their comparison with experiment have been reported^{176, 177, 180, 181} and supplemented by qualitative interpretation on the basis of molecular modelling.^{182, 183}

The solvation of polyatomic ions is also studied on the basis of integral equations using the RISM method. The calculations based on the molecular integral equations (25) are laborious and it was not until recently that they started to be actively used to study the solvation of polyatomic ions.¹⁸⁴ Note that even for an infinitely dilute solution, the standard RISM model should be modified for well-posed allowance for the dielectric shielding effects, because it results in a false estimate of the dielectric constant of the solvent. To eliminate this drawback, in the XRISM model,¹⁸⁵ it is proposed to renormalise the Coulomb interaction of ions in solution assuming that

$$u_c(r_{AB}) = \frac{Aq_A q_B}{r_{AB}}.$$

Here, the constant A is selected in such a way as to provide finally the required dielectric constant ε_0 . In practice, the constant A is determined from experimental data. Usually, it differs little from unity (for water, $A \simeq 0.98$), and this modification of the Coulomb potentials has only a slight influence on the thermodynamic parameters of the liquid. The XRISM calculations of the hydration of various ions provide qualitative agreement between the theory and experiment (see Table 3). Generally, these calculations give reliable information concerning various structural characteristics of hydrated ions. The activation energy ΔE for transfer of a water molecule from the region near the ion to the region of pure solvent has been calculated.¹⁶³ These data are consistent with experiment.¹⁶⁴

In the case of finite concentrations of solvated ions, the standard RISM and XRISM models lead to incorrect results, because the approximation of the linear response of the system to the external field created by a solvated molecule is violated. At low concentrations of ions, the plasma parameter

$$\zeta = \frac{l_B}{r_D}$$

[$l_B = e^2/(ek_B T)$ is the Bjerrum length, r_D is the Debye radius] is small and the linear response approximation is plausible. However, at high concentrations of solvated ions, the plasma parameter is no longer small (for NaCl concentrations of about 0.05 mol litre⁻¹ in water, $\zeta \simeq 0.5$). Hence, the ion-induced potential does not follow a linear dependence on the ion concentration and cannot be taken into account by mere renormalisation of the Coulomb interaction. For this case, the DRISM (Dielectric RISM) model has been developed;¹⁸⁶ in this model, the dielectric constant is included in the closure equation as the initial data. The calculations carried out using this model make it possible to estimate rather adequately the free energy and the salting-out coefficients for various concentrated salts.¹⁸⁷ It is noteworthy that DRISM calculations are needed in those cases where microscopic changes in the interaction of ions with a solvated macromolecule give rise to conformational rearrangements in the molecule, which involve rather large space.

In recent years, attempts have been made to use the 3DRISM models^{104, 107} or the method of molecular integral equations¹⁸⁸ to take into account the effect of the orientational correlations on the solvent structure near a polyatomic ion. Figure 8 shows the local structure of water around the Na⁺–Na⁺ ion pair calculated in terms of the 3DRISM model.¹⁸⁹ The deviation of the results obtained on the basis of this model from the results of MC and MD calculations is insignificant. Apparently, more accurate calculations could be carried out with appropriate calibration of the interaction potentials. Yet another promising route is to take into account the changes in the electronic structure of solvated ions caused by interaction with the solvent.

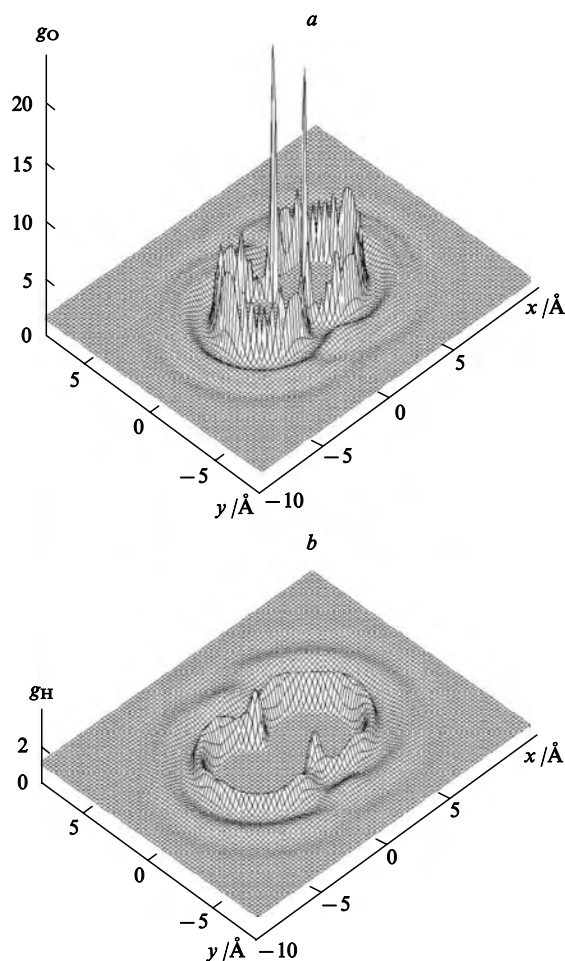


Figure 8. Molecule-atom ion-oxygen (a) and ion-hydrogen (b) correlation functions for the $\text{Na}^+ - \text{Na}^+$ pair in water.¹⁸⁹ The x, y, z coordinates of the sodium ions are $\pm 2.05, 0$ and 0 , respectively.

VIII. Polar molecules

The calculations of solvation for polar molecules are carried out in the same way as for ions. In the case of polar solutes, the effects of cutting-off the Coulomb interactions are usually neglected on the ground that the resultant electric field decays rather rapidly for these systems, *i.e.*, its potential

$$\varphi(R \rightarrow \infty) \propto R^{-n}, \quad n \geq 3,$$

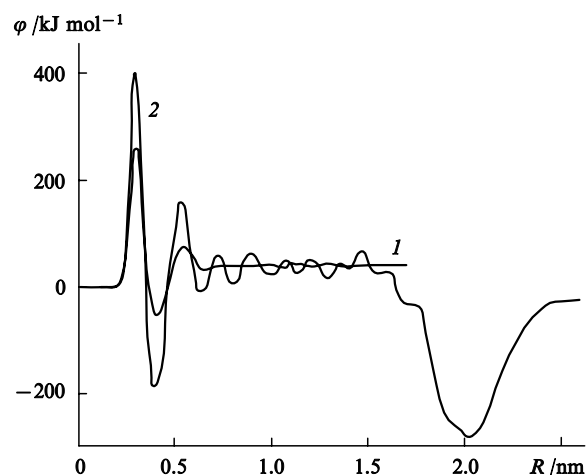


Figure 9. Electrostatic potential φ near the polar solute in water.⁸⁵ (1) calculation by the Ewald method, (2) calculation for the cluster of 1024 water molecules by the standard MD method.

and the errors caused by the cutting-off effects are insignificant. However, accurate calculations for polarisable solutes¹⁹⁰ have shown that the way of cutting-off the potential $\varphi(R)$ still influences, although to a lesser extent, the induced charge of the solvent molecule and, hence, the calculated thermodynamic and structural properties of the system. Figure 9 shows the electrostatic potential around a polar solute in water.⁸⁵

The modern trends in such studies take into account the many-particle interactions caused by the solute-induced polarisation of the solvent and turn to polarisable models of polar liquids (see, for example, Refs 191–193). These models (unlike non-polarisable ones) permit well-posed simulation of various processes in biological systems: electron transfer, solvatochromic changes of the electronic and vibronic spectra, *etc.* The results of computation of various characteristics of water in terms of polarisable and non-polarisable models of the solute and those found experimentally are summarised in Table 4. Richardi *et al.*¹⁸⁸ carried out computations within the framework of the same molecular model of water but on the basis of different methods. It can be seen that approximation (29) simulates rather closely statistic and dynamic characteristics of liquid water; the calculation of pressure is faced with difficulties because this value is determined by the balance of repulsion and attraction forces between molecules and is sensitive to the way of cutting-off the Coulomb potentials.

Currently, the most reliable estimates of the free energy of solvation of polar molecules are based on continuum models. Comparison of the theoretical and experimental data has shown

Table 4. Calculated and experimental values for the internal energy (U), pressure (P), dipole moment of the molecule (m), self-diffusion coefficient (D), relaxation time in the NMR method (τ_{NMR}), density (ρ) and dielectric constants ($\epsilon_0, \epsilon_\infty$) of water.

$U/\text{kcal mol}^{-1}$	P/kbar	m/D	$10^{-9} D/\text{m}^2 \text{s}^{-1}$	$\tau_{\text{NMR}}/\text{ns}$	$\rho/\text{g cm}^{-3}$	ϵ_0	ϵ_∞	Ref.
Calculation methods								
−9.86	0.02	2.62	2.0 ± 0.03	2.2	—	—	—	190 ^a
−10.21	−0.7	2.66	1.5 ± 0.01	2.8	—	—	—	190 ^b
−9.92	−2.9	2.62	1.8 ± 0.03	2.1	—	—	—	190 ^c
−9.92	—	2.712	1.81 ± 0.06	2.6	0.997	98 ± 8	1.689	193
−9.89	—	2.6	1.9 ± 0.1	2.1	1.014	79 ± 8	1.592	194
−9.87	—	2.29	2.62 ± 0.04	1.4	0.999	82 ± 2	1.0	195
−10.40	—	3.01	—	—	1.02	—	—	196
Experiment								
−9.92	—	—	2.3	2.1	0.997	78.3	1.79	197–201

^a Calculation in terms of the Ewald method. ^b Calculation using the cut-off Coulomb potential. ^c Calculation using the reactive field method.

that the difference between these values does not exceed 20%. This result is attained due to thorough parametrisation of models. However, at present, the continuum approaches tend to be upgraded, the modern phase in the modelling of solvation being characterised by active use of hybrid schemes. These schemes may include QM/MM computations²⁰² or the calculations in which some of the water molecules are explicitly taken into account, while other water molecules are taken into account in terms of a continuum approach.²⁰³ The results point to a higher efficiency of hybrid procedures compared to the conventional procedures of the continuum theory (see Table 2). For instance, calculations of the solvation of the $\text{Cl}^+ \cdots \text{Cl}^-$ complex based on a hybrid MD/CM model made it possible to estimate the electrostatic contribution to the free energy of solvation to within 1 kcal mol⁻¹ (see Ref. 122).

General equation (34) of the thermodynamic integration method can be regarded as an estimate for the change in the free energy related to the transition of the solvation system from one state to another; this change is described by the parameter λ . The selection of λ is rather free. It can be described as a multidimensional vector whose components correspond to different contributions to the free energy of the system. With this interpretation, thermodynamic integration is widely used for estimating the role of Coulomb contributions to the free energy of solvation (see, for example, Refs 83, 85). It can also be applied for estimating the changes in the free energy caused by quantum effects. For example, this procedure has been used²⁰⁴ to assess the quantum corrections to ΔG_s relying on the data of classical modelling as the initial conditions.

The method of integral equations also allows one to calculate the structural characteristics of solvation of polar molecules; however, the accuracy of the results obtained using the standard integral equations described above is much lower than in the MC or MD computations. This drawback is partially compensated by the relative ease of calculation of the solvation of large biomacromolecules. Thus for a fixed double helix conformation, RISM computations of hydration of a DNA fragment composed of 315 atoms²⁰⁵ and a mellitin molecule containing 436 atoms have been carried out.²⁰⁶ A calbindin molecule containing 722 atoms has been considered in a similar way.²⁰⁷ In the general case, the conformation of a biomacromolecule can be found by a self-consistent procedure based on hybrid calculations of the IMCF by the MC method and numerical solution of the RISM equations.^{208–211} At present, such calculations are carried out for peptides containing ~ 20 to 200 atoms. Figure 10 shows one of the conformations found for the hydrated C-peptide of ribonuclease A.²¹¹

Yet another version of hybrid calculations are those done for solvated molecules in which the electronic structure of the solute is calculated by quantum chemistry techniques, while the spatial

structure of the solvent is determined by the method of integral equations.^{212–220} Table 2 shows the results of calculations of ΔG_s on the basis of SCF–RISM computations (XSOL).¹⁵⁹ In this case, as in MC calculations, only qualitative agreement with experimental data is attained. As noted above, this is due to an ill-posed allowance made for the molecular orientations in the standard RISM procedure. Apparently, the results could be markedly improved by using the 3DRISM model or by solving the molecular integral equations. The conduction of such hybrid calculations has started only recently.^{217,218}

IX. Solvated quantum particles

In a study of solvation of a light quantum particle, an excess electron is considered most often. The interest in this type of studies is caused by two factors. First, such a quantum-and-classical hybrid system is convenient for demonstrating the potential of various hybrid schemes. Second, development of experimental procedures and the large amount of accumulated data on the behaviour of solvated electron (e_s) in various media²²¹ resulted in considering e_s as a unique test particle for testing the solution microstructure.

Early investigations of the solvated electron were based on the continuum approach;²²² it was assumed that e_s exists in a cavity surrounded by a dielectric medium with the constant ϵ . With this definition, the problem was reduced to the solution of the Schrödinger equation in the self-consistent field V_{ef} for the single-electron wave function $\phi(r)$. An alternative approach is to calculate the e_s characteristics on the basis of methods of the MC^{223–226} or MD quantum model (QMD).^{227–233} The application of these methods is based on the fact that the problem of the behaviour of a quantum particle in a liquid can be reduced to the equivalent problem of calculation of a classical polymer chain.²³⁴ A large number of calculations for the solvated electron in water,²²⁷ ammonia²²³ and metal–ammonia solutions²³⁵ have been reported. The results obtained are in good agreement with one another and correspond to experimental estimates. The modern studies also include SCF calculations, which take into account the discrete description of the solvent based on the method of integral equations.^{236–239} Detailed discussion of the application of these approaches has been reported;^{237,240} we will give only a brief outline of the calculation scheme. The interaction of the electron with molecules of the liquid results in redistribution of the solvent molecules, which is found from the electron–atom correlation functions $h_{\text{es}}(\mathbf{r})$ by solving integral equations²⁴¹

$$\rho h_{\text{es}}(\mathbf{R}) = \sum_j \int \int \omega_e(\mathbf{r}) c_{ej}(|\mathbf{r} - \mathbf{r}'|) \chi_{sj}(|\mathbf{r}' - \mathbf{R}|) d\mathbf{r} d\mathbf{r}', \quad (43)$$

where $\omega_e(\mathbf{r})$ is the electronic CF, which is a quantum analogue of the IMCF; $c_{ej}(\mathbf{r})$ is the direct electron–atom CF, $\chi_{sj}(\mathbf{r})$ is the generalised susceptibility of the pure solvent. The electron correlation function $\omega_e(\mathbf{r})$ is related to the electron wave function as²³⁷

$$\omega_e(\mathbf{r}) \simeq \phi^2(\mathbf{r})$$

and can be calculated by the variation method^{241,242} or by solving the Schrödinger equation with the potential V_{ef} .²³⁷ These studies of the hydrated electron (e_h) provide estimates for the energy and structural characteristics,^{241,242} which are in good agreement with experimental data: the calculated chemical potential e_h (see Ref. 241) differs from the experimental one²⁴³ by only 1%.

Yet another interesting example of the solvation of quantum particles is study of the bipolaron — two excess electrons that form a bound state — a ‘quasi-molecule’. Apparently, Feng *et al.*²⁴⁴ were the first to investigate this problem in detail for a number of liquids on the basis of the continuum approach. The numerical investigations by the MC method for water²⁴⁵ and for metal–ammonia solutions²³⁵ have shown that the bipolaron states are stable in water and in metal–ammonia solutions at a metal concentration of < 1%. As the concentration increases, the

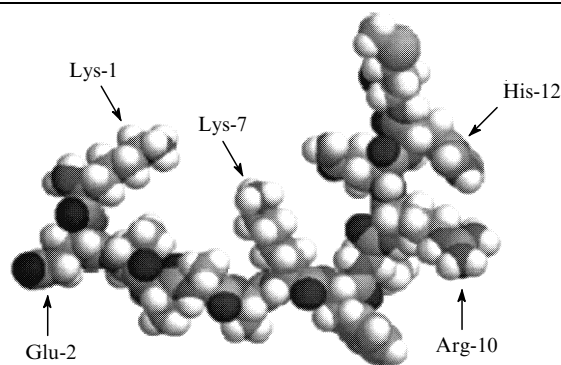


Figure 10. The most favourable conformation of C-peptide in aqueous solution.²¹¹

The arrows mark amino acids.

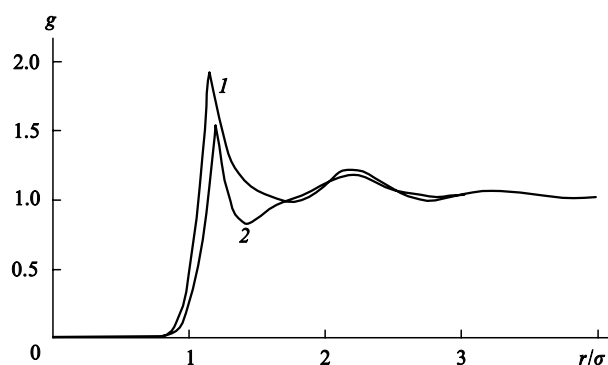
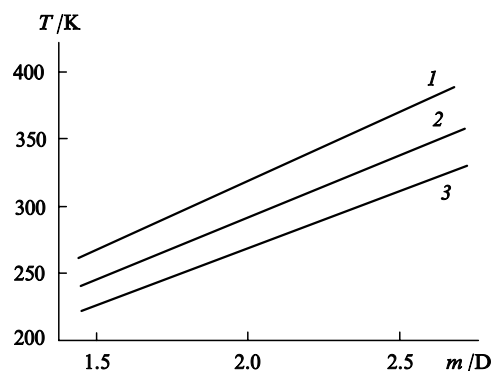
Table 5. Kinetic (E_k), potential (E_p) and total (E_t) energies, chemical potential (μ) and average radius (r_e) of the hydrated electron and bipolaron calculated by various methods.

Method	E_k /eV	E_p /eV	E_t /eV	μ /eV	r_e /Å	Ref.
Electron						
QMD	2.2	−5.0	−2.8	−2.2	2.1	227
QMD	1.8	−3.6	−1.8	—	2.4	236
MSA	1.33	−5.57	−4.24	−1.13	2.5	238
MSA	1.8	−3.6	−1.8	—	2.2	236
RISM	1.84	−6.08	−4.26	−0.96	2.9	242
Bipolaron						
QMD	4.05	−16.4	−7.71	−1.57	2.6	245
(H ₂ O) ₂₅₆						
MSA	2.34	−10.62	−9.67	−2.27	2.7	238

triplet state of the bipolaron decays, which is observed experimentally as a sharp decrease in the magnetic susceptibility.²⁴⁶ On further increase in the metal concentration, bipolarons are clustered and the electrons become delocalised.^{235, 247}

Both solvated electrons and bipolarons were studied using a hybrid approach which included the calculation of the electron structure by the density functional method and the solvent structure by the method of integral equations.²³⁸ Table 5 presents the main energy parameters of the hydrated electron and bipolaron calculated by various methods, while Fig. 11 presents the electron–solvent correlation functions $g(r, \theta = 0)$ for a singlet bipolaron and an electron solvated in a model polar liquid consisting of hard spheres. Qualitative analysis has shown²⁴⁸ that in the general case, the free energy functional includes various factors. The entropy contribution involved in the excluded volume cavity around the solute decreases the average radius of the bipolaron and favours an increase in its bond energy. The contribution caused by dielectric shielding produces an opposite effect. The competition of two contributions determines the stability condition for the bipolaron. The electron–electron correlations also result in an increase in the entropy factor due to the effects related to the formation of an ‘exchange-correlation hole’ and finally promote an increase in the bond energy. The calculations showed that bipolaron singlet states are stable in most polar liquids under normal conditions (Fig. 12).

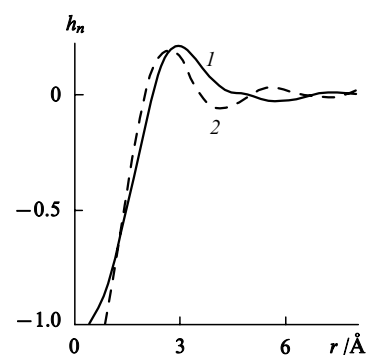
The simplest example of a solvated quantum particle is positronium (Ps). This neutral quasi-atom consists of an electron and a positron. Like atomic hydrogen, positronium has two spin states separated in energy, namely, a singlet state (parapositro-

**Figure 11.** Electron–solvent correlation function $g(r, \theta = 0)$ in the spherical coordinates for an electron (1) and a singlet bipolaron (2) solvated in a polar liquid as solid spheres with the radius $\sigma = 3.15$ Å and the dipole moment $m = 1.6$ D with the value $\rho\sigma^3 = 0.9$ (ρ is the average density of the solvent) at $T = 233$ K.²³⁸**Figure 12.** Diagram of bipolaron decomposition into single solvated electrons.²³⁸

Bipolarons are stable in the regions below the lines and decompose with temperature rise.

$\rho_0\sigma^3$: 0.8 (1), 0.9 (2), 1.0 (3).

nium) and a triplet state (orthopositronium). The interest in the study of this quasi-particle is related to the fact that, due to its electroneutrality, this particle can serve as a ‘probe’ for determining the character of molecular surfaces, the orientation of molecules in the liquid, and so on. Most often, continuum models are employed in the calculations of positronium. For example, a model taking into account the molecular structure of only the first coordination sphere of Ps has been considered.^{249, 250} Monte Carlo calculations for positronium solutions²⁵¹ and for distribution of the Ps density in water have also been carried out.²⁵² A hybrid scheme for the calculation of hydrated positronium including self-consistent DFT computations of the distribution of the Ps density and the calculation of water microstructure by the method of integral equations has been developed.²⁵³ The obtained results are consistent with experimental data. Figure 13 shows the Ps–H and Ps–O atom–atom correlation functions calculated for normal conditions. The form of these functions is typical of neutral solutes; however, in the case of positronium, they are smoother than in the case of neutral atoms. The procedure similar to that described in the study cited²⁵³ is fairly versatile and can be used for solving a broad range of problems related to the study of solvated positronium.

**Figure 13.** Correlation functions Ps–H (1) and Ps–O (2) for the positronium hydrated at room temperature.²⁵³

X. Tautomeric and conformational equilibria

The main goal of most molecular models of solvation is to study the conformational, tautomeric and other transformations of the solutes and to elucidate the conditions of formation of their dimers or other complexes. The scope of application of molecular models is very broad; therefore, without going into details, we

would only note characteristic features of the computation protocols involved.

Examples of application of the molecular models of solvation were given in the review.⁴⁰ This list is not exhaustive but continuum approaches clearly predominate. They are included in most packages of quantum-chemical programs and are most important in the study of binding of various ligands to the solute and in the studies related to the problem of 'recognition' in biomacromolecular reactions.^{254, 255}

In the case of continuum methods, several preferable schemes can be distinguished. Comparison of the calculations of the conformations of various peptides has shown²⁵⁶ that the GBSA model and the continuum calculations based on the solution of the Poisson – Boltzmann equation are best suited for the modelling of conformations. The corresponding estimates of the energy of conformational transitions give an error not exceeding 1–2 kcal mol^{−1} (see Ref. 256). The continuum models with distance-dependent $\epsilon(r)$ are less suitable for these purposes. The accuracy of calculations in terms of the GBSA model depends appreciably on the approximation of the cavity.⁴⁰ The calculations in which the whole region occupied by the solute is approximated as a single spherical or ellipsoidal cavity produce unrealistic results.

At present, various hybrid methods are used in which the electronic structure of the solute is calculated without taking into account the medium, then charge distribution on the solute is determined and, finally, the local structure of the solvent for the resulting charge distribution is calculated in terms of the MD or MC procedures.²⁵⁷ Unlike the continuum approaches, these calculations allow, in principle, not only estimation of the energy of conformational transitions and stability of the conformers but also determination of the enthalpy and entropy contributions to ΔG and the temperature dependence of the conformational transitions. They also provide the possibility of determining the accuracy of the classical molecular models. Comparison of the calculations using classical and hybrid models has shown, in particular, that the former give unsatisfactory results in the study of solvation of transition metal ions and polarisation of the solute molecule, while the latter produce more realistic results.²⁵⁸

In recent years, studies have been reported (see, for example, Refs 212–214) in which solvation was calculated in terms of a hybrid self-consistent procedure where the electronic structure of a conformer or a tautomer was calculated by quantum-chemical methods and the solvent microstructure was calculated by solving integral equations. These RISM – SCF models allow one to study chemical reactions in molecular liquids. The calculations were carried out for solute isomerisation in water^{213, 220} and tautomerisation in acetylacetone.²¹⁹ The absolute values of the solvation parameters determined on the basis of integral equations do not always correspond to experimental data; however, such estimates

are rather efficient for predicting thermodynamic and structural characteristics of the solvated complexes in various reactions (Table 6). In general, they are markedly more accurate than continuum models and almost as accurate as hybrid methods.

XI. Electronic spectra and solvatochromic shifts

The most detailed simulation of electronic spectra was carried out for the solvated electron. The absorption spectra of the solvated electron in ammonia,²²⁴ methanol,²⁵⁹ water²²⁵ and heavy water²³² were calculated. The resulting dependences of the absorption maximum and the peak width on the temperature and solvent density are in quantitative agreement with experimental results. The isotope effects²³² and the dynamics of variation of the spectrum²⁶⁰ have been studied in terms of nonadiabatic²⁵⁹ and adiabatic²²⁴ MD calculations. Simulation of the spectra of the solvated electron by the method of integral equations has been reported. These calculations also reproduce adequately the influence of temperature and ion concentration on the pattern of the absorption spectrum.²⁶¹ Figure 14 shows the calculated and experimental values for the shift of the absorption maximum of the hydrated electron in aqueous solutions of LiCl, MgCl₂ and LiClO₄.

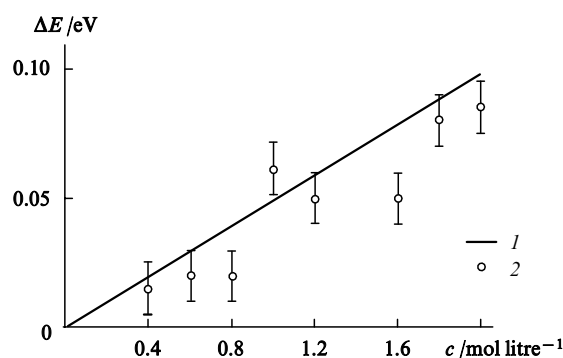


Figure 14. Shift of the maximum in the absorption spectrum of the hydrated electron in water – salt solutions depending on the salt concentration;

(1) calculation,²⁶¹ (2) experiment.²⁶²

Study of the solvatochromic shifts occupies an important place, especially in organic chemistry. There exists a correlation between the solvatochromic shift and the rates of chemical reactions in polar solvents.^{1, 263} The possibility of constructing polarity scales and using chromophores as probes for determining the relative polarity of the solvent has long been discussed.¹ The data obtained in this way provide much more detailed knowledge of the intermolecular potentials than conventional dielectric measurements, as solvatochromic shifts are sensitive to both electrostatic and short-range interactions.

We will briefly discuss some features of calculation of these shifts using betaine-30 as an example. The simplest approach used is based on the mean-spherical approximation,²⁶⁴ according to which the solvatochromic shift (ν_s) and the free energy of solvation (ΔG) are related as follows

$$\nu_s = \Delta G \frac{m_e(m_g - m_e)}{a^3}, \quad (44)$$

where m_e and m_g are the dipole moments of the solute in the ground and excited states, respectively. The free energy of solvation depends, in turn, on the size of the solute a and the dielectric constant of the liquid

$$\Delta G = f(\epsilon, a),$$

Table 6. Thermodynamic characteristics (kcal mol^{−1}) of some reactions for solute molecules.

Reaction	Solvent	ΔG	ΔH	$T\Delta G$	Ref.
Tautomerisation of acetylacetone	H ₂ O	−1.37 (−0.98)	−6.05 (2.7 ± 0.3)	−4.6 (3.7)	219
	DMSO	0.14 (0.29)	0.55 (1.8 ± 0.2)	0.41 (1.5)	219
	CCl ₄	0.11 (1.74)	1.02 (2.5 ± 0.3)	0.91 (0.8)	219
	pyridine	−3.9 (−4.6 ± 0.8)	—	—	159
Anomerisation	H ₂ O	−3.23	−4.20	−0.96	213

Note. The values in parentheses are experimental results.

the calculation of the function $f(\epsilon, a)$ according to the MSA method presents no difficulty.²⁶⁵ Using this approximation and relation (44), the solvatochromic shifts of betaine-30 in 110 solvents were found;²⁶⁴ the average deviation of the calculated values from experimental ones did not exceed 10%. It should be emphasised that two important points were taken into account, namely, the change in the dipole moment of the solute upon optical excitation and the predominant role of electrostatic interactions between the solute and the solvent.

It was shown using simple estimates²⁶⁶ that the contributions of the dispersion and induction interactions are also significant for the calculation of solvatochromic shifts. However, the results of calculation for betaine-30²⁶⁷ where these interactions were taken into account indicate that electrostatic interactions play crucial role in the appearance of this shift, which is mainly determined by the change in the dipole moment of the solute. The simplest approximation that assumes proportionality between the solvatochromic shift and the dipole moment²⁶⁷ leads to satisfactory results consistent with experimental data, although it is less accurate than hybrid calculations (Table 7). Shoeib *et al.*¹⁷² have attempted to include additionally the contribution of the electron polarisation of the solute by means of an appropriate renormalisation of the free energy of solvation. However, comparison of the data obtained by Chong and Hirata¹⁶³ with the results of hybrid calculations²⁶⁷ has shown that for this method, the role of electron polarisation is overestimated. According to calculations,²⁶⁷ the contribution of the electron polarisation to the solvatochromic shift does not exceed 5%.

Table 7. Solvatochromic shift (cm^{-1}) for betaine-30 in various solvents according to experimental data²⁶⁸ and calculations by various methods.^{172, 267}

Solvent	Experiment	Calculation by		Calculation by Eqn (44)
		INDO ^a	RISM	
Carbon tetrachloride	—	410	31	170
Chloroform	—	920	570	850
Acetone	1490	2730	—	1170
Acetonitrile	1160	4260	790	1510
Ethanol	2170	3070	—	2110
Methanol	2140	3570	2930	2510

^a Semiempirical quantum-chemical calculation.

In some publications, the solvatochromic shifts have been studied in terms of hybrid models.^{269–271} Detailed self-consistent calculations²⁷¹ demonstrated that accounting of the solvent can be restricted to the first coordination sphere of the solute (Fig. 15).

Finally, we will consider the dynamics of Stokes shifts. Continuum models are successfully used to study the dynamics of solvation phenomena; the complex dielectric constant $\epsilon(\omega)$ is used in these cases as a dynamic characteristic. Simple models^{272–274} have used the Debye parametrisation

$$\epsilon(\omega) = \epsilon_{\infty} + \frac{\epsilon_0 - \epsilon_{\infty}}{1 - i\tau_D\omega},$$

where ϵ_0 and ϵ_{∞} are the static and optical dielectric constants of the solvent, τ_D is the Debye relaxation time for the spherical approximation of the shape of the solute. There are different ways of modernisation of the Born model: more complex multimode parametrisation of the dielectric function, allowance made for the non-spherical shape of the solute molecule, account taken of the non-local electrostatic effects (as noted above, the last-mentioned point allows one to include the molecular structure of the solvent in the calculation scheme). The influence of the solute shape on the dynamics of Stokes shifts was first studied for the ellipsoidal cavities around the solute molecule^{275, 276} and then for cavities

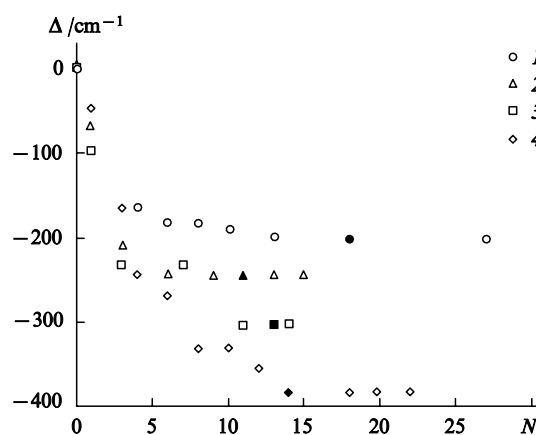


Figure 15. Calculated solvatochromic shift (Δ) vs. the number of solvent molecules (N) included in the quantum-chemical calculation.²⁷¹ (1) H_2O , (2) cyclo- C_6H_{12} , (3) C_6H_6 , (4) CCl_4 ; the dark dots show the data for the first coordination sphere of the solute.

having an arbitrary shape.^{277, 278} The molecular structure of the solvent was studied within the framework of the MSA method^{279–281} and by other methods,^{282, 283} and also using non-local models.²⁸⁴ However, in all of these calculations, the solute was assumed to be spherical. Early studies were mainly concerned with the asymptotic behaviour of the temporal correlation functions and the possibility of determining these functions from experimental data using the Stokes shift.^{272, 273, 276, 282, 283} The calculation could be improved if the data on the behaviour of the dielectric function in the region of medium and high frequencies, especially in the far infrared range, were available.^{275, 278, 285} An upgraded continuum model has been used to perform a systematic study²⁸⁶ of the influence of various factors on the dynamics of the Stokes shifts. In particular, the influence of the solute shape was studied in terms of single- and two-sphere models of the cavity surrounding the solute;¹⁷⁷ the intermediate spherical layer simulated the first coordination sphere of the solute. Yet another factor affecting the Stokes shift is related to the non-local effect.^{31, 33} The simpler models of the cavity predict simple monoexponential kinetics of the shift for Debye solvents where a single relaxation mode of the medium is considered.^{273, 274} This drawback is eliminated by taking into account either non-sphericity of the cavity^{275, 276–278} or the multimode relaxation of the medium. In the latter case, the kinetics²⁸⁶ is polyexponential and the results of calculations based on the local approach depend only slightly on the shape of the cavity. These calculations adequately reproduce the experimental data in the case where detailed information on the change in the dielectric constant is used as the input information.^{275, 278, 286}

A more complex situation arises when the MSA model and the non-local theories are used. Even for Debye solvents and spherical solutes, the calculations lead to polyexponential kinetics.^{279–281, 286} The local and non-local models produce different results. In non-local models, the oscillations of the correlation functions in the $0.1 \text{ ps} < t < 1 \text{ ns}$ range are smoother than in local approaches. These oscillations, which are not typical of the changes in the Stokes shifts observed experimentally, arise in all local models irrespective of the approximation of the solute shape. Another important difference is related to the asymptotic behaviour of the correlation functions. Non-local models yield much longer relaxation times than local models.²⁸⁶

XII. Electron transfer

Electron transfer plays a key role in many chemical and biological processes,²⁸⁷ and study of the electron transfer occupies an important place among applications of the molecular models of

solvation. The most important characteristic of this process is the rate constant for transfer K_{et} . In the Frank–Condon approximation in which the matrix element of the electron transition V_{et} does not depend on the nuclear coordinates, the constant can be found from the following equation:^{287–289}

$$K_{\text{et}} = V_{\text{et}}^2 \sqrt{\frac{\pi\beta}{E_{\text{r}}}} \exp\left[-\frac{\beta(\Delta F^\circ + E_{\text{r}})^2}{4E_{\text{r}}}\right], \quad (45)$$

where E_{r} is the reorganisation energy, ΔF° is the free energy of the reaction. The reorganisation energy is composed of the inner-sphere (*i.e.*, related to the internal degrees of freedom of the solute) and the outer-sphere (*i.e.*, related to the rearrangement of the solvent structure) components. In the continuum approach for spherically symmetrical charge distributions on the donor and the acceptor, outer-sphere reorganisation energy is often found from the equation²⁸⁷

$$E_{\text{r}} = C\Delta q^2 \left(\frac{1}{2a_{\text{A}}} + \frac{1}{2a_{\text{D}}} - \frac{1}{R_{\text{DA}}} \right), \quad (46)$$

where C is the Pekar factor, Δq is the charge being transferred, a_{D} and a_{A} are the effective radii for the donor and the acceptor, and R_{DA} is the distance of transfer. There exist numerous procedures for extending expressions (45) and (46) that take into account the real shape of the solute, quantum effects, deviations from the Frank–Condon approximation, and so on.²⁹⁰ In particular, for the intramolecular transfer of an electron, the influence of high-frequency quantum modes of the solute is commonly taken into account in an explicit form.^{291–298} However, in this case, too, the reorganisation energy E_{r} and the matrix element V_{et} still remain the key characteristics of the electron transfer. The problem is to elucidate the dependence of these values on the molecular and thermodynamic parameters of the surrounding medium. Here we discuss only aspects of the electron transfer concerned with its simulation on the basis of microscopic models and upgraded continuum theories.

Some effects cannot, in principle, be taken into account within the bounds of the continuum electrostatic models of the medium. These include, for example, the temperature dependence of the reorganisation energy. It can be included in a standard continuum calculation only through the temperature dependence of the dielectric constant of the solvent. However, this type of modelling is inefficient: the reorganisation energy really decreases with temperature rise,²⁹³ whereas the theoretical estimate based on the data on the dielectric constant predicts an increase in this energy. The error of calculation is due to neglect of the temperature dependence of the size of the cavity occupied by the solute. The size and the shape of the cavity are fixed in the continuum calculation and only transition to the molecular description of the solvent provides the possibility of reproducing the desired effect.

The continuum theory (in the local electrostatic variant) also cannot explain the presence of a noticeable outer-sphere reorganisation energy in non-polar solvents (benzene, dioxane, *etc.*), whose molecules are devoid of a permanent dipole moment. In these media, $\varepsilon_\infty = \varepsilon_0$ and the Pekar factor C is equal to zero, while the reorganisation energies found experimentally are equal to 0.1–0.2 eV.²⁹³

The simplest way of correcting the continuum calculations is to use the mean-spherical approximation for the solute model as hard spheres with an electric charge (on the solute) or a dipole moment (for solvent molecules). This approximation allows one not only to calculate the reorganisation energy but also to estimate correctly its temperature dependence (Table 8); however, its use is restricted by the assumption concerning the spherical shape of the solute inherent in the MSA theory. This version of the MSA model has also been used^{296,297} to study the reorganisation energy for the same solute (approximated by a sphere) in a series of solvents with different polarity including non-polar solvents.^{296,297} An alternative way of upgrading the continuum theory²⁹⁸ is to detail

Table 8. Calculated and experimental temperature characteristics of the free energy of solvation (ΔG) and reorganisation energy (E_{r}) for (tetrahydro-4H-thiopyran-4-ylidene)propanedinitrile dissolved in acetonitrile.²⁹³

Model	$a/\text{\AA}$	$\Delta G/\text{eV}$	$\frac{T\partial E_{\text{r}}}{\partial T}/\text{eV}$	$\frac{T\partial \Delta G}{\partial T}/\text{eV}$
Continuum	4.52	4.64	0.03	0.10
MSA	4.50	4.39	−0.19	0.37
Experiment	—	—	−0.23	0.32

the dielectric model of the medium. The solute is assumed to be surrounded by two cavities with different dielectric constants, namely, high-frequency and static ones (see Fig. 7). The cavities are constructed in the same way as in the PCM method. The modernised model explicitly takes into account the electronic structure and the real shape of the solute and implicitly, the molecular structure of the solvent in terms of the parameters of the cavity, *i.e.*, the dielectric constants and the atom radii r_∞ and r_{in}

$$r_\infty = kr_{\text{vdW}}, \quad (47)$$

$$r_{\text{in}} = \delta + r_\infty,$$

where k is a universal scale factor, r_{vdW} is the van der Waals radius, and δ depends on the particular solvent. This model can be used to calculate the reorganisation energy and the matrix element of transfer if these values depend little on the details of molecular structure around the solute. The optimal k and δ values are found by comparing the theoretical and experimental values for the free energy of solvation of small polyatomic ions.²⁹⁸ The k and δ values obtained in this way were used to calculate the reorganisation energies for many reactions of intramolecular electron transfer in steroid compounds.²⁹⁹ The results of calculations are consistent with experimental data,²⁹¹ which cannot be reproduced in the single-cavity model.^{300–302} However, like other continuum theories, this method cannot describe the temperature dependence of the reorganisation energy.

The method of integral equations also allows one to take into account, in an explicit form, the discrete pattern of charge distribution on the solvent molecules. The reorganisation energy E_{r} was calculated, in terms of the RISM theory,¹⁷² for betaine-30 solvated in various polar liquids. The results of calculations¹⁷² are in qualitative agreement with experimental data. Yet another line in the research into electron transfer related to the effect of the molecular structure of the solvent on the reorganisation energy is represented by studies performed by MD calculations.^{303–306} These works dealt with calculations of the diabatic surfaces of free energy, whose intersection area determines the transfer rate. In the macroscopic Marcus theory,³⁰⁷ the potential surfaces of the reactants and products are parabolic. The MD calculations³⁰⁵ have shown that the free energy surfaces found are close to parabolic surfaces, but under certain conditions, the reaction system behaviour can markedly deviate from the predictions of the Marcus theory [see Eqns (45) and (46)]. The deviations are great in the case of polarisation of neutral solutes,^{308–310} *i.e.*, in charge separation processes. They have also been observed for charged asymmetrical systems with different structures of the donor and acceptor centres.³¹¹ The deviations are assumed to be due to two compensative factors, namely, electrostriction and dielectric saturation, both being dependent on the charge of the reactants.³¹² The MD calculations of the reorganisation energy have now been carried out for several simplified model systems of electron transfer^{311–316} and for complex systems that mimic the electron transfer in proteins.^{317,318} Compared with routine MD calculations, these calculations require accurate handling of Coulomb interactions (see Section V) and taking into account electron polarisation. The latter is usually simulated by renorm-

alisation of the reorganisation energy by changing the Pekar factor C .³¹⁷

The calculation of the matrix element V_{et} requires thorough quantum-chemical calculations.^{292, 319} The result is sensitive to the choice of the initial and final diabatic electronic states between which the transition takes place. It is recommended to localise these states by the generalised Mulliken–Hush method according to which they are determined by diagonalisation of the matrix of the dipole moment of the electron transition.^{290, 320} An alternative method invariant with respect to the choice of the basis states has also been formulated.²⁹⁹ For complex biochemical objects, direct quantum-chemical calculation of the matrix elements V_{et} is impossible; therefore, it was proposed to estimate this matrix element by calculating the quasi-classical tunnelling flow of probability.^{321–324}

The number of works dealing with the effect of the solvent on the matrix element V_{et} is relatively low (see the review²⁹²). These calculations are based on upgraded continuum models²⁹⁹ or molecular schemes,³¹⁷ which allow one to determine the contribution of the effect of the molecular structure of the solute (conformation and effective radius) on the V_{et} value. This is exemplified in Table 9, which presents the results of calculation of characteristics of the electron transfer for a number of model $(\text{CH}_2)_n^-$ anions. The results confirm the tendency of V_{et} for exponential decrease following an increase in the distance R_{DA} between the donor and the acceptor, which has been discussed in the literature.²⁹⁰

Table 9. Calculated characteristics of electron transfer for a number of model $(\text{CH}_2)_n^-$ anions with the linear structure.²⁹⁹

n	E_{r}/eV	$\Delta F/\text{eV}$	$10^3 V_{\text{et}}/\text{eV}$	$R_{\text{DA}}/\text{\AA}$
4	0.86	0.035	257.0	3.80
6	1.37	0.28	61.9	6.26
8	1.70	0.41	14.7	8.74
10	1.92	0.48	3.77	11.23

XIII. Conclusion

The examples considered above of the use of molecular models for the study of solvation in polar liquids permit one to estimate qualitatively and, in some cases, even quantitatively the influence of the solvent on the change in the structural and thermodynamic properties of solvated particles and to study the physicochemical processes that accompany solvation. In essence, the molecular approach is meant to take into account two factors. The first one is mainly of entropic origin and is related to the excluded volume effect and the packing of molecules in the nearest environment of the solute particles. It is a consequence of the finite size of these particles. The second factor is due to the finite size of the solvent particles that interact with the solute. Both factors were ignored in the early solvation theories. In the modern continuum theories, the former factor is consistently taken into account, in particular, the size and shape of the solute are considered explicitly by specifying an excluded volume cavity in the continuum medium. This description is valid in the asymptotic limit

$$\frac{\text{size of the solvent particles}}{\text{size of the solute particles}} \ll 1$$

The theories that are commonly called molecular are beyond the scope of this restriction.

In the simplest molecular models of solvation, the solute and solvent particles are considered to be spherical, with point charges or dipoles at the centre of the sphere. At this level of description, it is usually possible to obtain analytical expressions or semianalytic

algorithms for the calculation of the response field, the solvation energy and other values. Abandoning of the spherical approximation, which is absolutely necessary for calculating real systems, inevitably converts the model physical theory into a cumbersome computation procedure. The computations are least cumbersome in the continuum approximation, whereas the use of ‘truly’ molecular calculations (MC or MD) increases the computational burden by a factor of 10^3 or more. The calculations of the correlation functions by the method of integral equations occupy an intermediate position, as regards laboriousness, in the series of modern computational methods of the solvation theory.

It is noteworthy that the structure of the medium can be ignored if the difference between the solute and solvent particles is much greater than the size of solvent particles. In this case, one can use hybrid schemes, which smoothly ‘sew together’ the continuum and molecular modes of the description of solvation effects and thus reduce the computational burden without substantial decrease in the reliability of the results obtained.

It is shown using particular examples that molecular models can be efficiently utilised to study various solvation systems ranging from salt solutions to dissolved biomacromolecules. The possibility of developing hybrid schemes in order to take into account changes in the conformation and the electronic structure of molecules in the solvent extends the scope of application of molecular models. The prospects of nanotechnology are associated with the study of a large number of complex liquids, which are characterised by high microheterogeneity and diverse supramolecular architecture which arises on the mesoscopic scale.³²⁵ The molecular models can serve as peculiar probes in the study of these mesoscopic structures, and new interesting results may be expected in this field.

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Supramolecular assemblies in eutectic alloys

V S Pervov, I D Mikheikin, E V Makhonina, V D Butskii

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Abstract. The main concepts of the theory of eutectics are analysed. The most essential results of investigations on eutectic alloys of inorganic compounds are surveyed. Evidence in favour of the supramolecular concept of eutectics is presented. This concept takes into account interactions of incommensurate substructures and gives an insight into the mechanisms of formation of supramolecular eutectic assemblies in boundary regions ('non-autonomous phases'). Using the static one-dimensional Frenkel–Kontorova model for finite systems, it is shown that the consideration of these mechanisms in terms of supramolecular chemistry simplifies analysis of the behaviour of inorganic eutectic systems in the course of crystallisation under conditions both close to and far from equilibrium, including crystallization upon quenching and under external actions. The supramolecular concept bridges gaps between the definitions 'compound', 'eutectic' and 'solution' in physicochemical analysis. The bibliography includes 83 references.

I. Main concepts and state-of-the-art in the theory of eutectics

Theoretical views of the nature of eutectic alloys were formed more than 80 years ago. Since then these views have gained wide acceptance. However, authors of a number of papers and monographs (see, for examples, Refs 1 and 2) stated their justified belief that the theory of eutectics is inconsistent with up-to-date knowledge. Thus, this theory fails to explain the fact that eutectics have low melting points, leaves unexplained the mechanism of the initial step of melting and gives no clear answer to the question as to why a 'mixture' of crystals of two compounds is molten and crystallises at the same temperature.² A sharp increase in the mutual solubility of components as the eutectic temperature passes through the liquidus line is inconsistent with the known

data that melting leads to only small changes in interatomic distances (melting of many metals and salts is even accompanied by a decrease in interatomic distances³).

Numerous studies of eutectics can be divided into three main groups. The first group involves data on the structures and morphology of eutectics (including attempts to classify eutectics). The second group includes theoretical studies of possible mechanisms of solidification of eutectic materials of different types. Results of recent studies of interphase and intergrain boundaries and structures of melts belong to the third group. Micromorphological structural features of eutectic composites ('eutectic grains' or 'colonies'^{4–6}) were most extensively studied in the 1920s–1980s.

Different classifications of eutectic structures were proposed. These classifications were presented in many reviews (see, for example, Refs 1, 4 and 5). However, attempts to combine these classifications into a single system failed because all known reviews were based on phenomenological data, which, generally, ignore many important factors, such as the chemical nature and structures of individual compounds, the degree of their chemical interaction, temperature and concentration parameters, conditions of crystallisation and cooling. That is why much recent attention has been focussed on investigations of particular objects. Nevertheless, early studies revealed certain general formal tendencies. For instance, it was demonstrated⁴ that crystal nucleation of eutectic phases occurs separately in organic systems solidified at relatively small supercooling: '...both crystals grow as though these processes were independent and crystal growth proceeds until the liquid completely disappears'.⁴ The so-called 'rough conglomerate of phases' is thus formed. In the second mode of growth typical of inorganic systems, nuclei appear at the contact interface of both phases. In the latter case, the basic phase gives rise to a coupled growth of colonies on a bicrystalline base. Taran¹ believed that this idea carries 'the germ of correct understanding' of the whole process of formation of a eutectic colony, *e.g.*, the colony is a product of crystal formation occurring in contact, *i.e.*, of cocrystallisation of two eutectic phases.

The best known classifications are those proposed by Brady,⁷ Portevin,⁸ Scheil⁹ and Hant and Jackson.¹⁰ Scheil's classification has gained wide acceptance. In this classification, the author attempted to take into account both morphological features and the assumed differences in the mechanism of crystallisation of eutectic alloys. All structures are classified into three groups, *viz.*, normal, degenerate (or separated) and anomalous. All eutectics characterised by the ordered arrangement of phases, *viz.*, lamellar, rod and globular, are assigned to normal structures. These eutectics have a colony structure, and individual colonies can

V S Pervov, I D Mikheikin Moscow State University of Engineering Ecology, St. Basmanaya ul. 21/4, 105066 Moscow, Russian Federation. Fax (7-095) 261 49 61. Tel. (7-095) 267 19 47.

E-mail: pervov@igic.ras.ru (V S Pervov)

Tel. (7-095) 267 19 60 (I D Mikheikin)

E V Makhonina, V D Butskii N S Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation. Fax (7-095) 952 20 62.

Tel. (7-095) 952 20 62. E-mail: evma@igic.ras.ru (E V Makhonina)

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always be separated by boundaries. The order appears due to the coupled growth of phases. The eutectic class depends on the rate of cooling. Very slow cooling can lead to 'degeneration of coupled growth', and eutectic phases crystallise separately to form degenerate (or separated) structures. Finally, there are systems in which coupled growth cannot take place at all (anomalous eutectics).⁹

In recent years, the terminology proposed by Brady⁷ has found ever-increasing application to the description of the eutectic morphology. Brady took the surface tension of components as the main classification criterion and classified eutectics as globular (both components have high but different surface tensions), lamellar (both components have high and approximately equal surface tensions), polygonal (one of the components has a substantially higher surface tension than another component) and crystalline (both components have low surface tensions). In the discussion of the morphology and structures of eutectic alloys, let us cite the conclusions made by Taran¹ after detailed analysis of the available classifications and abundant factual data. These conclusions concern not only the structures of eutectic colonies but also the mechanisms of their formation for interacting systems.

1. A colony can occur as a finely crystalline mixture of two phases (*i.e.*, a 'mechanical mixture of phases').

2. A colony can consist of a matrix built from the basic phase and inclusions of numerous crystallites of another phase. The basic phase is characterised by high entropy of melting and, correspondingly, by high surface tension at the interface with the melt. The development of a colony is accompanied by coupled growth of dispersed crystals and the matrix.

3. A colony contains two intergrown branched crystals of eutectic phases. The centre of the colony is the site of primary contact between the nucleated crystals. The formation of colonies occurs through their coupled growth.

As mentioned above, the structural features of crystallised eutectic alloys depend on the conditions of crystallisation of the system. The classical theory of crystallisation is based on studies by Gibbs and Volmer,^{11–13} who introduced the notion of metastable systems and constructed the apparatus of thermodynamics of phase interfaces. This theory is beyond the scope of the present review because it has been outlined in numerous handbooks and monographs. Let us only note that the Gibbs–Volmer theory does not allow one to predict the structures of crystallised multi-component alloys and determine the morphology of co-crystallised phases. This theory did not find application in the theory of eutectics, although the consideration of a eutectic alloy as a mechanical mixture of phases and the views of the separate crystal growth of each phase are seemingly consistent with the model implied in this theory. In our opinion, the reason is that the real crystallisation conditions very rarely satisfy the requirements of the thermodynamic model.

Presently, the less known concept of the phase field is used in many studies (including those devoted to the mechanisms of crystallisation of eutectic alloys). This concept has been proposed approximately simultaneously with the classical Gibbs–Volmer theory of phase interfaces. The phase-field approach is based on the assumption that a liquid–solid interface is determined as a gradual change in extensive quantities (continuous continuum^{14,15}).

For the solid and liquid phases in the system to be distinguished at any instant, the so-called order parameters describing the 'phase field' are introduced. The concept of the phase field was developed for modelling processes of solidification of two-component systems. According to these models, the free energy of the system depends on the temperature, phase field and concentrations of all components (*i.e.*, on the phase diagram). Computer simulations of solidification of eutectic alloys with different morphology (dendrite,¹⁶ lamellar,^{17–21} *etc.*^{18,21}) demonstrated that the theoretical model is in satisfactory agreement with experimental data. The drawbacks of the cited studies are the cursory consideration of the morphology and lack of information

on the structures of interphase boundaries. Besides, this model provides no clear explanation as to why the melting point of a eutectic is equal to its solidification temperature and it does not include parameters allowing for the description of distinctive specific properties of eutectic composites.

Obviously, the theories of phase interfaces and phase field, which include thermodynamic potentials as the initial parameters, can be used only if the system under consideration is close to thermodynamic equilibrium. Taking into account that an alloy can occur under conditions far from equilibrium (quenching), physical schemes were developed, which relate the morphological features of an alloy to diffusion processes. Considerations are carried out within the framework of stationary and non-stationary problems of diffusion. According to Chalmers and Weingard (Fig. 1),^{22,23} the appearance of periodic structures of eutectics (lamellar or rod) is determined by distances between the phase interface OA and two solid–liquid interfaces OB and OC in the vicinity of the point O. The width of lamellae depends on the rate of their growth and the influence of two opposite tendencies. One of these tendencies consists in the fact that the thicker is the lamella OB, the larger is the distance for which the structural components of the phase OC, which diffuse in the cross direction, should be moved and, correspondingly, the stronger is the driving force of diffusion. The latter is equal to $\Delta G^T(\text{melt}) - \Delta G^T(\text{cr})$, where $\Delta G^T(\text{melt})$ and $\Delta G^T(\text{cr})$ are the Gibbs free energies in the melt and crystal, respectively. At the same time, the thinner is the lamella, the stronger is the resistance to this force (determined by the contact surface OA). Therefore, diffusion is favoured by a small thickness of lamellae, whereas the principle of minimisation of the energy of the phase interface, by contrast, facilitates thickening of the lamellae. It can easily be concluded that a change in the rate of cooling should lead to a change in the mechanism of crystallisation due to the difference in the diffusion rate. Evidently, the above-considered mechanism is consistent with the Brady–Scheil classification (see above) and conclusions made in the studies.^{11,12}

In recent years, the Jackson–Hunt theory of formation of periodic structures upon crystallisation of eutectics^{24,25} has gained recognition. This theory takes into account the parameters of a phase diagram, surface tension and the rate of motion of the interphase boundary. Many studies were devoted to the development of the Jackson–Hunt model (see, for example, Ref. 26). Among these studies, noteworthy are investigations on the application of this theory to calculations of particular systems.²⁷ In a number of studies, account was taken of differences in the phase density,²⁸ the presence of external pressure,¹⁵ temperature gradient,²⁹ effect of electromagnetic fields³⁰ and differences in thermal conductivity of both components.³¹

An analogous approach was used in the study of the mechanisms of crystallisation of eutectics with rod or dendrite structures.³²

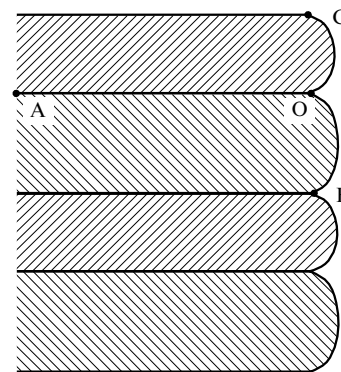


Figure 1. Mechanism of formation of lamellar eutectics according to Chalmers and Weingard.^{22,23}

The effects of rapid cooling (diffusion retardation) upon crystallisation of eutectics were investigated.^{20, 32, 33}

In spite of the fact that the results of calculations of particular eutectic structures with the use of the above-described models are in good agreement with the experimental data, it can be stated that the essential drawback of the available approaches is that they poorly describe interactions between components at the interface. In the review,² it was noted that it is this presence of an interface and solid–liquid interactions that are responsible for specific properties of eutectic alloys: ‘In a liquid eutectic alloy, the ‘structural complementarity’ between the dispersed medium and dispersed phase (the dimensional compatibility of the atomic arrangement at the interface) is better than that in a solidified alloy’. And later: ‘The eutectic composition corresponds to the phase ratio self-established in the melt at which the dispersed medium (melt) occurs in the state of solvation shells of dispersed particles. This specific nature of eutectics is responsible for their melting and crystallisation at a certain and constant temperature. A sacrifice in the dimensional compatibility of the atomic arrangement that occurs upon crystallisation is responsible for the elastic deformation of conjugated crystal lattices and a high elastic energy of the interphase surface’.²

These conclusions are confirmed by theoretical statements made by various authors at different periods of time. Commenting on the study by Bochvar,⁴ Taran¹ emphasised that ‘the fundamental idea is that two different crystals must be in contact with each other’. Based on the results of analysis of the structures of numerous eutectic alloys, Taran assumed that in the case of ‘the crystal-chemical difference between phases typical of the vast majority of eutectics,... the consideration of one of the phases as the basic one seems to be justified’.¹ This phase should possess ‘...a more complex crystal-chemical nature... The surface tension at the interface between this phase and the melt is high, which provides the possibility of nucleation and growth... of the second phase...’.¹ This basic phase can be determined with the use of the theorem of minimum entropy production in non-equilibrium processes. It was confirmed that this theorem is also applicable to particular simple eutectic structures, for example, to lamellar structures.³⁴ However, in a number of studies, this criterion was demonstrated to be insufficient. In the investigation,³⁵ the latter was attributed to the fact that characteristics of ‘pure’ phases are considered, whereas the presence of the second component is ignored, in particular, the entropy of mixing, which depends on interactions between the molecules of the components, is not taken into consideration. To characterise these interactions, new parameters, for example, the ‘parameter of surface roughness’ were introduced.³⁵

It should be noted that processes attendant on melting of crystals of different types (ionic, molecular, with different structures, etc.) were studied and described in detail.³⁶ The complexity of these processes in the pre-melting period (for example, positional and orientational disorder, the dependence on the type of unit cell of the initial crystal and its imperfection) suggests that the situation can become strongly complicated in the case of a mixture of interacting phases. In our opinion, all these changes should concern primarily the model of positional disorder because disordering of interacting structural units upon melting can be accompanied by their self-organisation giving rise to associates or something resembling a compound.³⁶

The concept of ‘interacting phases’ was supported by abundant experimental evidence. For example, interatomic interactions at the interface in crystallised eutectics were investigated. Analysis of X-ray emission and photoelectron spectra of eutectic alloys in the Al–Ge, Ag–Si, Ag–Ge (see Ref. 37) and Fe (Co,Ni)–Ge (see Ref. 38) systems demonstrated that the energy state of atoms in boundary layers of eutectic phases differs substantially from the state of atoms in the bulk of these phases and in the corresponding individual crystals. This specific state of boundary atoms is said to be ‘chemically active’.³⁶ These con-

clusions were made in studies of thin layers of eutectic alloys on substrates.³⁹

Let us discuss in more detail the remarkable and reliable experimental fact, viz., the orientational structural preference upon crystallisation of lamellar eutectics (the detection of this phenomenon was the aim of many investigations). In particular, it was proved⁴⁰ that the contact of phases along two crystallographic planes, viz., (111)Al–(211)CuAl₂ and (101)Al–(120)CuAl₂, is favourable for Al–CuAl₂ eutectics in the course of growth of a lamellar single crystal upon very slow cooling.

The consequences of interactions between components of eutectics in a molten state were also studied in sufficient detail. Thus, it was established^{41–47} that melts of eutectic systems in a particular temperature range above the liquidus line are characterised by ‘dynamic inhomogeneity’ manifested in the presence of ordered microregions, which are similar in composition and structure to eutectic colonies that form a structure of an alloy in the solid state. These ordered regions are called clusters, microgroups, cybotaxes, associates, dynamic short-lived complexes, heterophase complexes of atoms (or molecules), quasimolecules and fragments.² Hereinafter, we shall use the term ‘non-autonomous phase’ to refer to these ordered regions.

Many liquid alloys with eutectic compositions were studied by X-ray diffraction methods, which confirmed the presence of such non-autonomous phases. Studies of eutectic systems containing an intermediate phase revealed microgroups of atoms, which are similar in composition and structure to a chemical compound existing in the solid state (in the Tl–Te,⁴² Mg–Bi,⁴³ Fe–Si,⁴⁴ In–Sb,⁴⁵ etc. systems). For some binary amalgam systems, the substantiated conclusion was made that ordered structures, which are similar to chemical compounds, are retained in a melt.⁴⁷ In several studies, continuous series of solid solutions or metastable intermediate phases were detected in simple eutectic alloys obtained upon melt quenching.² These results are consistent, for example, with the conclusions⁴⁸ that eutectic melts are difficult to devitrify as well as with the data^{49, 50} that metastable solid solutions or compounds can exist after mechanochemical activation of eutectic alloys.

At the same time, it is known that microregions self-organised in a melt (non-autonomous phases) can be destroyed by external actions. For example, it was reported that the concentration in a eutectic melt changed under the action of centrifugal forces.²

When discussing the current state of the theory of eutectics, it should be noted that analogies between eutectics and chemical compounds were found. For example, Antipin and Vazhenin⁵¹ analysed two points of view, which are, in their opinion, of most importance. The first and most justified point of view consists in that eutectics are similar in nature to chemical compounds. The main argument is that most of eutectics obey the law of multiple ratios. The compositions of eutectics in melts of selected salts are given in Table 1.⁵¹

Table 1. Compositions of eutectics in molten salts.⁵¹

System	Chemical formula of the eutectic	Content of the second component (mol.%)	
		experiment	calculations
NaF–NaCl	NaF·2 NaCl	66.6	66.6
NaF–SrF ₂	2 NaF·SrF ₂	33.3	33.3
SrCl ₂ –NaCl	SrCl ₂ ·NaCl	50.0	50.0
LiCl–BaCl ₂	3 LiCl·BaCl ₂	25.0	25.0
KF–KI	KF·2 KI	66.0	66.0
NaF–KF	2 NaF·3 KF	60.0	60.0
NaF–LiF	2 NaF·3 LiF	61.0	60.0
KCl–KPO ₃	3 KCl·KPO ₃	20.0	20.0
KBr–KOH	KBr·3 KOH	75.0	75.0

It should be mentioned that Antipin and Vazhenin⁵¹ noted that more complex ratios (for example, $\text{NaCl} \cdot 14 \text{NaNO}_3$, $2 \text{NaF} \cdot 9 \text{NaI}$, $\text{NaCl} \cdot 6 \text{LiNO}_3$, *etc.*) were observed in some cases. These ratios could be considered as artificially selected. They referred to the data obtained by Geveling, who calculated that of 22 potassium halides, which form eutectics with other salts, 12 substances exactly correspond to multiple molar ratios. For three substances, the discrepancy is several tenths of a molar percentage. The remaining eutectics are not described by simple formulae. The authors of the cited monograph noted⁵¹ that 'this fact does not provide reason to reject certain stoichiometric ratios but can be indicative of their complexity' and believed that upon heating of a mechanical mixture of compounds forming eutectics, the liquid phase corresponding to the composition of the eutectic appears at a specified temperature only if certain ratios and conditions for contact between crystallographic planes of both substructures occur at the contact site. Antipin and Vazhenin⁵¹ concluded that, unlike chemical compounds characterised by the closest packing, a eutectic can be considered 'as the most weakly packed combinations of its constituent ions and atoms' and, hence, external actions, in particular, the pressure, 'can make the packing denser, *i.e.*, can, in the limit, give rise to a specific structure of a chemical compound'.⁵¹ In addition, studies were cited in which phase diagrams of either a eutectic or a chemical compound were obtained by varying the crystallisation conditions. Figure 2 illustrates the disappearance of a chemical compound and the appearance of a eutectic in the 2-chloronaphthalene–antimony trichloride system under certain experimental conditions.⁵¹

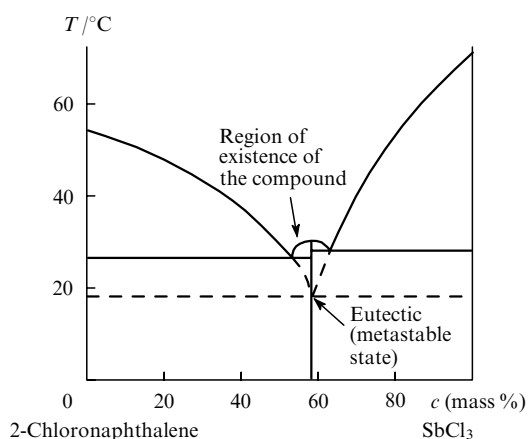


Figure 2. Phase diagram for the 2-chloronaphthalene–antimony trichloride system in the case of equilibrium and non-equilibrium crystallisation (c is the concentration of SbCl_3).⁵¹

Recently, the composition of a vapour over a eutectic melt was investigated.^{52, 53} Complex molecules of the MLnCl_4 and M_2LnCl_5 types ($\text{M} = \text{Rb}$ or Cs) were reliably detected in the vapour by high-temperature mass spectrometry. These results indicate that interactions in a melt, whose eutectic composition corresponds to the simple component ratio of 1 : 1, can be strong to an extent that congruent evaporation of the compound corresponding to the eutectic composition becomes possible. Therefore, the results of the above-mentioned studies can be considered as important experimental evidence in support of the proposed concept.

An alternative point of view consisting in that eutectics are heterogeneous mixtures, in the opinion of Antipin and Vazhenin,⁵¹ is based on two facts. First, the dependence of the eutectic composition on the external action, for example, on the pressure, can be attributed to a 'weak packing'. Second, a strong effect of the composition of impurities on the properties of eutectic alloys

cannot be explained within the framework of the concept presented in the monograph.⁵¹ However, it should be noted that the influence of impurities on the properties of eutectics has been considered in detail by Rebinder,⁵⁴ who explained this influence using the classical Gibbs–Volmer postulates and concepts of colloid chemistry.

To conclude this section, we cite one of the most recent definitions of the phenomenon of eutectics: 'The eutectic is a specific alloy (solution), whose components are partially miscible in the solid and liquid states and spontaneously form a thermodynamically equilibrium lyophilic dispersed system at certain temperatures. This system is characterised by substantial inter-phase interactions and solvation as well as by sedimentation stability. The composition of a eutectic corresponds to the ratio between eutectic phases, which is self-established in the melt and at which the dispersed medium completely occurs in the state of solvation shells of dispersed particles'.² It can be seen that the specific features of the formation of non-autonomous phases in eutectic alloys are described with the use of the notion of lyophilic systems characterised by interactions between dispersed particles. The terminology of colloid chemistry can eliminate particular contradictions in the theory of eutectics but it does not give a clear understanding of the mechanisms of processes occurring during melting and crystallisation of eutectic alloys. In our opinion, it seems more logical to use concepts of supramolecular chemistry for the determination of the nature of eutectic alloys and processes taking place during their formation. The formal possibilities of this approach will be considered in the next section. The drawbacks of the available notions can be to a large extent eliminated, first, by taking into account interactions between incommensurate substructures and, second, by developing a model, which describes mechanisms of these interactions and in which possible deformations and defects upon self-organisation of non-autonomous phases should be considered as a product of these interactions.

II. Main concepts and objects of inorganic supramolecular chemistry

J-M Lehn described supramolecular chemistry as the next step toward complexation of systems under study from molecules to supramolecules and organised supramolecular systems held together by non-covalent interactions.⁵⁵ This field of science deals with the chemistry of supramolecular assemblies and intermolecular interactions. Lehn assigned coordination bonds with metal ions as well as Coulombic, hydrogen, van der Waals and donor-acceptor interactions to intermolecular interactions.⁵⁵ The main property of self-organised supramolecular systems is their ability to perform molecular recognition. Recognition of components implies complementarity, *i.e.*, the mutual correspondence, both geometric and at the level of formation of intermolecular bonds, between the participants of the assembly (substrate and receptor). Although supramolecular chemistry has its roots in organic synthesis, coordination chemistry and studies of bioorganic and complicated organometallic complexes, Lehn particularly noted some objects of inorganic supramolecular chemistry admitting that the situation observed for these objects is rather inhomogeneous. In the study,⁵⁵ it was emphasised that intercalates, clathrates and host–guest structures exist only in the solid state. In the strict sense of the word, these structures are not discrete supramolecules but belong to solid supramolecular assemblies. Extended supramolecular assemblies (guests in extended[†] host structures) and discrete supramolecules occupy a special place.

[†] By 'extended' structures are meant one-, two- or three-dimensional infinite or semi-infinite crystalline substances with ionic or covalent bonds.

A more detailed classification of objects of inorganic supramolecular chemistry was presented in the review.⁵⁶ Among these objects are intercalates containing guests of different sizes in the host lattice, clathrates, framework silicates and complex molybdenum and vanadium phosphates. Because of the lack of the commonly accepted definitions and notions, the range of these objects is outlined very roughly.

In the present review, we restricted ourselves to the discussion of host–guest compounds as objects of inorganic supramolecular chemistry. These compounds allow one to study supramolecular assemblies in which the guest molecules form rather strong bonds with extended structures, factors influencing their complementarity (in particular, the geometric and topological complementarity between the components) and characteristic features of self-organisation. Extended assemblies enable one to consider the consequences of possible violations of the principle of complementarity and reveal the structural features of assemblies resulting from these violations. As will be demonstrated below, investigations of such objects can help in elucidating the mechanisms of formation of eutectic alloys.

It is known that formation of inorganic supramolecular assemblies can lead to violation of the principle of geometric and topological complementarity. Layered intercalates (in layered dichalcogenide matrices, graphite or clays) were particularly noted⁵⁶ as typical host–guest compounds examined in inorganic supramolecular chemistry. In all the above-mentioned cases, layers in the host lattice are linked by van der Waals interactions. Upon incorporation of guest molecules, the layers are pushed apart. It is known⁵⁷ that a change in the interlayer distance is an indication of the formation of an intercalate. This change depends on the size of the guest and can be 3–5 times larger than the initial crystallographic parameter of the host lattice. However, the ratio between the sizes of the guest molecules and cavities in the host lattice is not the only factor responsible for the limiting stoichiometry of an intercalate. It was demonstrated^{58,59} that the limiting stoichiometry of the intercalates A_aMX_2 (A is metal and MX_2 is a layered dichalcogenide matrix) is determined by the conditions of the matrix conduction band filling with electrons of the donor A (i.e., by electron stabilisation of the A_aMX_2 structure as a whole). The geometric factors are of secondary importance, as unambiguously evidenced by the small sizes of the M atoms in the A_aMX_2 systems, the absence of changes in the interlayer distances, the small limiting value of the parameter a and the dependence of a on the valence states of the A and M atoms.

The synthesis schemes for suprastructures developed in the study⁵⁶ consist in the following: the structure of a host should be constructed in such a way that it can be adapted to the structure of a guest. Successful examples of these retrosyntheses were cited in the study.⁶⁰ It should be noted that the so-called matrix crystals, which belong to a new type of inorganic supramolecular assemblies, have been discovered very recently.⁶⁰ Single crystals of synthetic opal were grown. These crystals contain cavities of a certain size, which form a regular cubic sublattice. The cavities were filled (from a melt under pressure) by crystalline and amorphous selenium as well as by sodium chloride. It was established that guest molecules always form quasilattices with unusually large parameters. Therefore, the geometric incommensurability of the sublattices is compensated by deformation of one of them (in this case, by deformation of the guest sublattice). Misfit compounds, which are a variety of intercalates in a layered dichalcogenide matrix, provide another example of incommensurability between the guest and host. Such compounds can also be assigned to objects of supramolecular chemistry. These are complex chalcogenides of the general formula $(AX)_{1+x}(MX_2)_y$ ($A = \text{Sn, Pb, Bi, Sb, Ln}$; $M = \text{Ti, V, Nb, Ta, Cr}$; $X = \text{S, Se}$; $x = 0.08–0.28$; $y = 1, 2, 3, \dots$) consisting of layers of two substructures, viz., AX (guest) and MX_2 (host). The guest layer (Q layer) forms a pseudocubic NaCl-type lattice. The host layer (H layer) occurs as a sandwich composed of hexagonal networks of the X atoms in which the M metal atoms have a trigonal-prismatic

(Nb, Ta) or octahedral (Ti, V, Cr) environment formed by the X atoms. The Q and H layers are incommensurate along one of the crystallographic directions (along one of the axes of the layer plane), the incommensurability being determined by the limiting value of x (at $y = 1$). Data on misfit compounds were generalised in the review⁶¹ in which it was noted that high thermodynamic stability of such compounds calls for revision of the topochemical laws of construction of supramolecular structures.[‡] Besides, it was hypothesised that in the process of organisation of supramolecular assemblies with incommensurate elements, the forces responsible for the retention of substructures (and their molecular recognition) compete with the forces linking these substructures.⁶¹ This can lead to morphological distortions of crystals and the appearance of different structural defects. The widespread opinion that the properties of misfit compounds are additive with respect to the properties of their constituent substructures was disproved in the study.⁶³ Numerous phase transitions were observed by measuring thermal capacity. The authors of the cited study⁶³ believed that these phase transitions are caused by temperature- and incommensurability-dependent defects of suprastructures.

Theoretical analysis^{64,65} confirmed the possibility of self-organisation of suprastructures from structures incommensurate along one crystallographic direction. Mechanisms of this self-organisation were proposed in the studies.^{64,65} The results of these investigations are briefly surveyed in the next section. Here it should be noted that (as will be demonstrated below) a consideration of eutectics, which, in the limiting case, are incommensurate along all three crystallographic directions, in terms of supramolecular chemistry allows one to answer many questions and eliminate unclear facts, which we have mentioned in the discussion of the available concepts of eutectics.

III. Static Frenkel–Kontorova model for finite systems

Interactions between substructures characterised by one-dimensional incommensurability (misfit compounds) were proposed to be considered as the behaviour of an elastic and less strong chain of finite length (guest) in the field of a rigid substrate (host) inducing a periodic potential (U)^{64,65} for elements of the chain (Fig. 3). This approach is a static version of the known Frenkel–Kontorova model.⁶⁶

A method was developed^{64,65} for the numerical solution of the problem of a search for energy minima of systems, which are composed of an elastic chain consisting of $N + 1$ atoms (i.e., containing N bonds) and a substrate, provided that the position of the chain on the substrate is determined by only one parameter (position of its end or beginning), whereas all other geometric elements of the chains are calculated according to recurrent equations. In calculations, the incommensurability parameter of subsystems $\gamma = b/h$ (b is the bond length in the free chain) and the ratio between their characteristic energies $z = 2\pi A/(kh^2)$ ($kh^2/2$ is the energy of stretching of the bond in the chain by a period of the substrate) are used as parameters of the problem. For convenience of discussion, the dimensionless potential energy (E) of chain–substrate systems (in units $kh^2/2$) per degree of freedom was introduced in the form $\varepsilon = E/(N + 1)$. In calculations, the incommensurability parameter of subsystems (γ) was varied within 0.5–1.5, and the optimum region of variation of the dimensionless

‡ It should be noted that the term ‘misfit’ is rather widely used in the literature. In particular, misfits between the parameters of crystal lattices of components of alloys are generally considered in metallurgy. For instance, in the study devoted to the development of compositions of high-temperature nickel alloys,⁶² the misfit characteristics were determined and the influence of these characteristics on processes of ordering and liquation depending on the morphological structural features were investigated.

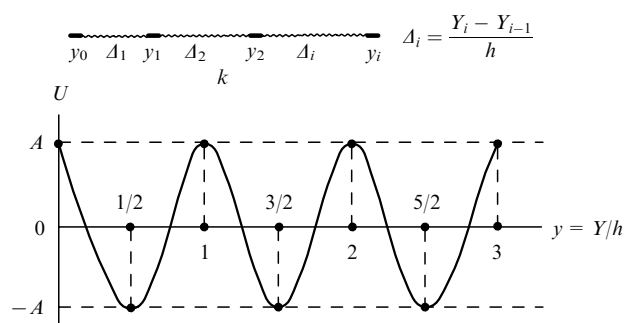


Figure 3. Frenkel–Kontorova model for a chain of a finite length;⁶⁶ y_0 is the position of the beginning of the chain; y_i is the dimensionless coordinate of the i th element of the chain ($i = 0, 1, \dots, N$) in units h , where h is the period of the potential of the substrate; Y_i is the absolute coordinate of the i th element of the chain; A_i is the length of the i th bond in the chain in units h ; k is the rigidity of the bonds in the chain; U is the potential energy; A is the amplitude of the potential of the substrate.

energy parameter z was determined from the real values of the corresponding constants for inorganic compounds. Leaving aside mathematical procedures (analytical and numerical solutions of

this problem were reported in detail in Refs 64 and 65), let us consider the most important conclusions drawn from the dependences obtained.

1. For different z and γ , the energy of the system in the ground state per degree of freedom (ε) increases as the number of bonds (N) increases. This indicates that beginning with a particular number of bonds, fragmentation (cleavage of the chain) becomes favourable. Obviously, in each particular case, the gain in energy upon fragmentation must be compared with the real bond energies in the corresponding substructure. Typical plots of the relative maximum bond deformations for a chain in the ground state [$\delta = (1/\gamma - 1) \times 100\%$] and the corresponding energies per degree of freedom (ε) vs. the number of bonds (N) at different incommensurability parameters γ and energy parameters z are shown in Figs. 4 *a–f*. It can be seen that an increase in N leads to a change in the configuration of the ground state. For example, if $\gamma = 1.1$ (see Fig. 4 *a*) and $z = 0.030$, the rigid chain is strongly stretched (or cleaved) on going from $N = 12$ to $N = 13$. If $\gamma = 0.9$ (see Fig. 4 *c*), a strong chain contraction occurs at the same parameters of the system.

2. The probability of fragmentation sharply increases as the initial incommensurability increases as well as upon the formation of strong chain–substrate bonds. For example, if $\gamma = 0.6$ (see Fig. 4 *e*), the deformation of one bond reaches 20% already at $z = 0.15$.

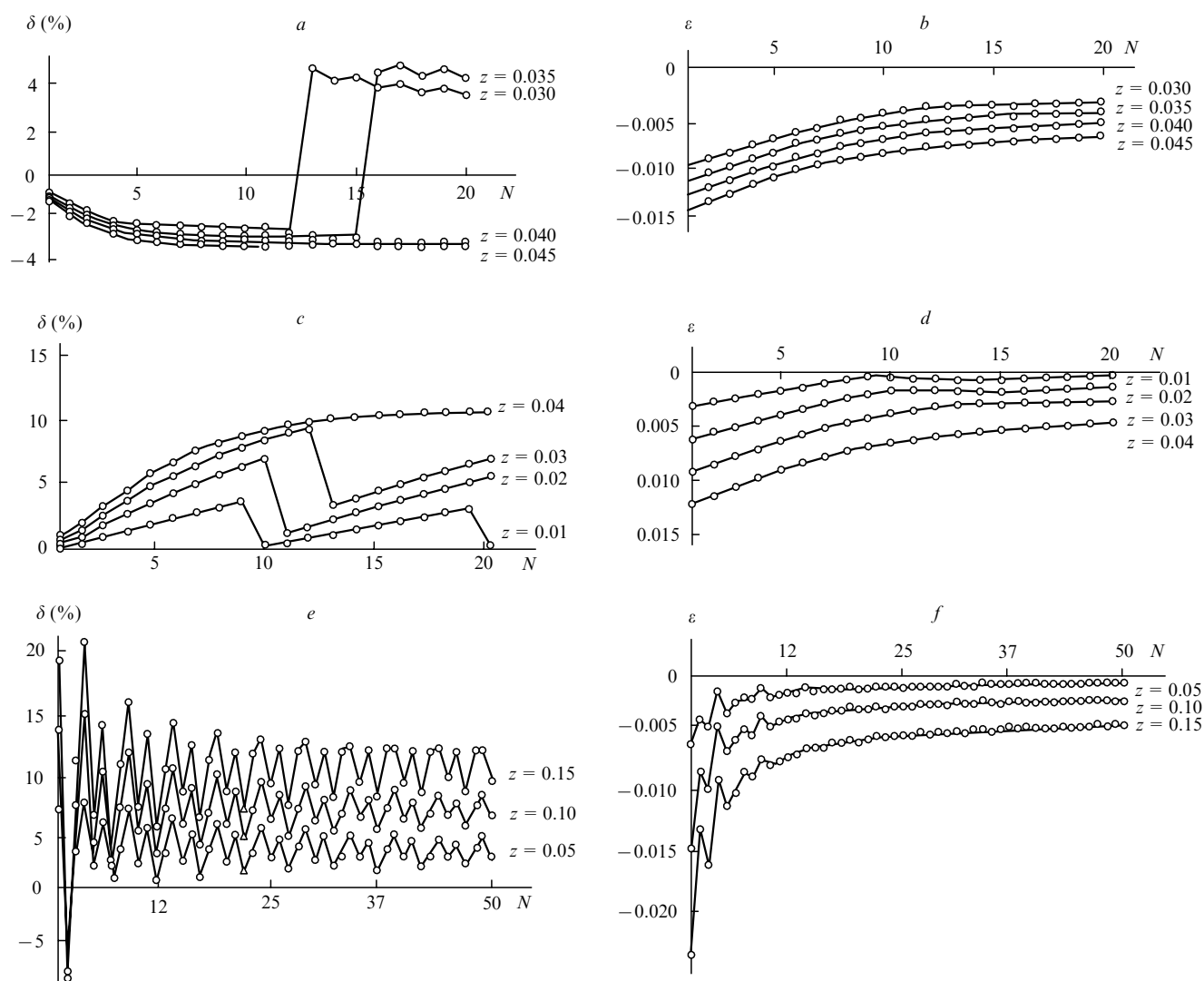


Figure 4. Plots of the maximum relative bond deformation (δ) in the chain in the ground state (*a*, *c*, *e*) and the energy per degree of freedom (ε) of the system (*b*, *d*, *f*) vs. the number of bonds (N) in the chain for $z < z^*$ and $\gamma = 1.1$ (*a*, *b*); 0.9 (*c*, *d*); 0.6 (*e*, *f*).⁶⁵ See comments in the text.

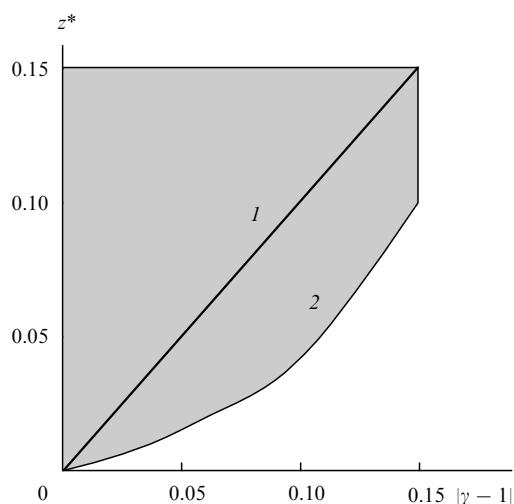


Figure 5. Estimation (1) and calculated (2) plots of z^* vs. γ . The region in which the ground state of the chain has the 1 : 1 configuration is dashed.⁶⁵

3. For chains with any rigidity and for a given incommensurability between the chain and substrate, there is the energy parameter z^* such that if $z > z^*$, the system occurs in the ground state (corresponding to the ratio of 1 : 1), i.e., $\gamma = 1.0$ (Fig. 5).

4. Excited metastable states of the system (conformers) also possess some interesting features. Calculations demonstrated that these states should be very stable. Regions of contraction or stretching in incommensurate systems are developed analogously to those in commensurate systems ($\gamma = 1.0$). This fact allows one to state that the deformation and fragmentation of substructures in real eutectic alloys depend substantially on the conditions of the synthesis (crystallisation).

5. The proposed one-dimensional model provides the answer to the question as to the mechanisms of mechanochemical actions on interacting substructures. The preliminary longitudinal contraction or stretching of the chain influences the incommensurability parameter γ , whereas the forces acting in the perpendicular direction affect the parameter z (via the dependence of the parameter A on the chain–substrate distance). The above-mentioned changes can lead to the formation of a suprastructure in the metastable state for non-excited γ and z .

Although these conclusions were made based on the results of investigations, which were far from completion, it is believed that they are of importance for an understanding of the mechanisms of formation of eutectic suprastructures from elements, which are, in the limiting case, incommensurate along all three crystallographic directions.

First, calculations demonstrated that the formation of assemblies from incommensurate elements cannot differ substantially from the formation of assemblies from commensurate elements if the synthesis conditions imply the presence of excited states. This is yet another argument in favour of the statement that the topological and geometric complementarity between the guest and host is not necessary, and, consequently, eutectics can be assigned to objects of supramolecular chemistry.

Second, one can follow the changes in the parameters of the model (as yet one-dimensional) depending on the external conditions (the effect of the temperature on the interaction potential, rigidity and bond energy, mechanical actions, etc.).

Third, the mechanism of fragmentation of interacting incommensurate substructures, i.e., the formation of thermodynamically stable nanocomposites, was established. In our opinion, the conclusions made for a one-dimensional model can be used for explaining certain phenomenological results of studies of eutectic alloys.

IV. Supramolecular concept in the theory of eutectics

As mentioned above, poorly defined terms in inorganic supramolecular chemistry arise from the fact that intercalated host–guest compounds are assigned to solid supramolecular structures according to the available nomenclature. Therefore, the term ‘compound’ is set equal to the term ‘supramolecular assembly’. At the same time, in solid-state chemistry it is generally agreed that compounds have individual structures. In our opinion, there is an approach eliminating these uncertainties. If an interaction between the initial substructures leads to their destruction giving rise to a new structure typical of a particular compound, conditions for the molecular recognition are violated. These objects fall outside the scope of supramolecular chemistry and the problems considered in the present review. However, if the energy released upon interaction between the initial structural elements is insufficient for their radical rearrangement, it can be used for production of various structurally less stable supramolecular assemblies. We believe that any alloys (eutectics, solid solutions, etc.) can serve as examples of such supramolecular assemblies. This provides the basis for our approach. Undoubtedly, these assemblies are consistent with the principle of molecular recognition because the initial structures are not destroyed. Evidently, the Gibbs energies of such assemblies should depend on their architecture and mutual arrangement of sublattices. For example, the fulfilment of the principle of complementarity depends to a lesser or greater extent on the incommensurability and rigidity parameters, the presence of defects and analogous factors. In syntheses under different conditions (for example, under different temperature modes of alloy solidification), the self-organisation of a suprastructure should be accompanied by the emergence of hierarchy of assemblies of different types. The main type (possessing the lowest energy under particular thermodynamic conditions) should correspond to the case of the limiting self-organisation, whereas all other types are non-equilibrium or metastable. A change in the synthesis conditions should lead to a change in the energy hierarchy of suprastructures.

Organisation of suprastructures from incommensurate elements can proceed according to three schemes. In the first scheme, we deal with rigid substructures, which rather weakly interact with each other. Since the energy effects are small, the self-organisation[§] is also insignificant. In a certain approximation, we arrive at the term ‘mechanical mixture of phases’ whose properties are additive with respect to the properties of its constituent structural elements.

According to the second scheme, non-rigidity of interacting substructures or external mechanical actions compensate insignificant incommensurability between these substructures upon the formation of a suprastructure. In this case, stresses giving rise to a change in the crystal morphology should appear in the resulting suprastructure, and the non-additivity of the thermal capacity and some other physicochemical properties can be observed. Apparently, this scheme can be used for explaining the formation of limited solid solutions. It is worthwhile to cite the reasoning of the authors of the study⁶⁹ who believed that the regions of existence of solid solutions in phase diagrams cannot be described in the context of classical thermodynamics because of their imperfection. These phases are non-equilibrium and, consequently, they must decompose as the system approaches equilibrium. It has long been noticed that some alloys quenched from a solid-solution region appear to be decomposed (the so-called ‘tweed’ or modulated structure is formed).^{70–73} In the study,⁷⁴ this phenomenon was interpreted as follows: ‘The concentration at which noticeable

[§] The meaning and differences of the terms ‘self-organisation’ and ‘self-assembling’ are extensively discussed in the literature. Cases when the initial components have different incommensurability and rigidity parameters were also described.^{67,68}

deviations from perfection take place in a particular solution depends substantially on the nature of the compounds involved in this solution. Solutions for which deviations from perfection cannot be observed throughout the concentration range are exceptionally rare and exist only if their components have similar chemical structures, possess similar thermodynamic characteristics, similar atomic sizes, identical crystal structures, *etc.* If atoms differ in size by more than 14%, a solid solution cannot be formed because the deformation energy of the crystal lattice substantially increases'. It was also noted that if only two types of interactions, *viz.*, attraction (tendency to ordering) and repulsion (tendency to phase separation), occur between components, two types of regions in which these tendencies are manifested should be observed in phase diagrams.^{74, 75} In the studies,^{76, 77} the thermodynamic, kinetic and morphological aspects of decomposition of substitution solid solutions characterised by either the positive or negative energy of ordering were considered. Using a model of free energy relaxation for separation and ordering, a method was developed⁷⁶ for the computer simulation of such transformations, including calculations of the effects of induced elastic stresses.

Therefore, the problems discussed in the present review, *viz.*, the possibility of self-organisation and defect formation in systems with interacting incommensurate structural elements, are directly related not only to eutectic alloys but also to solid solutions. Based on the available data, it can be assumed that the difference between the eutectic type of formation of an alloy in a binary system and the formation of a solid solution consists in the following.

In the case of small incommensurability, the molten components A and B are mutually soluble. The release of thermal energy responsible for the conditions of formation of a solution can be favoured by mechanical actions (thus, it was experimentally demonstrated⁷⁸ that these actions allow one to extend sharply the concentration region of existence of single-phase alloys; the mechanochemical synthesis of metastable solid solutions from eutectic phases was carried out in the studies^{49, 50}). If the components A and B have more substantial incommensurability and do not interact with each other (the negative energy of ordering), they undergo phase separation.

However, if the components A and B interact with each other, it is worthwhile to consider the third scheme associated with the mechanisms of structural compensation in the course of active self-organisation of assemblies, which are composed of incommensurate substructures, in eutectic alloys. This is true for cases when the potential of interactions between substructures is rather high and their non-rigidity and incommensurability lead to critical deformations or fragmentation of one of the substructures. The formation of assemblies can be accompanied by the appearance of various defects, nanocomposite structures, non-additivity of properties and morphological changes during crystal growth.

Evidently, eutectic supramolecular assemblies are generated as non-autonomous phases, *i.e.*, as phases formed in the vicinity of the contact surface of interacting substructures. However, under certain conditions, this non-autonomy can, in principle, turn into the organisation of the structure as a solid solution. Therefore, the proposed concept allows one to bridge the gap between the terms 'eutectic' and 'solid solution'. Obviously, non-autonomous phases in a molten state differ from those in the solid state because processes of self-organisation of substructures depend substantially on the temperature (crystal lattice parameters,⁷⁹ bond energies, interatomic distances² and rigidity are changed). Consequently, like in the case of solid solutions, the ground states of a supramolecular system and a set of excited states are functions of the temperature. In our opinion, estimation of the changes in the parameters of the system in the proposed one-dimensional theoretical model will enable one to predict the characteristic features of eutectic suprastructures formed in the quenching mode. As mentioned above, alloys prepared by quenching can retain the structure of assemblies formed at high temperature as long as is

wished due to thermodynamic stability of the conformers. Stability of eutectic suprastructures is responsible for the necessity of the constancy of their compositions and melting–solidification temperatures. The fact that eutectics have low-melting points and possess specific physiochemical properties can easily be explained taking into account that interactions between incommensurate structural elements are associated with bond deformation and considering that under particular conditions the total amount of defects in a non-autonomous phase should be approximately constant.

Measurements of heat capacities and the determination of their temperature dependences for a series of oxide eutectic alloys provided evidence that these non-autonomous phases play different roles in such systems. The GaSe–GaSe_{1.5} system was studied in the Se concentration range of 50%–60%, where the homogeneity region of gallium monoselenide and simple eutectics occurred.⁸⁰ For this purpose, samples, which were quenched from a melt and slowly cooled, were used. We studied the temperature dependences of the heat capacity⁸¹ for the PbO–ZnO (eutectic, 89 mol.% of ZnO, $T_m = 1134$ K),⁸² PbO–Y₂O₃ (eutectic, 95 mol.% of Y₂O₃, $T_m = 1103$ K)⁴⁸ and MoO₃–PbO (eutectic, 59 mol.% of MoO₃, $T_m = 933$ K) systems.⁸³ A special procedure was developed, which made it possible to decrease an error of the measurements of heat capacity to approximately 0.5%. The crystallographic characteristics of substructures and eutectic alloys were studied. It appeared that the heat capacities of eutectics, like those of misfit compounds, deviated toward the values calculated according to the additive scheme (by 4.0%–4.5% for PbO–ZnO and by 9%–10% for PbO–Y₂O₃ and PbO–MoO₃). The devitrification and crystallisation temperatures in the region of eutectic compositions and in the nearby concentration regions were also investigated. The results of these investigations demonstrated that there are no substantial difference between the structures of the 'host–guest' type, which fall into the category of supramolecular compounds and are consistent with the principle of molecular recognition, and eutectic assemblies.

In the context of the proposed concept, the orientational ordering in eutectic alloys (see above) can easily be explained. If the system is incommensurate along two or three crystallographic directions and the incommensurability parameter γ along different directions has different values, energetically most favourable positions will be chosen upon interaction between substructures of two components (A and B) in the course of self-organisation of assemblies.

Mechanochemical treatment of substructures can also lead to changes in the parameters of the system determining the self-organisation of assemblies.

Finally, the proposed concept provides an alternative insight to the mechanisms of modification of eutectics by adding the third component.

The known descriptions of quasi-equilibrium crystallisation of melts are based on the genetic relations between the phase diagrams of eutectics and solid solutions. A scheme of formation of a eutectic-type phase diagram after superposition of two phase diagrams of solid solutions is shown in Fig. 6. Weingard believed²³ that at the solidification temperature (T_{cr}), a melt with eutectic composition can be considered as if it were present on two liquidus lines. The liquid is in equilibrium with the solid phase with composition C₁ and another solid phase with composition C₂. Both solid phases are formed from the liquid with composition C_E. This mixture of two different solid phases is called a eutectic. It should be noted that the genetic relation between the state of a solid solution and eutectics is consistent with the conclusions drawn from the proposed theory. Recall that the results of analytical and numerical studies of the static one-dimensional Frenkel–Kontorova model eliminate sharp differences between commensurate and incommensurate substructures upon the formation of excited states of a suprastructure. At the same time, the supramolecular concept involving this theory

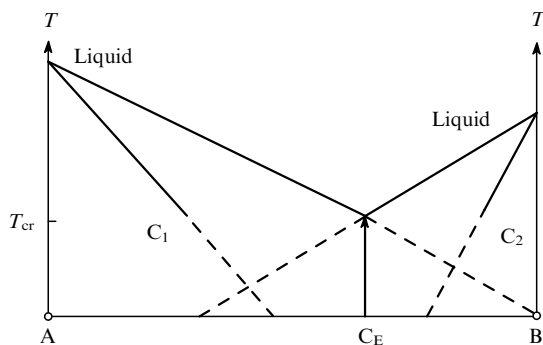


Figure 6. Scheme of formation of a eutectic-type phase diagram after superposition of two phase diagrams of solid solutions. See comments in the text.²³

bridges the gap between the notions of compound and solution by introducing a ‘supramolecular eutectic assembly’ as an intermediate.

As can be seen from Fig. 7, different composites can occur in a two-component (consisting of the phases A and B) eutectic alloy depending on the parameters of the system and external actions. This can be a mechanical mixture of phases (see Fig. 7, line 1), an associated solution (curve 2) or a supramolecular assembly (curve 3). The minimum of the potential corresponds to the ground state. The presence of excited states (conformers; region 4) implies an uncertainty in the composition and structure of the assembly. The exact concentration ratios can take place only upon the formation of a compound with an individual structure (point 5).

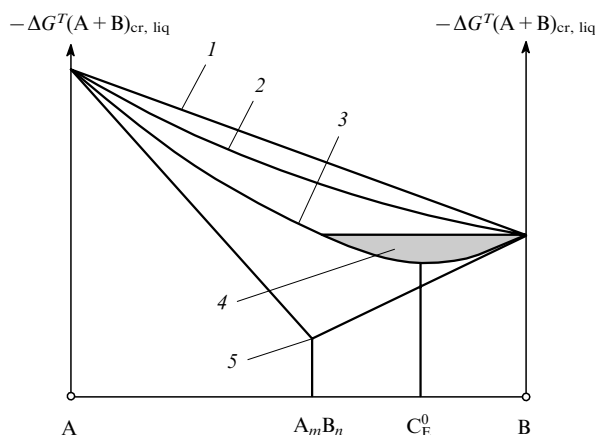


Figure 7. Types of interactions in a two-component A + B system; (1) a mechanical mixture of components, (2) an associated solution, (3) a supramolecular assembly, (4) a region of existence of metastable conformers (C_E^0 is a eutectic, the ground state), (5) a compound with an individual structure.

It can be stated that the proposed supramolecular concept in the theory of eutectics does not reject the classical views. The only difference is that the abstract thermodynamic criteria, such as the surface energy or surface tension, are changed for real parameters of interacting substructures, viz., the incommensurability, rigidity and interaction potential. These parameters are generally not used in supramolecular chemistry but are included in the static Frenkel–Kontorova model, which we propose for the description of different modes of self-organisation of systems characterised by one-dimensional incommensurability.

It should be noted that some of the notions used in the present review are discussed not for the first time. Thus, the terms

‘assembly’, ‘size dimensionality factor’ and ‘crystallographic factor’ have been used by Hume-Rothery *et al.*⁵

One would expect that the further development of theoretical approaches (primarily, the development of the two-dimensional static Frenkel–Kontorova model for finite systems) and the target studies of the dependences of the parameters of the model and structural features of the resulting suprastructural eutectic assemblies will allow one to accumulate data, which will make it possible to predict unambiguously properties of eutectic alloys.

V. Conclusion

The results surveyed in the present review provide evidence in favour of the supramolecular concept in the theory of eutectics. This concept is based on the assumption that a eutectic alloy containing the autonomous phases A and B (in a two-component system) must be studied with consideration for interactions between these phases. These interactions can be responsible for the formation of ordered microregions (non-autonomous phases) analogous to supramolecular assemblies. Depending on the interaction potential, incommensurability between the crystal lattices of the substructures A and B, their rigidity and extension, external mechanical actions, the conditions can be provided for the formation of defect composites, viz., non-autonomous phases with changed lattice parameters. The existence of such phases is confirmed by the data published in the literature and our experimental results. The mechanisms of self-organisation of such assemblies are discussed using the one-dimensional static Frenkel–Kontorova model. It was demonstrated that a change in the parameters of the model can lead to the formation of limited solid solutions. The relationships between the mechanisms of formation and ordering in metastable solid solutions and processes of formation of supramolecular assemblies in eutectic alloys are discussed. Along with the ground state of a non-autonomous phase (corresponding to the maximum level of self-organisation), there are a large number of excited states (conformers), which are similar in energy and whose transitions to the ground state should be kinetically hindered. At low interaction potentials and in the case of substantial rigidity of substructures A and B, eutectic alloys should be similar in properties to mechanical mixtures of the phases. The specific properties of eutectic alloys and the dependence of their structures on the synthesis conditions (temperature, rate of cooling, mechanical actions) depend on the amount of a non-autonomous phase and the degree of its organisation. Analysis of the results of investigations devoted to the structures and properties of eutectic alloys provided evidence that the proposed concept is consistent with abundant phenomenological data and is not contradictory to the classical theoretical notions.

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Methods for the synthesis of vinyl sulfides

N V Zyk, E K Beloglazkina, M A Belova, N S Dubinina

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Abstract. The published data on the methods for the synthesis of vinyl sulfides are considered and generalised. The main attention is given to methods based on electrophilic sulfenylation of unsaturated compounds. The bibliography includes 173 references.

I. Introduction

Vinyl sulfides play a prominent role in synthetic organic chemistry. They are extensively used as synthetic equivalents of enolate ions¹ and acyl anions.² In addition, vinyl sulfides are valuable intermediates in the synthesis of oxetanes,³ spirocyclic systems⁴ and other organic compounds.^{5–10} Vinyl sulfides also present interest as candidate pesticides and bactericides.^{11,12}

Among numerous methods for the synthesis of vinyl sulfides that have been described in the literature, three main groups can be selected: (1) electrophilic sulfenylation of unsaturated compounds; (2) nucleophilic addition of the RS group and nucleophilic substitution at the unsaturated carbon atom; (3) synthesis *via* radical intermediates. Other methods for the synthesis of vinyl sulfides can be illustrated by only a few examples, which include addition of hydrogen halides to alkynyl sulfides, elimination of various fragments from sulfur-containing compounds, reduction of sulfoxides, the Wittig–Horner reactions of arylthio-substituted phosphonates and the Peterson reaction.

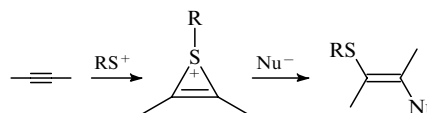
Some examples of the synthesis of vinyl sulfides can be found in reviews devoted to the synthesis of sulfides,¹³ applications of sulfonyl chlorides in organic synthesis¹⁴ and metal-catalysed formation of C–S bonds.¹⁵ A recently published review is devoted to the synthesis of fluorine-containing alkyl(aryl)vinyl sulfides.¹⁶ However, to the best of the authors' knowledge there are still no reviews devoted to the synthesis of vinyl sulfides. The present review is intended to bridge this gap. Here, we generalise

and analyse the data on the methods for the synthesis of vinyl sulfides published in the last 15–20 years. Besides, we thought it expedient to mention some other methods that were developed much earlier, but are still widely used.

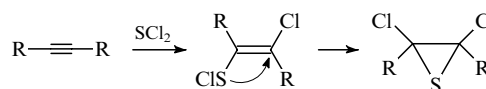
II. Electrophilic sulfenylation of unsaturated compounds

1. Electrophilic sulfenylation of alkynes

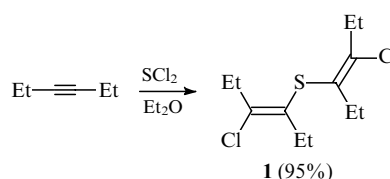
Electrophilic addition of divalent sulfur derivatives to alkynes is the most popular method for the synthesis of vinyl sulfides.



The addition of sulfur dichloride to alkenes and alkynes was studied in some detail back in the 1970's.^{17–21} Reactions of alkenes^{18–21} with SCl_2 afford chloroalkanesulfonyl chlorides which, in turn, react with the second alkene molecule to yield sulfides. It might be supposed that reactions of acetylenes with SCl_2 occur in a different manner and result in the formation of thiiranes, the addition products of the sulfonyl chloride group of the alkenesulfonyl chloride formed to the double bond.



However, it was found that SCl_2 reacts with hex-3-yne in dry ether in the same way as with alkenes to afford divinyl sulfide **1**. The latter is formed as a result of sulfenylation of an alkyne by the alkenesulfonyl chloride formed in the first step.¹⁷



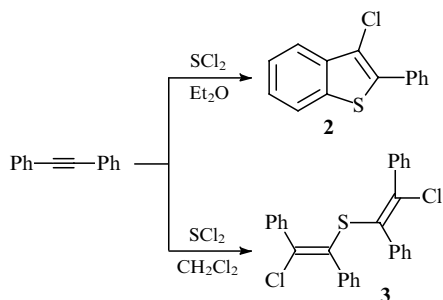
At the same time, the reaction of diphenylacetylene with sulfur dichloride in Et_2O results in 3-chloro-2-phenylbenzothiophene

N V Zyk, E K Beloglazkina, M A Belova, N S Dubinina Department of Chemistry, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax (7-095) 939 02 90. Tel. (7-095) 939 46 52. E-mail: zyk@org.chem.msu.ru (N V Zyk). Tel. (7-095) 939 22 92. E-mail: bel@org.chem.msu.ru (E K Beloglazkina), sma@org.chem.msu.ru (M A Belova)

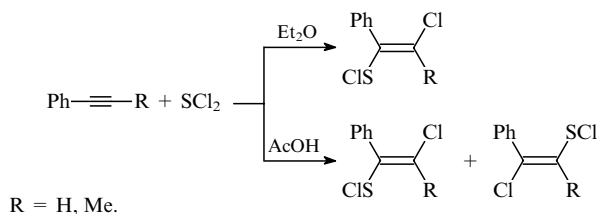
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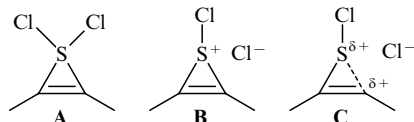
(2). The structure of the latter was established on the basis of its spectral characteristics and was confirmed by its conversion into the known 2-phenylbenzothiophene, although the reaction in dichloromethane gives divinyl sulfide **3** in high yield.¹⁷



The stereo- and regioselectivity of the addition of sulfur dichloride to phenylacetylene have been studied.¹⁷ It was found that the reaction of equimolar amounts of phenylacetylene and sulfur dichloride in Et_2O yields an anti-Markownikoff adduct with a *trans*-configuration of the substituents, whereas Markownikoff and anti-Markownikoff products are formed in acetic acid. 1-Phenylpropyne reacts with SCl_2 in a similar way.



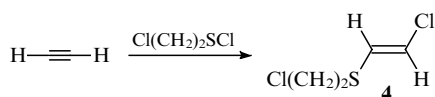
In highly polar solvents, *e.g.*, in acetic acid, the addition preferably occurs in accordance with the Markownikoff rule, while in less polar solvents, such as ethyl acetate, anti-Markownikoff adducts are preferably formed. It was thus suggested that this reaction occurs *via* one of the three intermediates **A–C** depending on the ion-stabilising characteristics of the solvent.



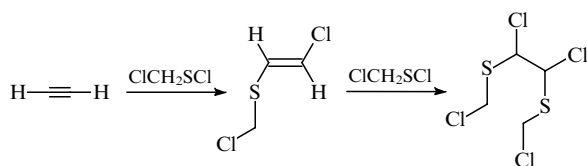
Steric factors compete successfully with the solvent effect.

Sulfenyl chlorides are one of the few sulfenic acid derivatives that add to multiple bonds without additional activation.

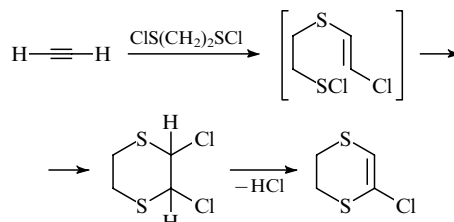
The first paper devoted to acetylene sulfenylation was published as early as 1946 within the framework of a search for methods for the synthesis of yperite and its analogues.²² The addition of 2-chloroethanesulfonyl chloride to acetylene was studied. *trans*-Configuration was ascribed to the monoadduct **4** formed.



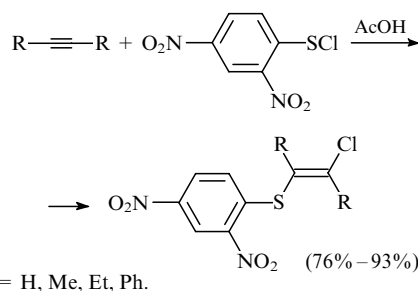
Later, it was shown²³ that the reaction of acetylene with chloromethanesulfonyl chloride yields an addition product of two sulfonyl chloride molecules to one acetylene molecule.



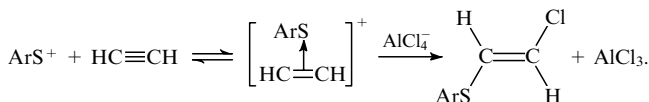
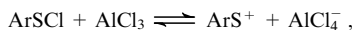
The reaction of acetylene with ethane-1,2-disulfonyl chloride underlies the synthesis of sulfur-containing heterocyclic compounds.²⁴



The reaction of 2,4-dinitrobenzenesulfonyl chloride with symmetrical acetylenes in glacial acetic acid yields exclusively *trans*-addition products.²⁴

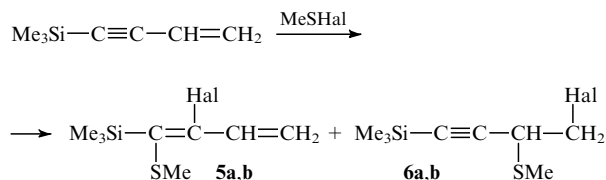


It was found that sulfonyl chloride reacts with acetylene in dichloroethane only in the presence of catalytic amounts of AlCl_3 .²⁵ The following reaction mechanism has been proposed:



However, in the case of higher acetylene homologues, *e.g.*, but-2-yne, hex-3-yne and diphenylacetylene, the presence of aluminium chloride is unnecessary.

As could be expected, electron-withdrawing groups deactivated the triple bond with respect to electrophilic reagents, while electron-donor groups activated it. Thus acetylenedicarboxylic acid does not react with sulfonyl chloride,²⁵ although methyl propiolate adds methane-, benzene- and *p*-substituted arenesulfonyl chlorides on heating.²⁶ Methanesulfonyl chloride adds to alkylthiovinylacetylenes exclusively at the triple bond.²⁷ The ratio of 1-trimethylsilylbut-3-en-1-yne adducts with methanesulfonyl halides (**5a**: **6a** and **5b**: **6b**) depends on the nature of the halogen atom in the sulfonylating reagent.²⁸

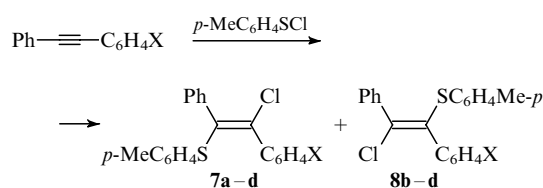


$\text{Hal} = \text{Cl}$ (**5a**, 90%; **6a**, 10%), Br (**5b**, 75%; **6b**, 25%).

Functionalised trimethylsilylvinylacetylenes $\text{Me}_3\text{Si}-\text{C}\equiv\text{C}-\text{CH}=\text{CRX}$ ($\text{X} = \text{CN, COMe, CO}_2\text{Et}$; $\text{R} = \text{H, Me}$) react with methanesulfonyl chloride at the triple bond.²⁹ Reactions of methane-, ethane- and *p*-toluenesulfonyl chlorides with nitroynes and their functional derivatives also involve exclusively the triple bond.³⁰

The effect of substituents in the benzene ring of diarylacetylenes on the addition of sulfonyl chlorides has been studied.³¹

The reaction of *p*-toluenesulfonyl chloride with diphenylacetylene in chloroform yields the monoadduct **7a** in quantitative yield. The reaction with *p*-methoxy-substituted diphenylacetylene proceeds in a similar way. Compound **7b** is the only reaction product (no isomer **8b** was found †).



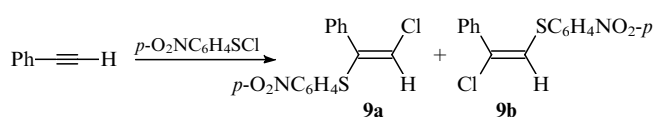
X = H (**a**), 4-MeO (**b**), 3-Cl (**c**), 4-Cl (**d**).

At the same time, the reaction of this sulfenylating agent with chloro-substituted diphenylacetylenes yields both isomers: for X = 3-Cl, the **7c**:**8c** ratio is 1:4, whereas for X = 4-Cl the **7d**:**8d** ratio is 3:2. Thus, the outcome of electrophilic addition of sulfonyl chlorides to substituted diphenylacetylenes is determined by the polar effects of the substituents.

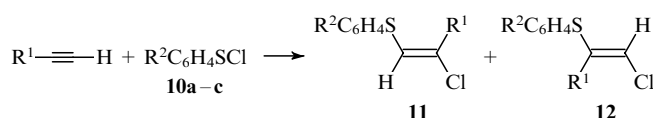
The rates of addition of sulfonyl halides to acetylenes and the structures of the reaction products depend on the nature of substituents in both the acetylene substrate and the starting sulfonyl halide. Thus the rate of addition of *para*-substituted arenesulfonyl chlorides to acetylene decreases in the following order: OMe > Me > H > Cl > NO₂. The methyl group and the chlorine atom in the *ortho*-position have little effect on the reaction rate, whereas the presence of a nitro group in the same position causes a 2000–3000-fold decrease in the reaction rate.³²

Studies on the kinetics of the addition of 2,4-dinitrobenzenesulfonyl chloride to hex-3-yne and phenylacetylene in acetic acid have shown that both reactions are overall second order and first order with respect to each reactant; the reaction products are represented exclusively by *trans*-isomers. In the case of acetylene, the addition product is formed exclusively according to the Markownikoff rule.³³

The effects of solvents on the ratio of Markownikoff and anti-Markownikoff addition products in reactions of sulfonyl chlorides with acetylenes have been studied.^{25,33,34} It was shown in particular that the reaction of *p*-nitrobenzenesulfonyl chloride with phenylacetylene in ethyl acetate gives predominantly the anti-Markownikoff adduct **9a**, whereas the same reaction in acetic acid yields predominantly the adduct **9b**.³⁴



The reaction product ratios of arenesulfonyl chlorides **10a–c** with phenylacetylene and but-1-yne in various solvents are presented in Table 1.³⁵



R¹ = Et, Ph; R² = 4-Me (**a**), 4-NO₂ (**b**), 2-NO₂ (**c**).

All of the adducts formed are *trans*-addition products. A reaction scheme has been proposed³⁶ where a complex of the chloride ion with the thiirenium cation is formed in the first step. Further transformations of this ionic complex depend on the nature of the solvent and the structure of the cation; these determine the quantitative ratio of the reaction products. Thus conversions within tight ion pairs result in anti-Markownikoff

† It is worth mentioning that formation of the adduct **8b** in this reaction cannot completely be excluded. Apparently, it is present, but in insignificant amounts (< 5%).

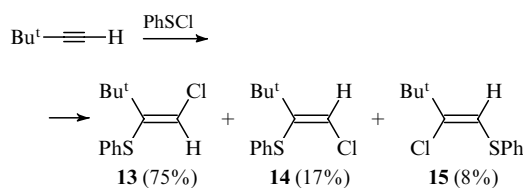
Table 1. Yields of the adducts **11** and **12** prepared by sulfenylation of but-1-yne and phenylacetylene.³⁵

R ¹	R ²	Solvent	Yield (%)	
			11	12
Ph	4-Me	EtOAc	100	0
	4-Me	CHCl ₃	65	35
	4-Me	AcOH	29	71
	4-NO ₂	EtOAc	85	15
	4-NO ₂	CHCl ₃	65	35
	4-NO ₂	AcOH	20	80
	4-NO ₂	MeCN	67	33
	2-NO ₂	EtOAc	57	43
	2-NO ₂	CHCl ₃	45	55
	2-NO ₂	AcOH	11	89
Et	4-NO ₂	EtOAc	100	0
	4-NO ₂	AcOH	100	0
	2-NO ₂	EtOAc	80	20
	2-NO ₂	CHCl ₃	67	33
	2-NO ₂	AcOH	58	42

adducts, while the dissociation into a chloride anion and an organic cation yields Markownikoff products.

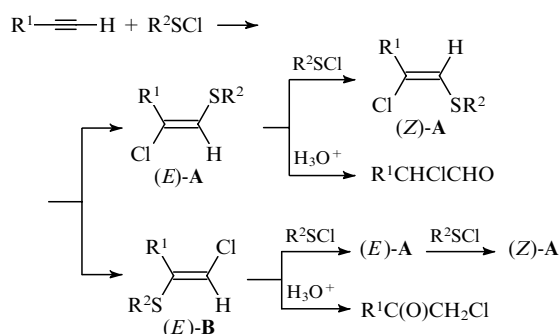
Catalytic amounts of trifluoroacetic acid and hydrogen chloride added to the reaction mixture have different effects on the structures and ratios of the reaction products of *p*-nitrobenzenesulfonyl chloride with phenylacetylene in ethyl acetate.³⁷ In the presence of hydrogen chloride, the ratio of Markownikoff and anti-Markownikoff *trans*-isomers changes simultaneously with the formation of *cis*-isomers. It has been found³⁷ that *cis*-isomers are formed as a result of isomerisation of the original *trans*-adducts. It is noteworthy that the nature of the acid influences neither the course of the reaction of but-1-yne with *p*-nitrobenzenesulfonyl chloride nor the ratio of the isomers formed.

The formation of *cis*-isomers in the chlorosulfenylation of certain alkynes has been observed earlier.³⁸ *cis*-Addition products have also been obtained in the reaction of benzenesulfonyl chloride with *tert*-butylacetylene.³⁹



These studies have shown that compounds **13** and **14** are converted into a thermodynamically more stable isomer **15** upon heating or UV irradiation in benzene.

Later, it was found^{40,41} that reactions of sulfonyl chlorides with alkynes are *trans*-stereospecific and afford a mixture of Markownikoff [adduct (*E*)-A] and anti-Markownikoff products

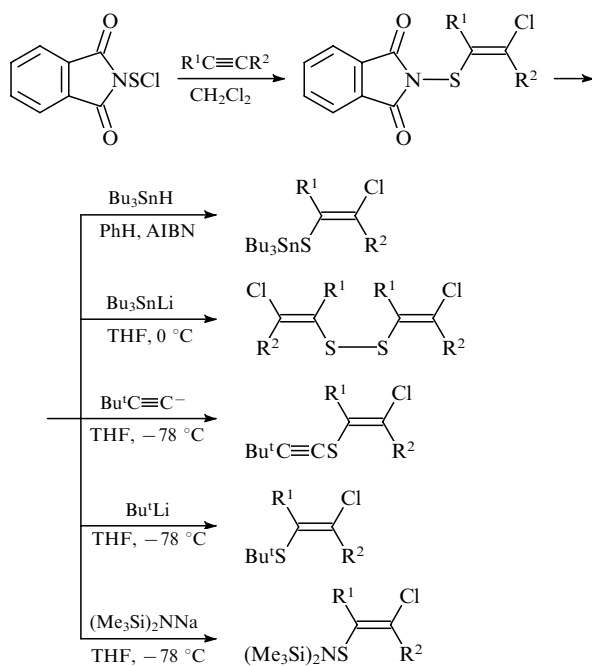


R¹ = Prⁱ, Buⁿ, Bu^t, Ph; R² = Me, C₆H₄Me-*p*, C₆H₄Cl-*p*.

[adduct (*E*)-**B**] which are converted into Markownikoff *cis*-isomers (*Z*)-**A** in the presence of an excess of sulfenyl chloride or catalytic amounts of trifluoroacetic acid.

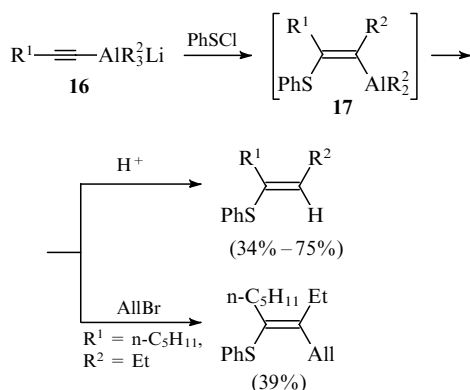
Aldehydes and ketones can in principle be prepared^{40,41} from β -chlorovinyl sulfides synthesised upon acid hydrolysis.

A method for electrophilic sulfonylation of alkynes with phthalimidosulfonyl chloride, which can be regarded as a synthetic precursor of sulfenic acid derivatives, has been developed.⁴² The nucleophilic substitution of the phthalimide group at the sulfur atom enables the preparation of hitherto unavailable vinyl sulfides and alkenesulfenamides. Some of them manifest pesticidal and bactericidal activities.¹¹



$\text{R}^1 = \text{R}^2 = \text{Me, Ph}$; $\text{R}^1 = \text{Bu}^n, \text{R}^2 = \text{H}$; $\text{R}^1 = \text{Ph, R}^2 = \text{H}$;
AIBN is azobisisobutyronitrile.

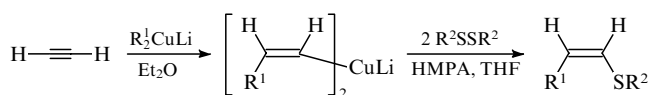
Yet another convenient approach to the synthesis of vinyl sulfides has been described.⁴³ Complexes **16** formed in the reaction of lithium acetylides with trialkylaluminium were used as the starting substrates. The reactions of these complexes with benzenesulfonyl chloride afford the intermediates **17** which yield vinyl sulfides upon hydrolysis or on treatment with allyl halides.



$\text{R}^1 = \text{n-C}_5\text{H}_{11}$; $\text{R}^2 = \text{Me, Et, Bu}^i, \text{n-C}_8\text{H}_{17}$; $\text{R}^1 = \text{n-C}_{10}\text{H}_{21}, \text{R}^2 = \text{Et}$.

The formation of side products, such as $\text{R}^1\text{C}\equiv\text{CR}^2$, $\text{R}^1\text{C}\equiv\text{CSPH}$, PhSSPH and PhSR^2 , is a disadvantage of this reaction.

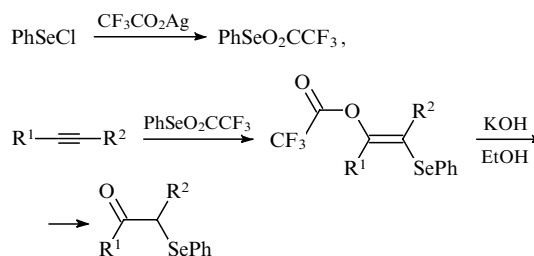
Vinyl sulfides can also be synthesised in a reaction of acetylene with alkylolithium cuprates.⁴⁴



$\text{R}^1 = \text{Et, Bu}^n, \text{n-C}_7\text{H}_{15}$; $\text{R}^2 = \text{Me, Bu}^i, \text{Ph, Bn}$;
HMPA is hexamethylphosphoramide.

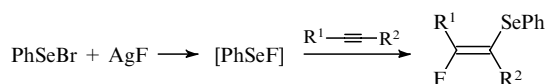
It is of note that in many studies devoted to electrophilic addition various selenium and tellurium derivatives were investigated along with sulfenyl chlorides. Thus reactions of areneselenenyl and arenesulfonyl chlorides containing 4-MeO, 4-Me, 4-Cl, 4-Br, 3-Br, 4-NO₂ and 3-NO₂ groups in the benzene ring with various unsaturated compounds have been studied.⁴⁵ It was shown⁴⁶ that the addition of sulfonyl and selenenyl halides (Hal = Cl, Br) to the triple bond of 1,4-dichlorobut-2-yne and subsequent dehydrohalogenation can be used for the synthesis of novel 1,3-disubstituted butadienes.

It was found⁴⁷ that reactions of areneselenenyl chloride and bromide with silver trifluoroacetate yield reactive complexes which are added to alkynes to give α -arylseleno-substituted esters. Hydrolysis of the latter yields α -arylseleno-substituted ketones.



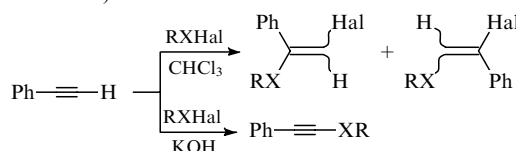
$\text{R}^1 = \text{Ph}$; $\text{R}^2 = \text{H, Me}$; $\text{R}^1 = \text{R}^2 = \text{Et}$.

Later,⁴⁸ fluoroselenenylation of a vast variety of alkyl- and dialkyl acetylenes was performed using sonication of an alkyne–phenylselenenyl bromide–silver fluoride mixture.



$\text{R}^1 = \text{R}^2 = \text{Et, Pr, Bu, Ph}$; $\text{R}^1 = \text{Et, R}^2 = \text{Ph}$;
 $\text{R}^1 = \text{Pr, iso-C}_5\text{H}_{11}, \text{R}^2 = \text{Me}$.

The addition of sulfonyl, selenenyl and tellurenyl halides to phenylacetylene has been studied and their reactivities have been compared.⁴⁹ It was shown that the reaction rate decreases in the following order: $\text{AlkSHal} > \text{AlkSeHal} > \text{AlkTeHal}$. If the reaction is carried out in chloroform, a mixture of addition products is formed, whereas addition–elimination products are formed under conditions of phase-transfer catalysis (KOH–crown ether–PhMe).

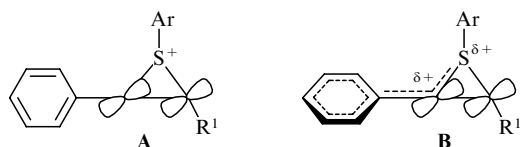


$\text{R} = \text{Me, Et, Pr}^i, \text{Bu}^n$; $\text{X} = \text{S, Se, Te}$; $\text{Hal} = \text{Cl, Br, I}$.

Much attention in the majority of papers devoted to reactions of sulfonyl chlorides with alkynes is given to the nature of reaction intermediates. The reaction of 2,4-dinitrobenzenesulfonyl chloride with 1-phenyl-prop-1-yne in CHCl_3 yields exclusively *trans*-addition products; the reaction mixture contains 94% of the Markownikoff adduct.⁵⁰ It was found that this reaction is second order and occurs in two steps. The first, rate-determining step is the formation of a cyclic intermediate (a thiirenium ion); the second step consists of its opening. The second reaction is *trans*-stereo-

specific rather than regioselective. The predominance of one of the isomers in the reaction mixture testifies to a non-symmetry of the cyclic intermediate.

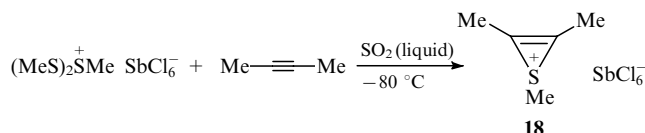
Further studies^{51–54} of chlorosulfonylation of substituted acetylenes by sulfonyl chlorides in various solvents, *e.g.*, tetrachloroethane,^{51,52} acetic acid⁵³ and SO₂ (see Ref. 54), revealed that the effects of the alkyl substituents at the triple bond on the rate of ArSCL addition are adequately described by the Taft correlation equation. Steric factors prevail over electronic ones only in the case of *tert*-butyl-substituted alkynes. The effects of aryl substituents at the triple bond are not so unambiguous. The data obtained^{51–54} have made it possible to propose a theory for the cyclic structure of the reaction intermediate **A** and to postulate the role of the benzene ring in the delocalisation of the positive charge in the thiirenium ion (structure **B**) (see also Refs 17 and 20).



More recent studies⁵⁵ into kinetic isotope effects of the solvent in addition of 4-chlorobenzenesulfonyl chloride to alkenes and alkynes in AcOH and AcOD corroborated the earlier proposed mechanism.^{50–54}

The kinetic aspects of reactions of arylacetylenes and styrenes with arenesulfonyl chlorides have been studied in detail; the rate constants and the activation barriers have been established.^{56,57}

The isolation of trimethylthiirenium hexachloroantimonate (**18**) formed in a reaction of di(methylthio)methylsulfonium hexachloroantimonate with an excess of but-2-yne provided direct evidence for the role of thiirenium intermediates in the addition of sulfonyl chlorides to acetylenes.⁵⁸ This salt retained stability in liquid SO₂ at temperatures up to –60 °C.



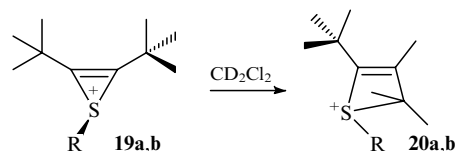
The ¹H NMR and ¹³C spectra of compound **18** and the corresponding spectra of 2,3-diethyl-1-methylthiirenium ion isolated from hex-3-yne could be recorded.⁵⁸

The use of alkynes containing bulkier substituents, *e.g.*, [di(*tert*-butyl)acetylene, 3-methyl-1-phenylbut-1-yne and 3,3-dimethyl-1-phenylbut-1-yne] increased the stabilities of thiirenium ions, and 1-methyl-2-phenyl-3-(*tert*-butyl)thiirenium and 1-methyl-2,3-di(*tert*-butyl)thiirenium hexachloroantimonates and tetrafluoroborates were isolated as white crystals at 20 °C.^{59,60} The structures of 1-methyl-2,3-di(*tert*-butyl)thiirenium hexachloroantimonate, tetrafluoroborate and hexafluorophosphate were established using X-ray diffraction analysis.⁶¹ The

nucleophilic stereo- and regiospecific Markownikoff attack of the chloride ion on the sulfur atom of the thiirenium ring in the absence of stabilising non-nucleophilic anions (SbCl₆[–], BF₄[–]) yields the corresponding (*E*)-chlorovinyl sulfides.⁶⁰

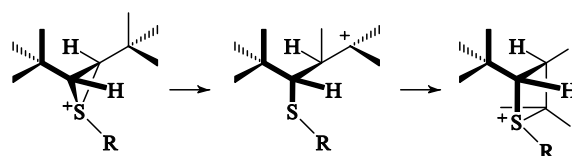
The structures, stabilities, reactivities and rearrangements of thiirenium and thiiranium ions have been studied by a group of Italian investigators.^{62–66}

¹H NMR studies have shown⁶² that compounds **19a,b** containing thiirenium rings are quantitatively isomerised in deuteriodichloromethane into thietene derivatives **20a,b** within several hours.

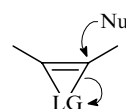


R = Me (**a**), C₆H₄Cl-*p* (**b**).

It is believed^{63,64} that the rearrangement mechanism (S_N2-Vin) of thiirenium cations is similar to that of their saturated analogues, *viz.*, thiiranium ions.



The S_N2-Vin mechanism implies an attack of the nucleophile (Nu) lying in the plane of the molecule from the side opposite to the leaving group (LG). This results in the formation of a planar transition state which resembles that in S_N2.

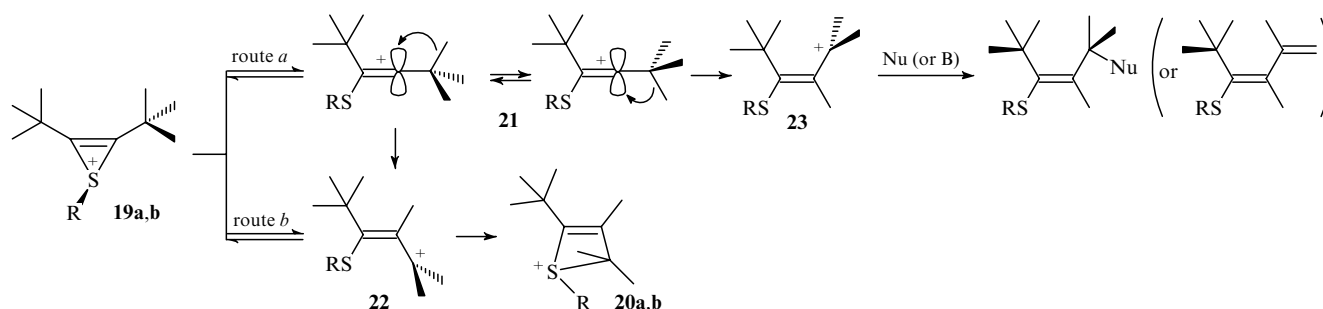


Theoretically, the rearrangements of the thiirenium ion may proceed according to two routes (Scheme 1, routes *a* and *b*). Route *a* leads to the linear intermediate **21** for which a 1,2-methyl shift is possible. This shift yields *Z*- and *E*-isomers of carbenium ions **22** and **23**. It is of note that only one of these isomers, *viz.*, the isomer **22**, can be converted into thietene derivatives **20a,b**, whereas the second ion (isomer **23**) reacts with a nucleophile or a base to give addition or dissociation products. Route *b* is no other than the S_N2-Vin mechanism, which yields exclusively compounds **20a,b**.

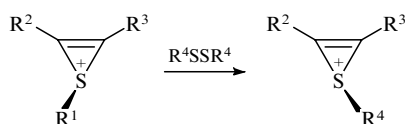
The quantitative conversion of compounds **19a,b** into compounds **20a,b** is in favour of a rearrangement according to route *b*.

Later, it was found⁶⁵ that thiirenium hexachloroantimonates react with dialkyl disulfides at 20 °C to yield substitution products.

Scheme 1

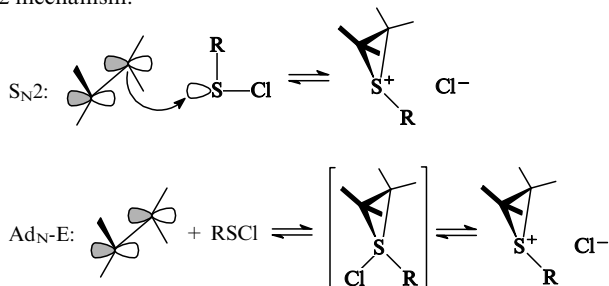


R = Me (**a**), C₆H₄Cl-*p* (**b**); B is a base.

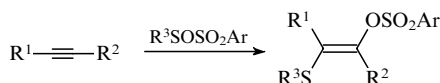


$R^1 = \text{Me}, \text{C}_6\text{H}_4\text{Cl-}p$; $R^2, R^3 = \text{Bu}^t, \text{Ph}, \text{Ad}$ (Ad is adamantyl);
 $R^4 = \text{Me}, \text{Et}, \text{Pr}^i$.

Steric hindrances created by substituents at the sulfur atom and the carbon atoms of the thiirenium ring strongly affect the reaction rate. An analysis of the kinetic data has led to a hypothesis that attack on the sulfur atom occurs in the plane of the ring parallel to the C=C bond. Such a direction corresponds to the maximum electron density of the lowest unoccupied molecular orbital (LUMO) of the thiirenium ions (*ab initio* calculations data^{65,66}). Taking into account the effects of the substituents on the reaction rate and the calculated data, Fachini *et al.*⁶⁵ put forward a hypothesis that nucleophilic substitution at the sulfur atom in thiirenium ions follows an addition–dissociation mechanism *via* a sulfurane-like intermediate rather than the $\text{S}_{\text{N}}2$ mechanism.



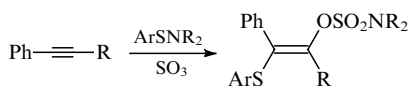
o-Sulfonylarene sulfonates react with unsaturated hydrocarbons like sulfonyl chlorides to give *trans*-adducts (1 : 1).⁶⁷



$R^1 = \text{H}, \text{Me}$; $R^2 = \text{Ph}$; $R^3 = \text{Me}, \text{Ph}, 4\text{-MeC}_6\text{H}_4$;
 $\text{Ar} = 2,4,6\text{-(NO}_2)_3\text{C}_6\text{H}_2, 2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3, 4\text{-NO}_2\text{C}_6\text{H}_4, 4\text{-BrC}_6\text{H}_4$.

The orientation of substituents in the products of this type of reaction suggests that their mechanisms are similar to the mechanism of addition of sulfonyl halides to the triple bond.

The addition of weak electrophilic reagents to the multiple bonds requires the presence of activating reagents. A search for such agents has led to a vast variety of novel sulfonylating systems. Thus the use of readily available inorganic Lewis acids, *e.g.*, sulfuric anhydride and its complexes with pyridine,⁶⁸ thionyl and sulfonyl chlorides⁶⁹ as well as phosphorus halides and oxyhalides,^{70,71} zinc, magnesium and tin iodides,⁷² as activating reagents has made it possible to perform electrophilic addition reactions with sulfenamides and sulfonates,^{68–72} thio- and dithio-bisamines,^{69,70,72,73} disulfides⁷⁴ and many other sulfur-containing compounds, which themselves cannot add to the multiple bond. This has made it possible to extend the range of reactants and to develop novel methods for one-step synthesis of substituted vinyl sulfides which cannot be prepared by other methods. The activation of arenesulfenamides by sulfuric anhydride is one of such reactions.^{68,75}



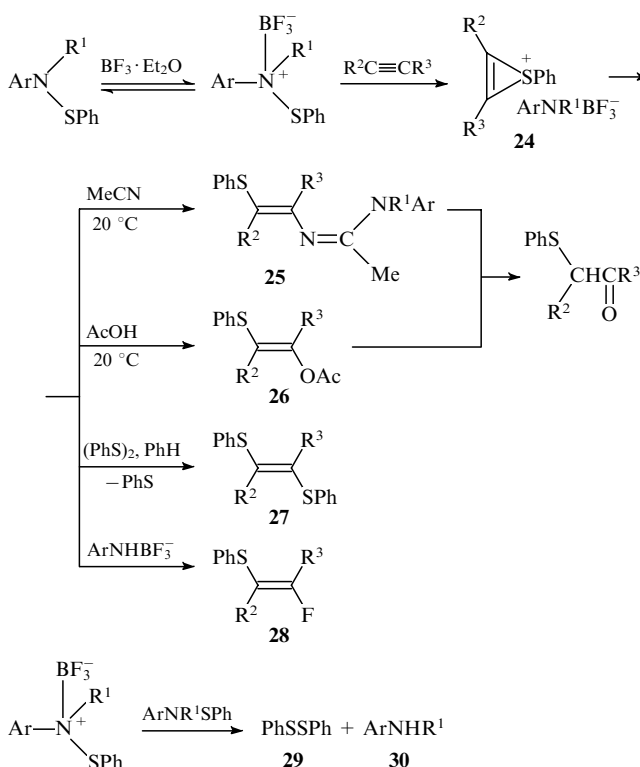
$R = \text{H}$ (13%–15%), Ph (12%–14%).

It is sulfonyl sulfamate that is formed upon insertion of sulfuric anhydride at the sulfur–nitrogen bond that adds to the

triple bond. However, this reaction has not gained wide acceptance for the preparative synthesis of aryl β -sulfamatovinyl sulfides because of low yields and side processes.

The studies by Italian investigators^{76–83} were devoted to reactions of arenesulfenamides with unsaturated compounds in the presence of boron trifluoride. The synthetic applications of these reactions have been investigated. It was found in particular that the reaction of *p*-nitrobenzenesulfenamide with alkynes in the presence of boron trifluoride (20 °C) can be used for the preparative synthesis of β -substituted vinyl derivatives. It was found that BF_3 converts inactive arenesulfenamides into highly reactive species (presumably into reactive BF_3 –sulfenamide complexes⁷⁸) which undergo nucleophilic substitution at the sulfur atom to give thiirenium ions **24** (Scheme 2).

Scheme 2



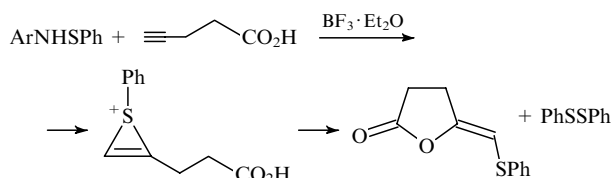
$\text{Ar} = \text{Ph}, \text{C}_6\text{H}_4\text{Me-}p, \text{C}_6\text{H}_4\text{OMe-}p, \text{C}_6\text{H}_4\text{Cl-}p, \text{C}_6\text{H}_4\text{NO}_2\text{-}p$;
 $R^1 = \text{H}, \text{Me}$; $R^2 = \text{H}$; $R^3 = \text{Pr}^n, \text{Bu}^n, \text{Bu}^t, \text{Ph}$;
 $R^2 = \text{Me}$; $R^3 = \text{Me}, \text{Pr}$; $R^2 = R^3 = \text{Et}$.

The nucleophilic opening of the thiirenium ring in the intermediate **24** is *trans*-stereospecific and highly regioselective and yields vinyl sulfides according to the Markownikoff rule. The ring opening in nucleophilic solvents, such as acetonitrile^{75,78} and acetic acid,⁷⁹ is accompanied by formation of β -amidino- (**25**) and β -acetoxyvinyl sulfides (**26**),^{78,79} respectively, in good yields. Compounds **25** and **26** are convenient starting reagents for the synthesis of β -oxosulfides.⁸²

The addition of PhSSPh in non-nucleophilic solvents, such as dichloromethane and benzene, results in bisulfides **27**.⁸⁰ Alkyl-substituted acetylenes react with thiirenium cations in the presence of ArNHBF_3^- to give β -fluorovinyl sulfides **28**.⁸⁰ In all cases studied, diphenyl disulfide **29** and substituted anilines **30** are formed along with the main reaction products.

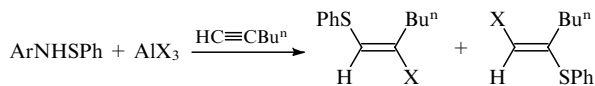
The reaction of boron trifluoride-activated *p*-nitrobenzenesulfenamide with alkyl- and arylacetylenes in chlorobenzene (80 °C) occurs *trans*-stereospecifically and regioselectively and yields β -fluorovinyl sulfides **28**.⁸⁰

If the sulfenamide molecule contains nucleophilic sites involved in the opening of the thiirenium ring, heterocyclic compounds are formed.⁸³



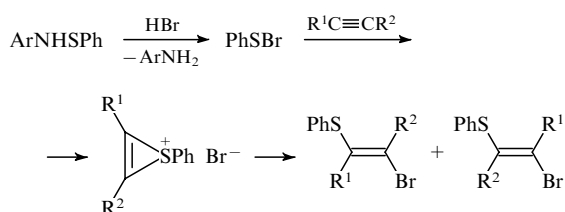
Ar = C₆H₄NO₂-*p*.

The activation of arenesulfenamides by Lewis acids, such as AlCl₃ or AlBr₃, affords *E*-isomers of β-halogenovinyl sulfides.⁸³



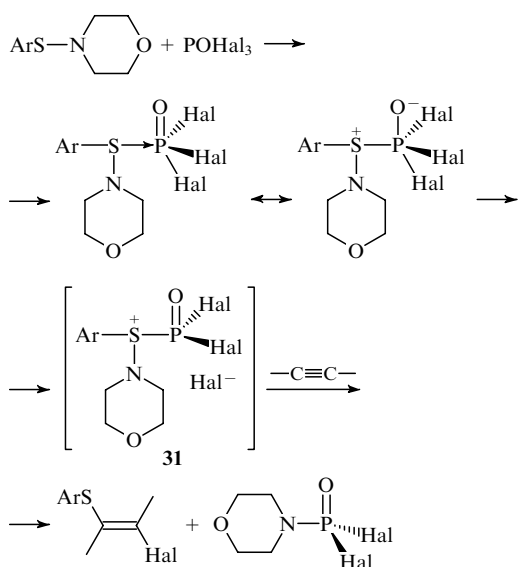
X = Cl (55%), Br (35%).

The *p*-nitrobenzenesulfenamide–HBr system was recommended as a bromosulfenylating reagent.^{83,84} The sulfenyl bromide formed adds *trans*-stereoselectively and regioselectively to alkenes and alkynes against the Markownikoff rule. The mechanism of this reaction seems to be similar to the mechanism of addition of sulfenyl chlorides to multiple bonds.



Ar = C₆H₄NO₂-*p*; R¹ = H: R² = Prⁿ, Buⁿ, Bu^t, Ph;
R¹ = Me, R² = Ph; R¹ = Et: R² = Et, Ph.

Arenesulfenamides activated by phosphorus oxyhalides are promising sulfenylating reagents for alkynes.^{85–87} It is believed that the role of reactive sulfenylating species in this reaction is played by complexes of the type **31**; the positive charge on the sulfur atoms is higher than that on the starting sulfenamide.⁸⁸



Ar = Ph, C₆H₄NO₂-*p*, C₆H₄NO₂-*o*; Hal = Cl, Br.

The complexes **31** react with alkynes according to the electrophilic substitution mechanism. In the final addition step, the halogen atom of phosphorus oxyhalide acts as a nucleophile; this reaction yields β-halogenovinyl sulfides.^{71,85,87}

According to kinetic data, no sulfenyl chlorides are formed in reactions of arenesulfenamides with phosphorus oxychlorides. The data presented in Table 2 suggest that the reaction time of

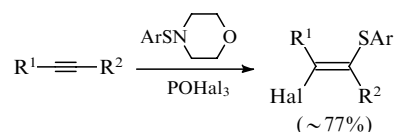
Table 2. Addition of sulfenyl chlorides and arenesulfenamides to unsaturated hydrocarbons.

Alkyne or alkene	Sulfenyl chloride or arenesulfenamide	Activating reagent	Reaction time	Ref.
H ₂ C=CH ₂	2,4-(NO ₂) ₂ C ₆ H ₃ SCl	—	16 h	89
HC≡CH	2,4-(NO ₂) ₂ C ₆ H ₃ SCl	—	5 days	25
EtC≡CH	4-NO ₂ C ₆ H ₄ SCl	—	12 h	35
PhC≡CH	2-NO ₂ C ₆ H ₄ SCl	—	30 days	35
PhC≡CH	2-NO ₂ C ₆ H ₄ SN	POCl ₃	20 h	87
C ₆ H ₁₃ C≡CH	4-NO ₂ C ₆ H ₄ SN	POCl ₃	1.5 h	85, 87

POCl₃-activated *N*-(4-nitrophenylthio)morpholine with alkynes is much less than that of nonactivated sulfenyl chlorides.

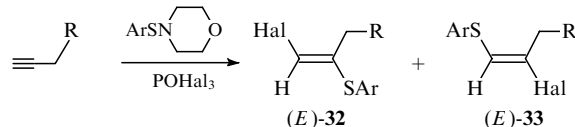
The rates of dehydration of sulfenyl bromides into disulfides often exceed the rates of their addition to multiple bonds, which decreases the yields of the final products.^{22,90} At the same time, arenesulfenamides activated by phosphorus oxybromide react readily with alkenes,⁷¹ alkynes^{85,86} and dienes⁸⁸ to give high yields of bromosulfides. No new stable compounds are formed upon mixing of sulfenamides with POCl₃ or POBr₃ in dichloromethane in the absence of alkenes (TLC data).⁸⁷

The reaction of POHal₃-activated arenesulfenamides with acetylene and its derivatives in dichloromethane chloride is *trans*-stereospecific.^{85,87}



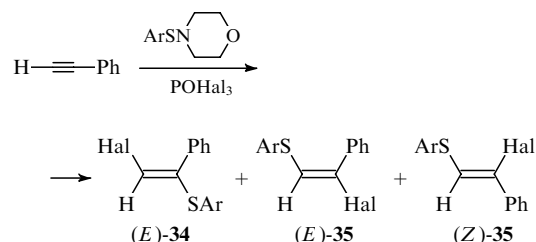
R¹ = R² = H, Prⁿ; Ar = Ph, C₆H₄NO₂-*p*, C₆H₄NO₂-*o*, C₆H₄Me-*p*;
Hal = Cl, Br.

The addition of arenesulfenamides to terminal alkynes yields a mixture of isomeric aryl β-halogenovinyl sulfides (total yield 50%–90%), which represent addition products formed both against (**32**) and according to the Markownikoff rule (**33**).^{85,87} The anti-Markownikoff product **32** prevails.



R = Prⁿ, Buⁿ, n-C₅H₁₁; Ar = C₆H₄NO₂-*p*, C₆H₄NO₂-*o*.

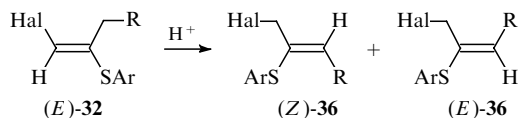
The *cis*-isomers of aryl β-halogenovinyl sulfides (*Z*)-**35** are formed in reactions of arenesulfenamides with phenylacetylene along with the *trans*-addition products (*E*)-**34** and (*E*)-**35**.^{85,87}



Ar = Ph, C₆H₄NO₂-*p*, C₆H₄NO₂-*o*; Hal = Cl, Br.

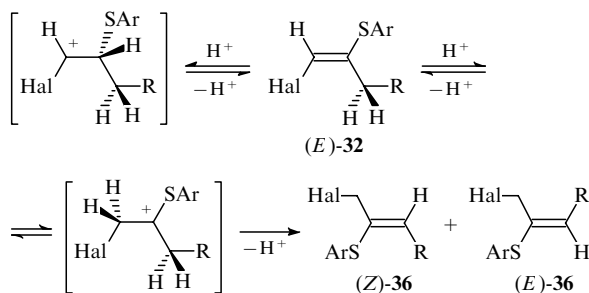
2-Arylthio-1-halogenoalk-1-enes (*E*)-**32**, the products of anti-Markownikoff halogenosulfenylation of terminal alkynes,

undergo isomerisation into 2-arylthio-1-halogenoalk-2-enes (*E*)-**36** and (*Z*)-**36** under the action of catalytic amounts of protic acids.^{85, 87}



R = Prⁿ, Buⁿ, n-C₅H₁₁; Ar = C₆H₄NO₂-*p*, C₆H₄NO₂-*o*.

The following mechanism for the acid-catalysed isomerisation of 2-arylthio-1-halogenoalk-1-enes has been proposed:⁸⁶



R = Prⁿ, Buⁿ, n-C₅H₁₁.

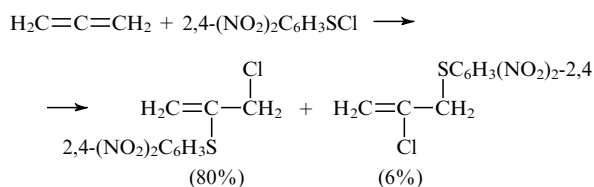
Here, the protonation of the double bond in compounds **32** and subsequent deprotonation with the formation of a mixture of isomeric alkenes is the key step. The ratio of the isomers is determined by their relative thermodynamic stabilities.

It should be emphasised that only one of the initially formed halogenovinyl sulfides, *viz.*, the anti-Markownikoff isomer **32**, undergoes isomerisation under conditions of acid catalysis to give a mixture of *E*- and *Z*-isomers of 2-arylthio-1-halogenoalk-2-ene **36** with the predominance of the *Z*-isomer. Under these conditions, the Markownikoff adduct (*E*)-**33** is partly converted into a *Z*-isomer. Apparently, the formation of more thermodynamically stable alkenes is the driving force of the isomerisation in both cases.

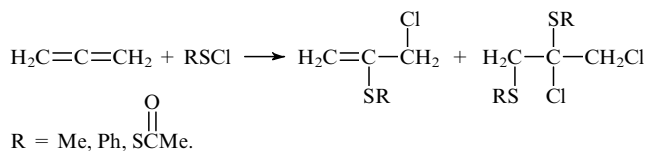
2. Electrophilic sulfonylation of allenes

It is of note that reactions of sulfonyl halides with conjugated and non-conjugated dienes do not usually afford vinyl sulfides; therefore, electrophilic sulfonylation of these unsaturated compounds is not considered in this review. Here, only the sulfonylation of cumulated dienes, *i.e.*, allenes, will be discussed in detail.

In 1960, Jacobs and Johnson⁹¹ established that 2,4-dinitrobenzenesulfonyl chloride reacted with allene to give 3-chloro-2-(2,4-dinitrophenylthio)prop-1-ene as an addition product (yield ~ 80%). In the authors' opinion, this reaction occurs regioselectively with the anti-Markownikoff attack by the electrophilic sulfur atom on the central atom of the allenic system. Such a regioselectivity is not unexpected, since the addition of sulfonyl chlorides to alkenes largely occurs against the Markownikoff rule. Small amount of a compound with a tentative structure of 2-chloro-3-(2,4-dinitrophenylthio)prop-1-ene could be isolated.

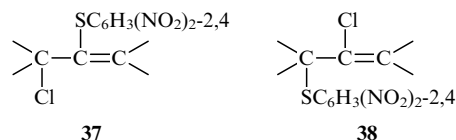


Later, it was found⁹² that reactions of allenes with other sulfonyl chlorides always yield mainly anti-Markownikoff products. Bisadducts (up to 20%) are formed in small amounts along with monoadducts.

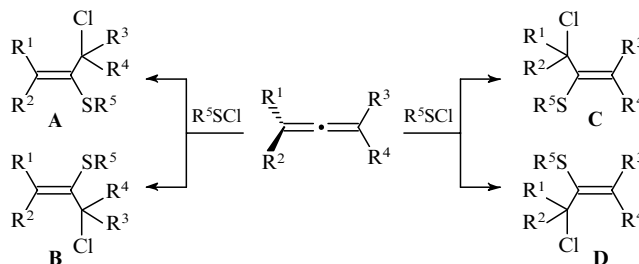


A classical mechanism including the intermediate formation of the episulfonium ion has been proposed for these reactions.^{91, 92}

The addition of 2,4-dinitrobenzenesulfonyl chloride to various allenes has been studied.⁹³ It was shown that adducts of the type **37** containing a 2,4-dinitrophenylthio group at the double bond are the main reduction products; regioisomeric compounds of the type **38** were formed in smaller amounts and with only some of the substrates studied.

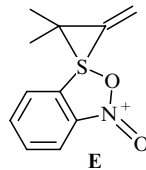


In early studies, stereochemical aspects of reactions of sulfonyl chlorides with allene derivatives have not been considered; the first paper⁹⁴ devoted to the detailed analysis of this problem appeared only in 1979. Evidently, addition of a sulfonyl chloride to a tetrasubstituted allene containing four different substituents may afford four stereoisomers **A–D**.



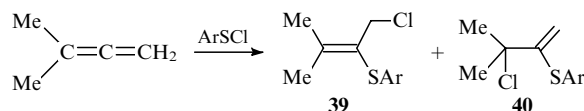
It was shown⁹⁴ that electrophilic species always attack only the central atom of the allenic system. The stereochemistry of the addition reaction is determined by steric factors, which favour the predominant formation of (*E*)-isomers. The formation of Markownikoff products of the type **38** was explained by the rearrangement of the adducts of the type **37** formed under conditions of kinetic control.

The kinetics of addition of sulfonyl chlorides to allenes and the effects of substituents in sulfonyl chlorides on the rate and stereochemistry of the reaction have been studied.^{95–97} It was found that steric and electronic factors have little effect on the addition of sulfonyl chlorides to allenes.⁹⁷ It was therefore concluded that steric effects are critical only in the case of arenesulfonyl chlorides containing *ortho*-substituents in the benzene ring. It was even suggested⁹⁶ that specific intermediates **E** are formed in reactions of allenes with *o*-nitrobenzenesulfonyl chloride; however, this hypothesis has not been strictly proven.



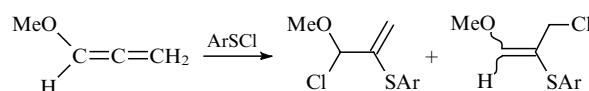
In a more recent study,⁹⁸ using the example of the reaction of 1,1-dimethylallene with various sulfonyl chlorides it was shown that the ratios of the products **39** and **40** strongly depend on the reaction conditions and the nature of the aryl substituent in the sulfonyl chloride. Thus the adduct **39** is mainly formed in C₂H₂Cl₄ at 20 °C, whereas the adduct **40** is mainly formed in CH₂Cl₂ at –78 °C. As far as the nature of the aryl substituent in a sulfonyl

chloride is concerned, the adducts **40** are almost exclusively formed for Ar = Ph, 4-MeC₆H₄, while a mixture of the adducts **39** and **40** (2:1) is formed for Ar = 4-ClC₆H₄ and 2,4-(NO₂)₂C₆H₃, respectively.



Ar = Ph, 4-MeC₆H₄, 4-ClC₆H₄, 2,4-(NO₂)₂C₆H₃.

Similar conclusions were made with respect to the reaction of 1-methoxyallene with arenesulfonyl chlorides.⁹⁹ Treatment of chlorosulfonylation products of 1-methoxyallene with water yields α -arylthiosubstituted aldehydes.

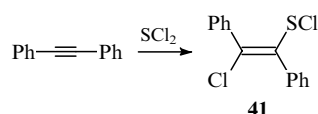


Ar = 4-MeC₆H₄, 4-ClC₆H₄, 2,4,5-Me₃C₆H₂.

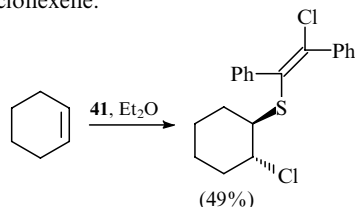
Chloro- and bromoselenenylation reactions of allenes¹⁰⁰ were found to be very similar to the sulfonylation reactions.

3. Electrophilic vinylsulfonylation of alkenes

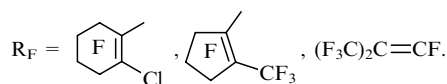
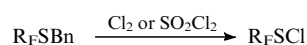
As mentioned above, the addition of sulfur dichloride to alkynes usually results in divinyl sulfides. However, it was possible to isolate¹⁷ an intermediate product, *viz.*, 2-chloro-1,2-diphenylethenesulfonyl chloride (**41**), upon treatment of diphenylacetylene with SCl₂ and to investigate its properties.



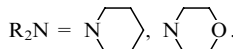
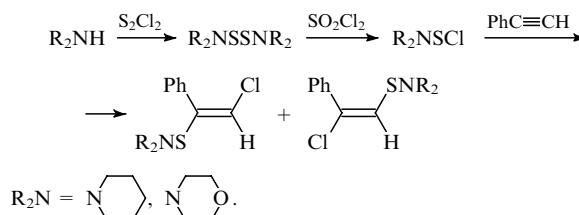
It was shown, in particular, that this compound adds to cyclohexene.



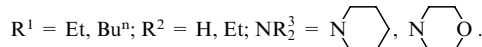
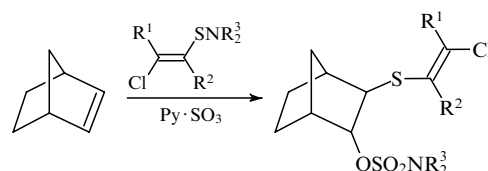
There is very little evidence on reactions of α,β -unsaturated sulfonyl chlorides, which may be attributed to their inaccessibility and low stability.¹⁷ It is known, for example, that chlorination of some benzyl, perfluoroalkenyl and perfluorocycloalkenyl sulfides results in the chlorolysis of the C–S bond with retention of the double bond in the fluorinated substituents.¹⁰¹ The perfluoroalkene- and perfluorocycloalkenesulfonyl chlorides formed are efficient sulfonylating reagents, which easily add to multiple bonds.



Later, a new method for electrophilic vinylsulfonylation of alkenes by ethenesulfenamides in the presence of activating reagents, such as sulfuric anhydride and its complexes with tertiary amines (Py·SO₃, Et₃N·SO₃) or ammonia, was proposed.^{102, 103} Ethenesulfenamides were prepared from readily available dithiobisamines.

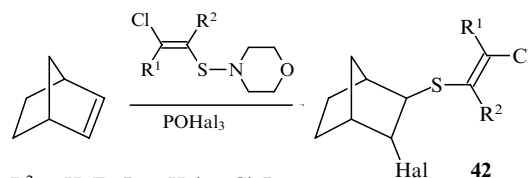


The insertion of sulfotrioxide into the S–N bond of vinylsulfenamides has enabled the sulfamatovinylsulfonylation of some cage alkenes.^{102, 103}

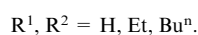
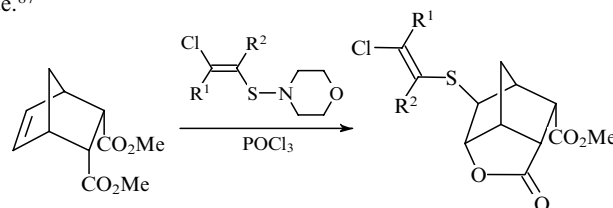


An attempt to perform vinylsulfonylation of conformationally labile alkenes, such as cyclohexene and hex-1-ene, was unsuccessful, since the products formed appeared to be extremely unstable.¹⁰⁴

Similar results were obtained in the electrophilic vinylsulfonylation of alkenes by ethenesulfenamides activated by phosphorus oxyhalides.⁸⁷ Thus stable compounds (*e.g.*, product **42**) were obtained in reactions with cage alkenes (norbornene, norbornadiene, camphene, dimethyl 5,6-di-*endo*-norbornenedicarboxylate), while the vinylsulfonylation products of conformationally labile alkenes, *e.g.*, cyclohexene, could not be isolated because of their low stability.⁸⁷

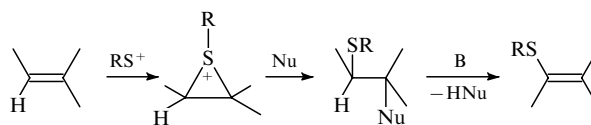


The feasibility of conjugate addition was demonstrated in the example of a reaction of phosphorus oxychloride-activated ethenesulfenamides with dimethyl 5,6-di-*endo*-norbornenedicarboxylate.⁸⁷



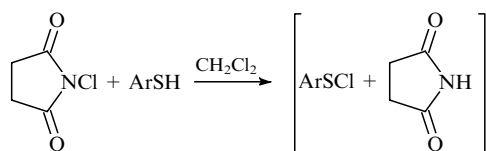
4. Electrophilic sulfonylation of alkenes with subsequent α,β -elimination

Electrophilic sulfonylation of alkenes with subsequent α,β -elimination is yet another convenient method for the synthesis of vinyl sulfides. Both reaction steps are carried out under mild conditions and give fairly good yields of reaction products.^{105–109}

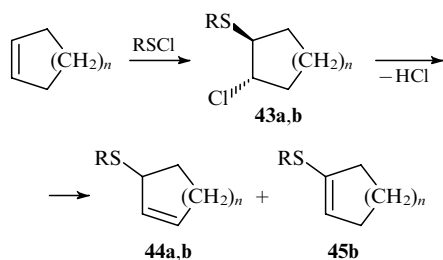


B is a base.

Sulfenyl halides are usually precursors of reactive species RS^+ . Dehydrohalogenation is carried out with different bases, *e.g.*, sodium methoxide, potassium *tert*-butoxide (in diethyl ether, DMSO or THF),¹⁰⁵ triethylamine,^{106, 107} sodium carbonate,¹⁰⁸ potassium fluoride (in DMSO or THF)¹⁰⁹ and silver trifluoroacetate.¹⁰⁹ A convenient method for the *in situ* synthesis of starting arenesulfonyl chlorides, which excludes isolation and purification of sulfenyl chlorides, has been described.¹⁰⁸



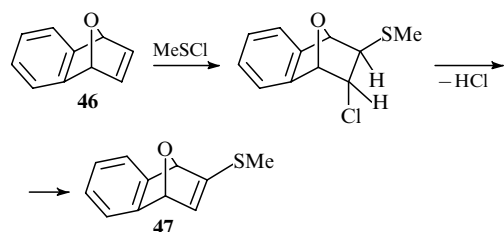
There are two possible directions of elimination, which yield allylic or vinylic sulfides. In many cases, the formation of allylic rather than vinylic sulfides is more preferable. Thus it has been shown¹⁰⁵ that 1-alkylthio-2-chlorocyclohexanes **43a** undergo elimination with great difficulty and give exclusively 3-alkylthiocyclohexenes **44a**. The formation of alkenes containing an allylic RS group proves that *anti*-elimination is more preferable for cyclohexane systems with a diaxial arrangement of the hydrogen atom [at C(3)] and the leaving group (the chlorine atom). The proton at C(1) is in a *gauche*-position relative to the chlorine atom in any conformation of cyclohexane **43a** which is unfavourable for the elimination.¹⁰⁵



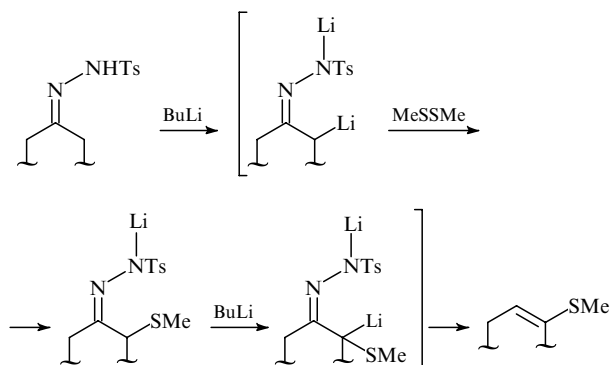
$n = 2$ (a), 1 (b); $R = \text{Me, Et}$.

On the other hand, the dehydrohalogenation of sulfenylation products of cyclopentene **43b** occurs more smoothly and yields a mixture of 3-alkylthio- (**44b**) and 1-alkylthiocyclopentenenes (**45b**) (1 : 1). The equal probability of formation of allylic and vinylic thioethers suggests that *syn*-elimination is the most probable route for this system.

syn-Elimination is the only route for the chlorosulenylation products of the cage alkene **46**, which gives a quantitative yield of vinyl sulfide **47**.



Dialkyl disulfides can also be used as electrophilic sulfenylating species. Their reactions with *C,N*-lithiated tosylhydrazones and subsequent α,β -elimination lead regioselectively to vinyl sulfides; the yields of the latter depend on the nature of substituents in the starting tosylhydrazones.¹¹⁰

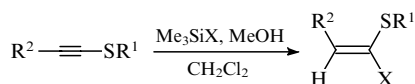


III. Synthesis of α -halogenovinyl sulfides by electrophilic hydrohalogenation of alkynyl sulfides

Regioselective addition of hydrogen halides (HCl, HBr, HI) to alkynyl sulfides is also related to the class of electrophilic reactions. However, it can be placed in a separate group, because it is not accompanied by the formation of a new C–S bond. This reaction is the simplest and most efficient approach to the synthesis of α -halogenovinyl sulfides (see Ref. 111 and references cited therein).

Reactions of aqueous hydrohalic acids (37% HCl, 48% HBr, 51% HI) or saturated hydrogen halides in benzene with alkynyl sulfides are regioselective and yield mixtures of *Z*- and *E*-isomers that are difficult to separate.

The recently developed procedure for the synthesis of α -halogen-substituted vinyl sulfides and vinyl ethers by addition of a hydrogen halide generated *in situ* from a trimethylsilyl halide in dry methanol at low temperature is devoid of this defect.¹¹² This reaction is highly regioselective and affords nearly quantitative yields of vinyl sulfides.¹¹³

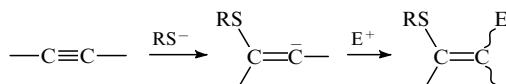


$R^1 = \text{Me, Ph}$; $R^2 = \text{Bu}^n, n\text{-C}_7\text{H}_{15}, \text{cyclo-C}_6\text{H}_{11}, \text{BnCH}_2$;
 $X = \text{Cl, Br, I}$.

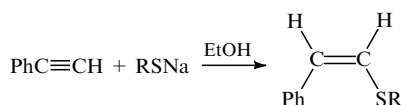
IV. Methods for the synthesis of vinyl sulfides based on nucleophilic reactions

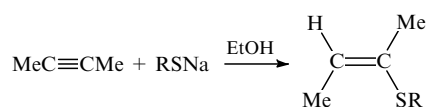
1. Nucleophilic thiolation of alkynes

Nucleophilic thiolation of alkynes is one of the oldest, but nevertheless valuable methods for the synthesis of nonsymmetrical unsaturated sulfides. On the whole, this reaction can be described by the following scheme:



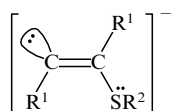
Thiols and alkali metal thiolates are most commonly used as thiolating reagents^{114–116} with proton as the electrophile. The use of thiolates enables the synthesis of stereochemically pure products. Thus reactions of phenylacetylene and but-2-yne with various thiolates occur exclusively as *trans*-addition.¹¹⁶





R = Me, C₆H₄Me-*p*.

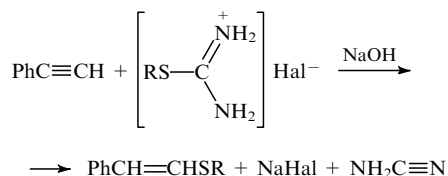
Such a stereoselectivity can be attributed to the fact that this reaction proceeds *via* a carbanion in which the negative charge on the carbon atom (the free electron pair) and the lone electron pairs on the sulfur atom tend to be arranged as far as possible from one another.



R¹ = H, Me, Ph; R² = Me, C₆H₄Me-*p*.

Thiols add to non-symmetrical alkynes in a non-stereoselective manner.¹¹⁷

A reaction described by Trofimov and co-workers¹¹⁸ can also be regarded as a convenient method for the synthesis of alkyl (β-substituted vinyl) sulfides. It was found that thiolation of phenylacetylene by thiolate anions generated from *S*-alkylisothiuronium salts under the action of alkali occurs smoothly under mild conditions in both protic (ethanol) and aprotic (DMSO, DMF, *N*-methylpyrrolidone) solvents. The yields of alkyl styryl sulfides in dimethyl sulfoxide reached 98%.

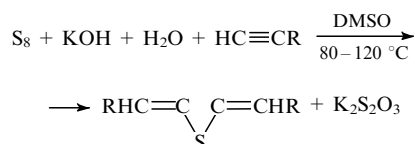


R = Me, Prⁿ, All; Hal = Br, I.

The *in situ* generation of thiolate anions from *S*-alkylisothiuronium salts in the presence of alkali excludes the use of free thiols and, as a consequence, the occurrence of competing free-radical reactions.¹¹⁸

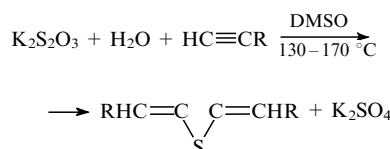
Alternative methods for the *in situ* generation of thiols include decomposition of xanthates and dithiocarbonates¹¹⁹ and alkylthioimidinium salts.¹²⁰ Electrochemical generation of thiolate anions is carried out in the absence of alkali. It is possible to synthesise sulfides by this method in up to 97% yields.¹²¹

The salient advantages of alkyne thiolation by elemental sulfur in the presence of potassium hydroxide and catalytic amounts of water required for the proton transfer are simplicity of the procedure, availability of reactants and high yields of divinyl sulfides.¹²²



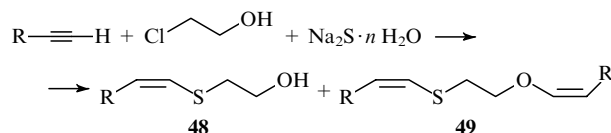
R = H, Ph.

The reaction is carried out at 80–120 °C exclusively in aprotic dipolar solvents (DMSO, HMPA), which are rather stable on heating in the presence of strong bases. In other solvents (*e.g.*, dioxane), the reaction does not occur or proceeds with low efficiency. It was shown¹²² that at higher temperatures (130–170 °C) the potassium thiosulfate formed can also react with acetylene thereby increasing the yield of the final product.



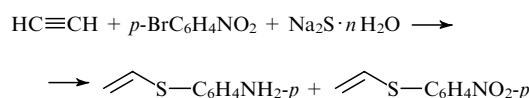
R = H, Ph.

The reactions of acetylene and its derivatives with ethylene chlorohydrin and aqueous sodium sulfide afford 2-hydroxyethyl vinyl sulfides **48** and 2-vinyloxyethyl vinyl sulfides **49**.¹²³



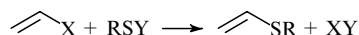
R = H, Ph.

If the reaction in DMSO is carried out in a flow reactor, it can be stopped at the stage of formation of sulfide **48**. Taking into account the accessibility of the starting reagents, this synthetic procedure can sometimes be rather convenient despite low (5%–20%) yields of the reaction products. This approach was used in the synthesis of *p*-nitrophenyl and *p*-aminophenyl vinyl sulfides.¹²³



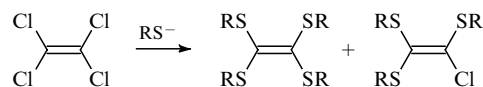
2. Nucleophilic substitution at the unsaturated carbon atom

Nucleophilic substitution at the unsaturated carbon atom is yet another popular synthetic procedure.



Vinyl halides (X = Cl, Br, I) are most commonly used as substrates, while thiols¹²⁴ and alkali metal,^{125–127} copper¹²⁸ and magnesium⁶ thiolates serve as a source of thiolating species.

Thus tetrachloroethylene reacts exothermally with sodium thiolates as suspensions in aprotic solvents (*e.g.*, DMF, DMSO, HMPA) at atmospheric pressure to afford tetra[alkyl(aryl)thio]ethylenes in 60%–80% yields. Tri[alkyl(aryl)thio] derivatives are formed as side products.¹²³



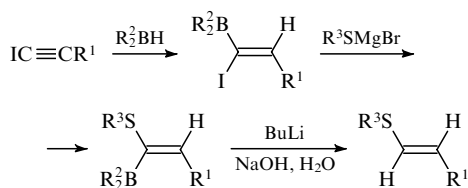
R = Et, Prⁿ, Prⁱ, C₆H₁₃, C₈H₁₇, (CH₂)₂OH, Ph.

Substitution at the double bond occurs more easily in the presence of catalysts, such as Ni (see Ref. 126) and Pd complexes.¹²⁷ Nonpolar aprotic solvents (benzene, toluene, dimethoxyethane) are used in catalytic reactions, whereas alcohols are usually used in the absence of catalysts.

Reactive thiolating species can also be generated *in situ*, if the reaction is carried out in alkaline media. Alkali metal hydroxides (NaOH, KOH)¹²⁹ or potassium carbonate in acetone¹²⁴ are most often used as deprotonating reagents.

Similar reactions were used in the synthesis of vinyl selenides.¹²⁶ High (70%–80%) yields of vinyl sulfides and vinyl selenides is a salient advantage of this method.

A highly stereospecific method for the synthesis of vinyl sulfides from alkynes, boranes and magnesium thiolates has been developed.⁶ This approach can be used for the synthesis of a broad range of vinyl sulfides.



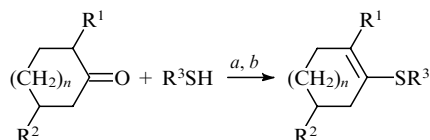
$\text{R}^1 = \text{Bu}^n, n\text{-C}_6\text{H}_{11}$; $\text{R}^2 = \text{Me}_2\text{CHCHMe}$; $\text{R}^3 = \text{Bu}^n, \text{Bu}^t, \text{Ph}, \text{Bn}$.

All reagents used in this reaction are readily available and relatively inexpensive; moreover, all reactions can be carried out in a one-pot procedure.

3. Addition of thiols to the C=O bond of carbonyl compounds

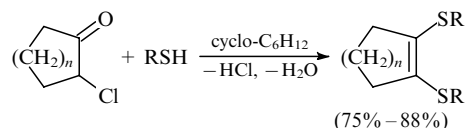
In recent years, the method based on addition of thiols to ketones under conditions of acid catalysis followed by dehydration of the hemiketals formed has been widely used for the synthesis of vinyl sulfides. Both protic¹³⁰ and Lewis acids [AlCl_3 ,¹³¹ P_2O_5 (see Refs 131 and 132), *etc.*] are used as catalysts.

Thus heating of a mixture of a cyclic ketone, a thiol and a catalyst in benzene afforded the corresponding vinyl sulfides in up to 80% yields.¹³²

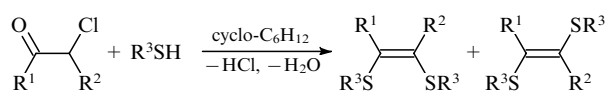


$\text{R}^1, \text{R}^2 = \text{H}, \text{Me}, \text{Pr}^i$; $\text{R}^3 = \text{Et}, \text{Pr}^n$; $n = 1, 2, 3$;
(a) $\text{PhH}, \text{AlCl}_3, \Delta, 15 \text{ min}$; (b) $\text{PhH}, \text{P}_2\text{O}_5, \Delta, 1 \text{ h}$

This approach¹³³ was used for the synthesis of di(alkylthio)alkenes from a series of cyclic and acyclic α -chloro ketones; the former are starting compounds in [4+2]-cycloaddition reactions used for the synthesis of novel acetylene compounds.¹³⁴



$n = 1, 2$; $\text{R} = \text{Et}, \text{Pr}, \text{Bu}$.

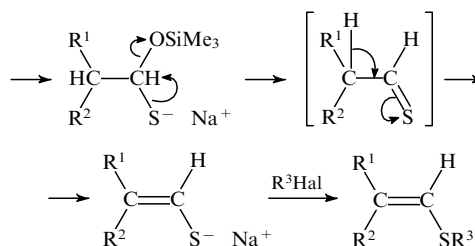
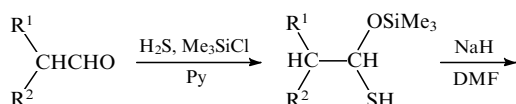


$\text{R}^1 = \text{Me}, \text{Et}, \text{Pr}^n, \text{Bu}^n, \text{Bu}^t, \text{Ph}$; $\text{R}^2 = \text{H}, \text{Me}, \text{Et}, \text{Pr}^n$; $\text{R}^3 = \text{Et}, \text{Pr}, \text{Bu}$.

The Michael addition of thiols to cyclic α, β -unsaturated carbonyl compounds, such as 3-oxo-2,3-dihydrothiophene 1,1-dioxides, with subsequent opening of the ring also affords vinyl sulfides (see Section VI).

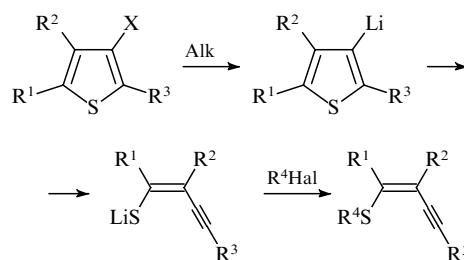
4. Nucleophilic vinylthiolation

Much attention has recently been given to methods based on nucleophilic vinylthiolation. In many reactions, nucleophilic species are generated *in situ*, *e.g.*, upon treatment of aldehydes with Me_3SiCl and H_2S in pyridine.¹³⁵

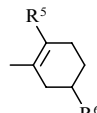


$\text{R}^1 = \text{H}$; $\text{R}^2 = \text{Me}, \text{Et}, \text{Pr}^i$; $\text{R}^1 - \text{R}^2 = (\text{CH}_2)_5$;
 $\text{R}^3 = \text{Ph}(\text{CH}_2)_2, \text{Bn}, \text{cyclo-C}_6\text{H}_{11}, \text{Pr}^n, \text{Bu}^n$; $\text{Hal} = \text{Cl}, \text{Br}, \text{I}$.

The vinylthiolating species can easily be generated through the opening of the thiophene ring under the action of organolithium compounds^{136, 137} or metals (Li, Na) in liquid ammonia in the presence of alcohols.¹³⁸

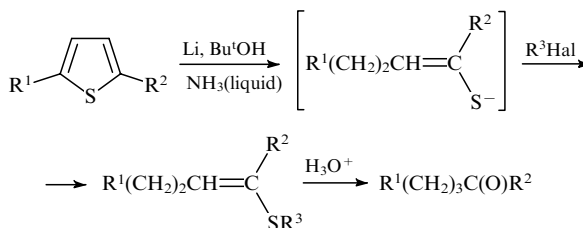


$\text{X} = \text{Br}, \text{I}$; $\text{R}^1 = \text{H}, \text{Me}, \text{Et}, \text{Bu}^t, \text{Ph}$; $\text{R}^2 = \text{H}, \text{Me}$; $\text{R}^3 = \text{H}, \text{Me}, \text{Et}$,

Bu^t, Ph ,  ($\text{R}^5 = \text{Me}, \text{R}^6 = \text{H}$; $\text{R}^5 = \text{Pr}^i, \text{R}^6 = \text{Me}$);

$\text{Alk} = \text{Et}, \text{Bu}$; $\text{R}^4 = \text{Et}, \text{Bu}, \text{CO}_2\text{Et}, \text{CH}_2\text{CO}_2\text{Me}, \text{Bn}$; $\text{Hal} = \text{Cl}, \text{Br}$.

The cleavage of the thiophene ring takes place under the action of solvated electrons; subsequent alkylation of the thiolate formed gives rise to various unsaturated sulfides which are further converted into the corresponding ketones.^{138, 139}

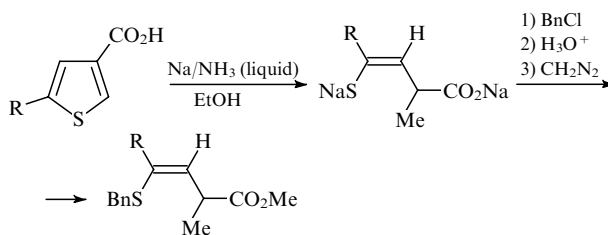


$\text{R}^1 = \text{H}, \text{Me}$; $\text{R}^2 = \text{Me}, \text{Et}, \text{C}_9\text{H}_{19}, (\text{CH}_2)_2\text{NEt}_2, (\text{CH}_2)_4\text{NEt}_2, (\text{CH}_2)_6\text{NEt}_2$; $\text{R}^3 = \text{Me}, \text{Et}, \text{Bu}^n, (\text{CH}_2)_4\text{CO}_2\text{Et}, \text{CH}_2\text{COPh}$,

$\text{CH}_2\text{CH}(\text{Me})\text{OH}, \text{CHCH}_2\text{OH}, \text{CH}_2\text{CHCH}_2\text{O}$; $\text{Hal} = \text{Cl}, \text{Br}, \text{I}$.

In the last step, epoxides can be used as alkylating reagents.¹³⁹

The opening of the thiophene ring in thiophene-3-carboxylic acids¹⁴⁰ results in enolthiolate; its benzylation and subsequent esterification give high yields of alkyl (Z)-4-benzylthio-2-methyl-alk-3-enoates.



$\text{R} = \text{H}, \text{Me}$.

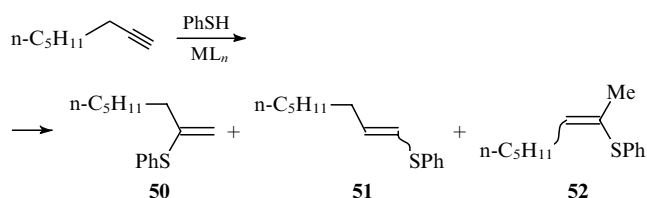
V. Methods for the synthesis of vinyl sulfides based on reactions occurring *via* radical intermediates

1. Addition of thiols to alkynes

The addition of thiyl radicals to multiple carbon–carbon bonds is a well-known reaction, which has found wide acceptance in organic synthesis. Normally, thiyl radicals are generated from thiols or disulfides by thermolysis, photolysis¹⁴¹ or treatment with radical initiators.^{142, 143} The radical addition of thiols to alkynes occurs regioselectively against the Markownikoff rule and yields a mixture of stereoisomers.

Reactions of thiols with acetylenes are catalysed by nickel,^{15, 144} platinum,^{144–146} palladium,^{144, 146} rhodium^{144, 147, 148} and ruthenium complexes.¹⁴⁸

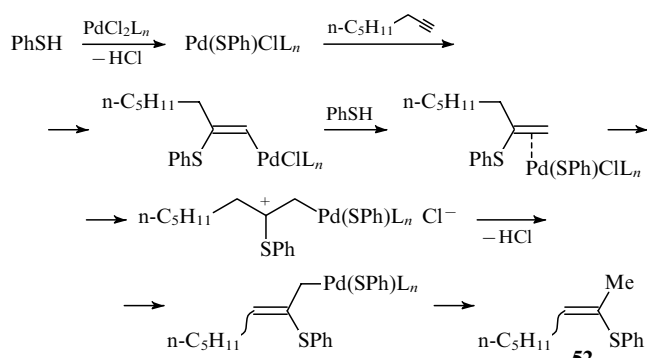
The addition of benzenethiol to various alkynes has been studied in detail.^{144, 147} The effects of the structure of the starting substrate, the nature of the catalyst and the solvent on the yields of reaction products have been investigated. Using the reaction of oct-1-yne with benzenethiol as an example, it was demonstrated¹⁴⁷ that the addition follows the Markownikoff rule in the presence of palladium(II) acetate and yields compound **50**. However, reactions catalysed by other divalent palladium complexes, *e.g.*, PdCl₂(PhCN)₂ or PdCl₂(MeCN)₂, afford the anti-Markownikoff product **51** and the double-bond-migration product **52**.



ML_n = Pd(OAc)₂, PdCl₂(PhCN)₂, PdCl₂(MeCN)₂, Pd(PPh₃)₄, Pt(PPh₃)₂(CH₂=CH₂), RhH(CO)(PPh₃)₃, RhCl(PPh₃)₃.

Both Markownikoff and anti-Markownikoff adducts are formed in the presence of RhH(CO)(PPh₃)₃ and the Wilkinson complex RhCl(PPh₃)₃. However, in-depth studies of the addition of benzenethiol to oct-1-yne in the presence of RhCl(PPh₃)₃ have shown that in ethanol only the *E*-isomer of the anti-Markownikoff product is formed. Thus different regioisomers can be prepared from the same starting compounds (alkyne and thiol) by varying the solvent and the catalyst.

It was also found that the double bond in addition products of thiols to alkynes migrates in the presence of metal complex catalysts. Thus the Markownikoff adducts (*e.g.*, compound **50**) formed in reactions of alkynes containing propargyl hydrogen atoms with benzenethiol in the presence of PdCl₂(PhCN)₂ are further isomerised under the action of the catalyst to give alkenes of the type **52** containing a non-terminal double bond. The following reaction scheme has been proposed:



L = PhCN, n = 2.

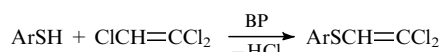
It was also shown that isomerisation does not take place if alkynes contain no propargyl hydrogen atoms. Moreover, the presence of an amino group in the alkyne molecule prevents the migration of the double bond.

The addition of various thiols to substituted acetylenes in the presence of a ruthenium complex catalyst has been studied.¹⁴⁹ This reaction yielded a mixture of *cis*- and *trans*-alkenes; their ratio varied depending on the nature of substituents in the starting alkyne.

2. Substitution at the unsaturated carbon atom

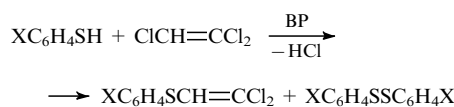
The replacement of the halogen at the double bond by an arylthio or an alkylthio group yields vinyl sulfides and may occur as both nucleophilic substitution and *via* radical intermediates. These reactions are usually carried out in the presence of initiators (*e.g.*, benzoyl peroxide^{146, 150, 151}) or upon UV irradiation.^{152, 153} In this case, the formation of side products (diaryl disulfides) is insignificant.

For the first time, radical chlorovinylation of benzenethiol and 4-toluenethiol with trichloroethylene in the presence of benzoyl peroxide (BP) was used for the synthesis of aryl β,β-dichlorovinyl sulfides in 1966.¹⁵⁴



Ar = Ph, C₆H₄Me-*p*.

It has been shown¹⁵¹ that aryl β,β-dichlorovinyl sulfides are formed as the main products in reactions of trichloroethylene with arenethiols irrespective of the nature of the substituent in the benzene ring.¹⁵¹ Diaryl disulfides are formed as side products, but their content is not very high. Saturated sulfides of the type ArS(Cl)CHCHCl₂ are not formed at all.



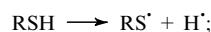
X = H, 4-MeO, 4-Me, 3-Me, 4-Cl.

Free-radical chlorovinylation of aliphatic thiols by trichloroethylene also results in β,β-dichlorovinyl sulfides.¹⁵¹ UV irradiation of reaction mixtures is optimum for thermolysis; the trichloroethylene : thiol ratio varies from 3 : 1 to 4 : 1.

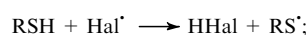
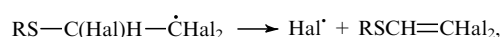
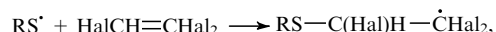
Reactions of 1,2-dichloroethylene with thiols upon UV irradiation yield β-chlorovinyl sulfides RSCH=CHCl and disulfides RSCH=CHSR in addition to saturated products.¹⁵¹

A similar UV-induced reaction of tribromoethylene with benzenethiol yields β,β-dibromovinyl phenyl sulfide.¹⁵³ A general scheme for the substitution of the thiol group for the halogen atom in trichloro- and tribromoethylenes has been proposed:^{151, 153}

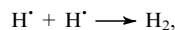
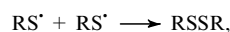
Initiation



Chain growth



Chain termination



It should be noted that some reactions of thiols with tribromoethylene yield aryl monobromovinyl sulfides as side products,¹⁵³ similar reactions with trichloroethylene do not give aryl monochlorovinyl sulfides.¹⁵¹

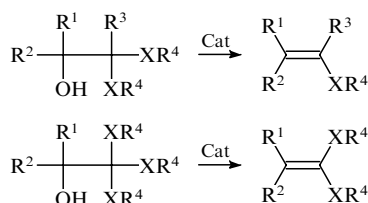
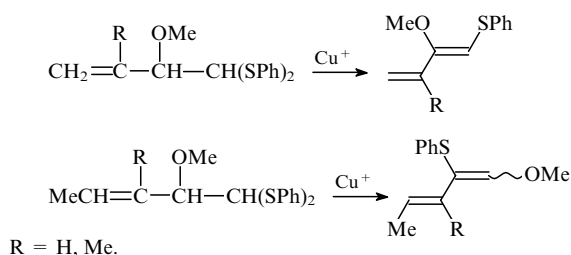
VI. Miscellaneous methods for the synthesis of α,β -unsaturated sulfides

1. Elimination from sulfur-containing compounds

a. α,β -Elimination from dithioacetals and dithioketals

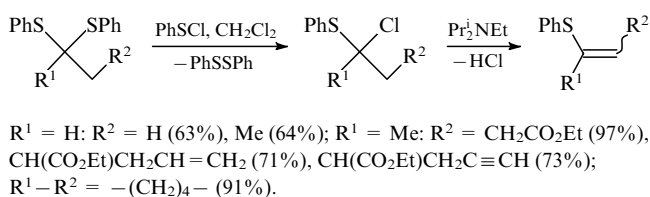
The method for the synthesis of vinyl sulfides based on α,β -elimination of thiols from dithioacetals and dithioketals has found wide acceptance owing to the ease of preparation of the starting compounds. Usually, thiols are eliminated from dithio compounds by treatment with Simmons–Smith reagent,¹⁵⁵ phosphorus iodides,¹⁵⁶ mono- or divalent copper salts^{157,158} or mercury trifluoroacetate.¹³² The main disadvantage of these reactions is their nonstereoselectivity.

Phosphorus iodides, copper salts and thionyl chloride are widely used for α,β -elimination of thiols from acetals, α -hydroxy-, α -alkoxythio(seleno) ketals and orthothioesters.^{159,160}



X = S, Se; R¹ = n-C₅H₁₁, n-C₇H₁₅, cyclo-C₃H₅, Ph; R² = H, Me; R³ = H; R⁴ = Me, Ph; Cat = P₂I₄, PI₃, CuY, CuY₂, SOCl₂.

Yet another approach to the conversion of dithioketals into vinyl sulfides has been proposed.¹ It consists of treatment of thioacetals and thioketals with benzenesulfonyl chloride and subsequent elimination of HCl from the α -chloro sulfide formed.

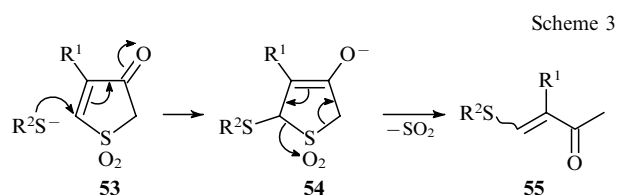


High yields and applicability of this method for a broad range of substrates make it extremely promising.

b. Elimination of sulfur dioxide from the Michael adducts of thiols to 3-oxo-2,3-dihydrothiophene 1,1-dioxides

Boiling of 3-oxo-2,3-dihydroxythiophene 1,1-dioxide **53** (R¹ = H) with benzenethiol in toluene in the presence of catalytic amounts of pyridine results in the elimination of SO₂ and the formation of a 5:1 mixture of *Z*- and *E*-isomers of 4-phenylthiobut-3-en-2-one.¹⁶¹ In THF, this reaction occurs in the absence of a base.¹⁶² The reaction of substituted 3-oxo-2,3-dihydroxythiophene 1,1-dioxides with aliphatic thiols proceeds in a similar way.¹⁶²

Although the mechanism of this reaction has not been strictly proven, it is believed¹⁶² that it occurs as a cheletropic disrotatory conversion **53** → **54** (Scheme 3), although a two-step mechanism with the initial formation of the sulfinate anion and a subsequent loss of SO₂ is not excluded. Exclusive formation of the *E*-isomer of compound **55** (R¹ = H, R² = Ph) upon heating of the intermediate **54** in ethanol is the supporting evidence in favour of a

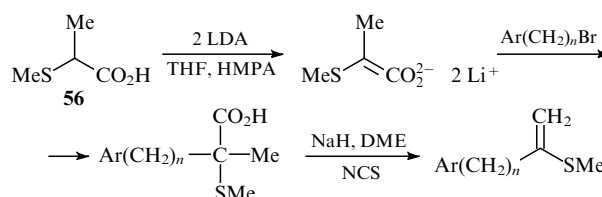


R¹ = H, Me; R² = Ph, Bu, (CH₂)₂CO₂Me.

concerted mechanism. The *Z*-isomers **55** are formed in subsequent conversions of *E*-isomers.

c. Decarboxylation of α -methylthiocarboxylic acid salts

Regioselective syntheses of terminal vinyl sulfides can be implemented using mild decarboxylation of (α -methyl)(α -methylthio)alkanoic acids **56** with *N*-chlorosuccinimide (NCS) and sodium hydride in dimethoxyethane (DME).¹⁶³

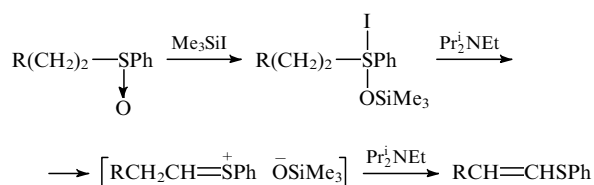


LDA is lithium diisopropylamide; Ar = Ph, 3-MeOC₆H₄, 3,4-(CH₂O₂)C₆H₃; n = 2–5.

No regioisomer with a non-terminal double bond was found in this reaction. However, it was concluded¹⁶³ that reactions in protic solvents, *e.g.*, Bu^tOH, lead to the reduction of the oxidative potential of *N*-chlorosuccinimide and the establishment of a rapid equilibrium between the regioisomers, as a result of which the regioselectivity of the reaction decreases.

2. Reduction of sulfoxides with subsequent α,β -elimination

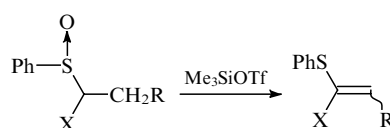
Reduction of sulfoxides to sulfides usually occurs under mild conditions and with good yields and does not require any complex equipment. Trimethylsilyl iodide in combination with bis(trimethylsilyl)amine or sterically hindered tertiary amines is one of the most efficient reagents for the reduction and subsequent α,β -elimination of sulfoxides.¹⁶⁴



R = n-C₆H₁₃.

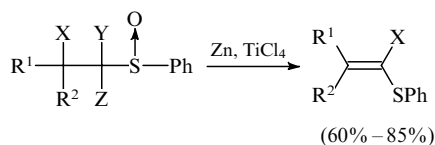
Treatment of α -chloroalkyl sulfoxides with trifluoroacetic anhydride and sodium iodide in acetone at low temperatures affords vinyl sulfides in high yields.²

Trimethylsilyl trifluoromethanesulfonate (Me₃SiOTf) can be used in the synthesis of α -cyano- and α -alkoxycarbonyl-substituted vinyl sulfides.⁵



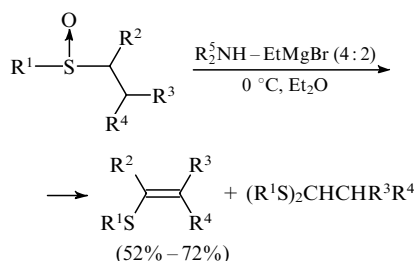
R = H, Et, Prⁿ, cyclo-C₆H₁₁; X = CN, CO₂R.

Sulfoxides containing a halogen or a hydroxy group in the α - and β -positions easily undergo reductive elimination in diethyl ether under the action of Zn and TiCl_4 .¹⁶⁵



$\text{R}^1, \text{R}^2 = \text{H, Alk, Ar}; \text{X} = \text{H, OH}; \text{Y} = \text{H, Cl, Br}; \text{Z} = \text{H, Cl}.$

A method for the reduction of sulfoxides containing hydrogen atoms in α - and β -positions was developed in 1995,¹⁶⁶ which involves their treatment with *in situ* generated magnesium amide $\text{Mg}(\text{NH}_2)_2$.

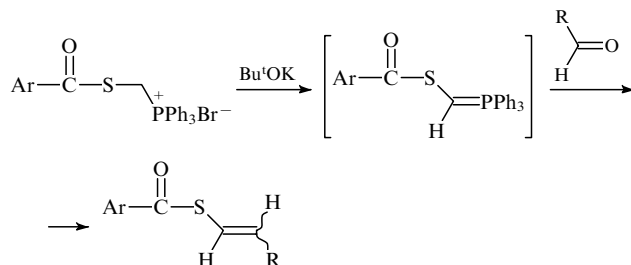


$\text{R}^1 = \text{Bu}^n, \text{Ph}, 4\text{-MeC}_6\text{H}_4; \text{R}^2 = \text{H, Me, Ph}; \text{R}^3 = \text{H, Me, Et, Ph};$
 $\text{R}^4 = \text{H, Me}; \text{R}_2^5\text{NH} = 2,2,6,6\text{-Me}_4\text{C}_5\text{H}_6\text{NH}, \text{Pr}_2^i\text{NH}.$

3. Methods for the synthesis of vinyl sulfides based on the Wittig–Horner and Peterson reactions

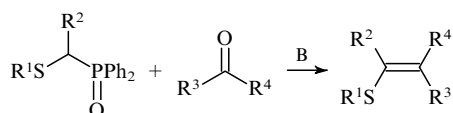
a. Synthesis of vinyl sulfides using the Wittig–Horner reaction

The Wittig reaction using sulfur-containing reagents can be used for the synthesis of vinyl sulfides.¹⁶⁷

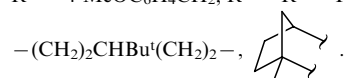


$\text{Ar} = \text{Ph}, 4\text{-MeC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4;$
 $\text{R} = \text{Me, Et, Ph}, 4\text{-NO}_2\text{C}_6\text{H}_4, \text{PhC}\equiv\text{C}, 2\text{-NO}_2\text{C}_6\text{H}_4\text{CH}=\text{CH}.$

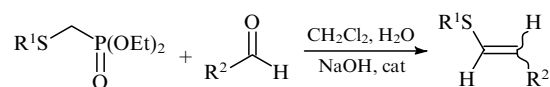
However, the Wittig–Horner reactions where phosphonates are used instead of phosphonium salts have found wider application in the synthesis of α,β -unsaturated sulfides.^{3, 168, 169} This reaction is carried out in the presence of strong bases, such as NaH (see Ref. 3) or Bu^nLi .^{168, 169}



$\text{R}^1 = \text{Me, Ph}; \text{R}^2 = \text{H, Et, Pr}^i, \text{Bn}; \text{R}^3 = \text{H}; \text{R}^4 = \text{Ph, n-C}_6\text{H}_{13},$
 $4\text{-MeOC}_6\text{H}_4, \text{PhCH}=\text{CH}, 3,4\text{-(CH}_2\text{O}_2\text{)}_2\text{C}_6\text{H}_3; \text{R}^3 = \text{Me},$
 $\text{R}^4 = 4\text{-MeOC}_6\text{H}_4\text{CH}_2; \text{R}^3 = \text{R}^4 = \text{Ph, Bn}; \text{R}^3 - \text{R}^4 = -(\text{CH}_2)_4-,$



Sometimes, these reactions require BF_3 for their completion.¹⁶⁹ They can also be carried out under conditions of phase-transfer catalysis.¹⁷⁰

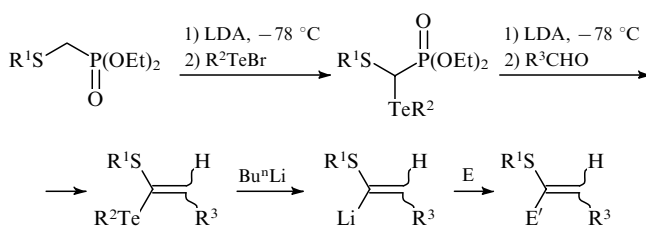


$\text{R}^1 = \text{Me, Ph}; \text{R}^2 = \text{Ph}, 4\text{-Me}_2\text{NC}_6\text{H}_4.$

Quaternary ammonium bases and crown-ethers are used as catalysts in phase-transfer reactions. In this case, the ratio of (*E*)- and (*Z*)-vinyl sulfides formed varies depending on the catalyst.¹⁷⁰

High yields of vinyl sulfides are an indisputable advantage of the given method; however, in some cases the synthesis of sulfur-containing Wittig reagents presents a complicated synthetic problem.

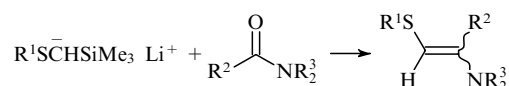
The use of the Wittig–Horner reaction enables the synthesis of some thio(telluro)acetals of substituted ketenes where the aryltelluro groups can be readily and selectively modified.¹⁷¹



$\text{R}^1 = \text{Me, Ph}; \text{R}^2 = \text{Ph}, \text{Bu}^n; \text{R}^3 = \text{H, Ph}, 2\text{-furyl}, 4\text{-MeC}_6\text{H}_4,$
 $4\text{-ClC}_6\text{H}_4, \text{Pr}^n, \text{Pr}^i; \text{E} = \text{H}_2\text{O, MeI, PhCHO}; \text{E}' = \text{OH (62\%),}$
 $\text{Me (86\%), PhCHOH (85\%).}$

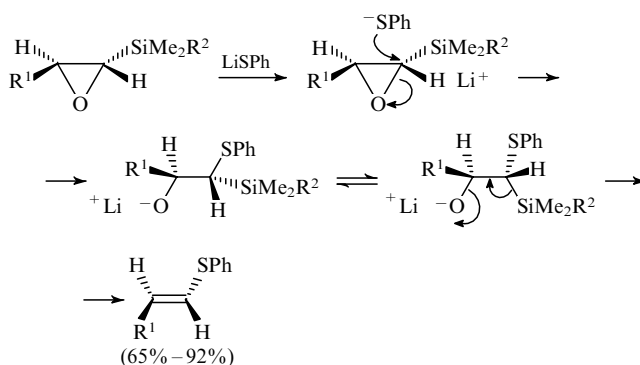
b. Synthesis of vinyl sulfides using the Peterson reaction

The Peterson reaction, *i.e.*, the synthesis of vinyl sulfides from α -metallo-silanes, plays an important role in organic synthesis. Thus lithium derivatives of arylthiomethyltrimethylsilanes react with ketones to give vinyl sulfides.¹⁷² Various carboxylic acid derivatives, *e.g.*, amides, can be used for the synthesis of β -substituted vinyl sulfides instead of ketones.

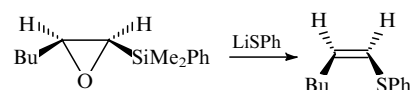


$\text{R}^1 = \text{Me, Ph}; \text{R}^2 = \text{H, Bu}^t, \text{Ph}; \text{R}_2^3 = \text{Me}_2, (\text{CH}_2)_2, (\text{CH}_2)_5.$

A method for the synthesis of vinyl sulfides has been developed which is based on the reaction of epoxysilanes with lithium phenylsulfide and subsequent Peterson *syn*- α,β -elimination.¹⁷³ This method is distinguished for high yields, regio- and stereo-specificity.



$\text{R}^1 = \text{H, Bu, Ph, SiMe}_3, \text{SiMe}_2\text{Ph}; \text{R}^2 = \text{Me, Ph}.$



VII. Conclusion

The choice of a method for the synthesis of vinyl sulfides is determined by the nature of the substrate as well as by the stability and availability of the starting reagents. Some of the methods considered in this review, e.g., the addition of sulfonyl chlorides to acetylenes or nucleophilic substitution for the thiolate ion, were developed as early as the middle of the last century, but are still widely employed owing to the simplicity of equipment and experimental procedures. However, the yields of such classical reactions are not always satisfactory, which stimulates the search for more complex, perhaps, but nevertheless more efficient methods for the synthesis of vinyl sulfides.

Among a variety of methods recently developed for the synthesis of vinyl sulfides, reactions of arenesulfenamides with alkynes in the presence of phosphorus oxyhalides hold especially great promise.^{69–74} The simplicity of equipment, the availability of starting reagents and high yields of reaction products make this method a reasonable alternative to the existing chloro- and bromosulfenylation procedures. Addition of thiols to alkynes in the presence of metal complex catalysts is yet another promising approach,^{15, 144–149} which allows regioselective sulfenylation of nonsymmetrical alkynes. The success of the synthesis of the target regioisomer depends on the choice of a metal complex catalyst.

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^d — *Chem. Heterocycl. Compd. (Engl. Transl.)*

Synthesis, some properties and structural features of 1,2-thiaphosphacyclanes

I L Odinets, N M Vinogradova, T A Mastryukova

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Abstract. Synthetic routes to 1,2-thiaphosphacyclanes bearing both tri- and tetracoordinate phosphorus atoms, and their reactivity and structural features based on data from X-ray diffraction analysis are discussed. Particular emphasis is placed on the rare case of ring-chain halogenotropic tautomerism in the series of 1,2-thiaphosphacyclanium salts and related compounds. The bibliography includes 107 references.

I. Introduction

In recent years, there has been an increase in the interest in the chemistry of heterocyclic compounds, development of synthetic routes and investigation of properties of novel types of heterocycles, mostly due to their practical applications, *e.g.*, in agrochemistry and pharmaceutical chemistry. In full measure, this applies to phosphorus-containing heterocyclic compounds. Noteworthy is the known peculiarity of phosphorus-containing heterocyclic compounds compared to their acyclic analogues, which is manifested in the unusual structures (conformational and stereochemical) of the reaction products. Cyclic phosphorus compounds are often invoked with the purpose of studying the mechanisms of chemical transformations of organophosphorus compounds, moreover, they are effectively used as synthons in organic synthesis. Phosphorus-containing heterocyclic compounds, in particular, phosphates, play an important role in biochemical processes.

Among fairly numerous phosphorus-containing heterocyclic compounds known presently, saturated and unsaturated phosphacyclanes¹ and polyheterophosphacyclanes^{2–6} have been investigated in most detail. General synthetic procedures have been proposed for the synthesis of 1,3,2-diheterophosphacyclanes based mostly on the interaction of phosphorus acid chlorides with nucleophiles (polyhydric alcohols, thiols and amines). Mono-

heterophosphacyclanes are represented in the literature mainly by 1,2-oxaphosphacyclanes. Basic publications concerning the synthetic routes to these compounds date from the 1960–1980. 1,2-Oxaphosphacyclanes have found wide industrial application, particularly as non-inflammable hydraulic fluids and plasticisers,^{7,8} additives to lubricants,⁹ flame retardants,^{10,11} thermostabilisers of synthetic fibres^{12–14} and surfactants.¹⁵ Some P,O-heterocyclic compounds are used as synthons for hard-to-reach compounds.^{16–19}

1,2-Monoheterophosphacyclanes having other heteroatoms in the ring, *e.g.*, sulfur or nitrogen, have been investigated to a far lesser extent because of the absence of convenient preparative methods to obtain them. At the same time, cyclic P,S-containing systems represent a highly promising class of organophosphorus compounds. In particular, it is known that some P,S-heterocycles are used as antioxidant additives in motor oils, polymers and agrochemicals,^{20–22} and also as co-monomers for polymers possessing complexation properties²³ and ligands for metal complex catalysts.²⁴ Cyclic esters of phosphorus thioacids are widely used in biochemical studies and as sulfur analogues of nucleotides.^{25,26} Some saturated P,S-heterocyclic compounds, such as 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide²⁷ (currently known as the Lawesson reagent, LR), are of great utility in organic synthesis as mild thiylating agents for carbonyl and phosphoryl compounds and also as reagents in the synthesis of unsaturated 5- and 6-membered heterocyclic compounds containing a P,S-moiety.^{28,29}

Though the number of publications concerning the saturated 1,2-thiaphosphacyclanes is rather limited, it seemed expedient to summarise the information on this topic available in the literature taking into account the clear prospects of these compounds. We have paid attention to the synthesis, structural features and tautomerism of this interesting but still poorly investigated class of heterocyclic compounds.

II. 1,2-Thiaphosphiranes

Three-membered saturated P,S-heterocycles, *i.e.*, 1,2-thiaphosphiranes, became available only when synthetic approaches to stable dicoordinate phosphorus compounds were developed.

1. Synthesis of 1,2λ⁵-thiaphosphiranes

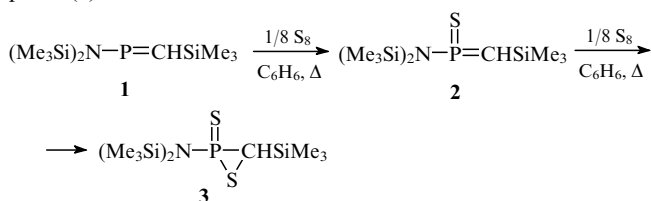
The only general synthetic route to 2-thioxo-1,2λ⁵-thiaphosphiranes presently known is based on the addition of elementary sulfur to methylenephosphines. Niecke and Wildbrecht³⁰ were the first

I L Odinets, N M Vinogradova, T A Mastryukova A N Nesmeyanov
Institute of Organoelement Compounds, Russian Academy of Sciences,
ul. Vavilova 28, 119991 Moscow, Russian Federation.
Fax (7-095) 135 50 85. Tel. (7-095) 135 93 56.
E-mail: odinets@ineos.ac.ru (I L Odinets),
vinograd1@yandex.ru (N M Vinogradova).
Tel. (7-095) 135 63 73 (T A Mastryukova)

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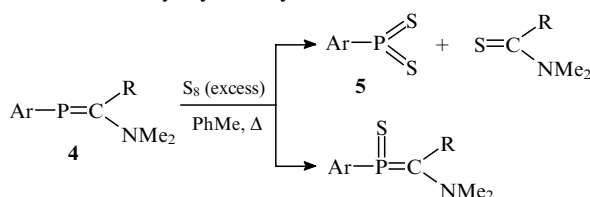
Uspekhi Khimii 72 (9) 884–901 (2003); translated by I L Odinets

to obtain a compound with such a heterocycle starting from [bis(trimethylsilyl)amino]trimethylsilylmethylidene- $\sigma^2\lambda^3$ -phosphine (**1**).



This reaction proceeds in two steps: the addition of one equivalent of sulfur affords $\sigma^3\lambda^5$ -methylidene(thio)phosphorane **2** in high yield (90%), which reacts with the second equivalent of sulfur according to the [1 + 2]-cycloaddition affording 2-thioxo-1,2 λ^5 -thiaphosphirane **3**. A small amount of the latter as a by-product is formed in the first step. If the reaction of methylidene-phosphine **1** is carried out directly with two equivalents of sulfur the desired 2-thioxo-1,2 λ^5 -thiaphosphirane **3** is obtained in virtually quantitative yield.

It should be noted that not all cases of the reactions of phosphalkenes with sulfur result in the formation of stable $\sigma^3\lambda^5$ -methylidene(thio)phosphoranes, the pentavalent tricoordinate phosphorus compounds. In particular, the reaction of 2,4,6-tri-*tert*-butylphenyl(dimethylaminomethylidene)phosphines **4** with sulfur yields metadithiophosphonate **5**^{31,32}, which does not dimerise to the corresponding analogue of the Lawesson reagent because of the bulky aryl moiety.



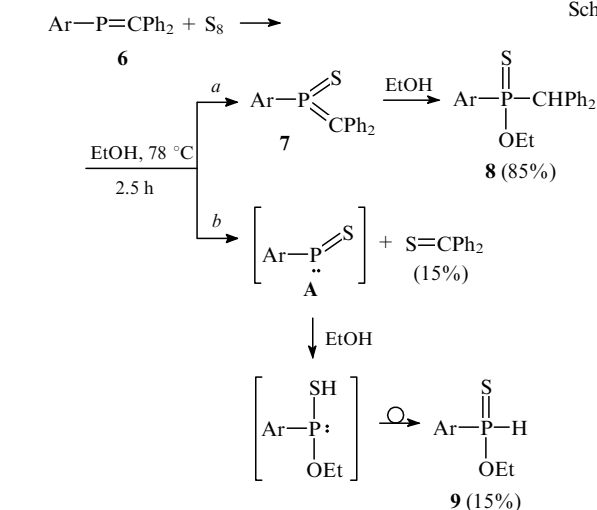
Ar = 2,4,6-Bu₃C₆H₂, R = H, Me.

No thiaphosphiranes were also found among the addition products of the sulfur to 2,6-dimethylphenyl(diphenylmethylidene)phosphine (**6**) in boiling ethanol,[†] though in this case methylidene(thio)phosphorane **7** is really formed in the first step.^{32,33} It was not possible to isolate phosphorane **7** because of its extreme instability, but its formation was confirmed by NMR and mass spectrometry techniques and also by its reaction with ethanol affording *O*-ethyl 2,6-dimethylphenyl(diphenylmethyl) thiophosphinate **8** (Scheme 1, path *a*, attack on the lone electron pair of the phosphorus atom).³² Concurrently with the addition of one equivalent of sulfur leading to the phosphorane **7** (path *b*), cleavage of the P=C multiple bond in the starting methylidene-phosphine takes place (path *b*), as the energies of these reactions are similar. Such a cleavage results in thiobenzophenone (15%), and after addition of ethanol to an unstable intermediate **A**, *O*-ethyl H-phosphinothioate **9** (15%).

However, if this reaction is carried out in benzene, it is possible to obtain the desired addition product of two sulfur atoms, 2-thioxo-1,2 λ^5 -thiaphosphirane **10**. Refluxing of methylidene-phosphine **6** with 5.7 equivalents of sulfur in benzene for 3 h provided the maximum yield of the product **10** (34%).³² With a lesser amount of sulfur, a mixture of methylidene(thio)phosphorane **7** and the starting methylidene-phosphine **6** was formed containing only traces of 1,2 λ^5 -thiaphosphirane **10**. An increase in the temperature up to 90–100 °C (sealed tube) afforded an analogue of the Lawesson reagent, *i.e.*, compound **11**, which is the dimerisation product of arylmetadithiophosphonate **12**, and

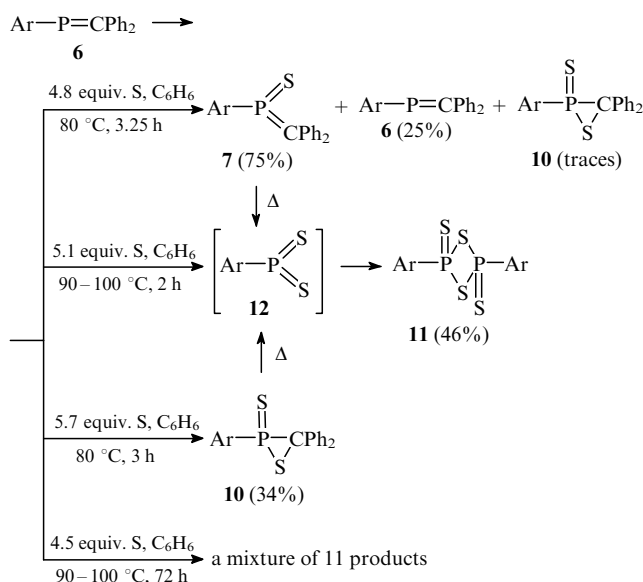
[†] No reaction of 2,6-dimethylphenyl(methylidene)phosphine with sulfur occurs in EtOH or benzene at room temperature.³²

Scheme 1



Ar = 2,6-Me₂C₆H₃.

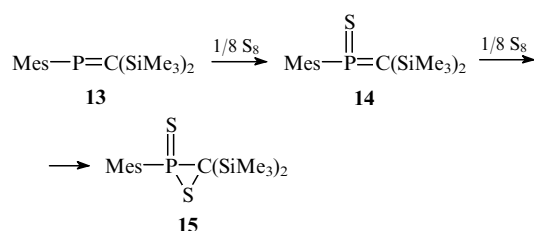
prolonged heating under the above-mentioned conditions gave a mixture of eleven unidentified phosphorus-containing compounds.



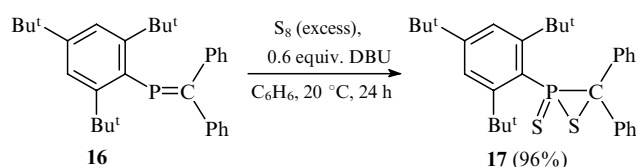
Ar = 2,6-Me₂C₆H₃.

Obviously, the stability of methylidene(thio)phosphoranes like the stability of 2-thioxo-1,2 λ^5 -thiaphosphiranes depends on the nature of substituents at the phosphorus atom and at the methylene carbon atom. On the whole, the set of these substituents is rather limited and comprises bulky groups [(Me₃Si)₂N, (Bu^t)(Me₃Si)N, Ph, 2,4,6-Me₃C₆H₂, 2,4,6-Bu₃C₆H₂, 2,6-Me₂C₆H₃, SiMe₃], which stabilise both the starting methylidene-phosphine and the addition products of sulfur. The trimethylsilyl group at the methylene carbon atom and bis(trimethylsilyl)amino-³⁰ and mesityl (Mes)^{34,35} groups at the phosphorus atom manifest the greatest stabilising effect.

The reaction of mesityl[bis(trimethylsilyl)methylidene]phosphine (**13**) with sulfur gives methylidene(thio)phosphorane **14** and the corresponding 1,2 λ^5 -thiaphosphirane **15**, which were obtained in the crystalline form for the first time. This made it possible to carry out the X-ray diffraction investigation (see below).³⁴

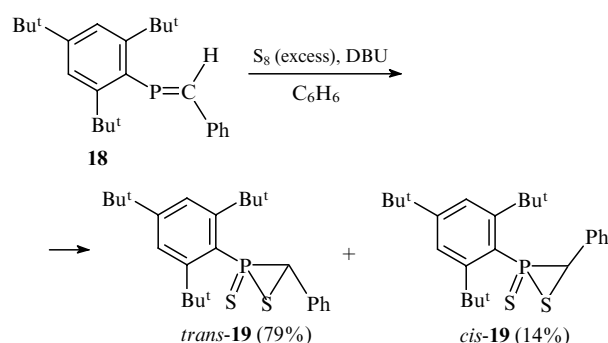


Later, by the example of 2,4,6-tri-*tert*-butylphenyl(diphenylmethylene)phosphine (**16**) it was shown that the use of bases [e.g., 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)] allows one to perform the addition of sulfur to triarylphosphaalkenes under very mild conditions (under room temperature) and to obtain the corresponding 2-thioxo-1,2λ⁵-thiaphosphirane **17** in virtually quantitative yield.³⁶ At higher temperatures, the yield of the cyclic product decreases significantly due to its instability under these conditions.³⁷

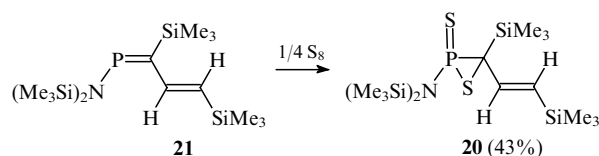


It may be suggested that the presence of different substituents at the methylene carbon atom of methylenephosphine would result in the formation of λ⁵-thiaphosphiranes as a mixture of two stereoisomers, and this was observed in one study.³⁸

The reaction of (*E*)-benzylidene(2,4,6-tri-*tert*-butylphenyl)phosphine (**18**) with sulfur afforded 1,2λ⁵-thiaphosphirane **19** as a mixture of isomers differing in the mutual arrangement of aryl groups. Taking into account the possible steric repulsion of the bulky aryl groups, the authors ascribed the *trans*-configuration to the major isomer.

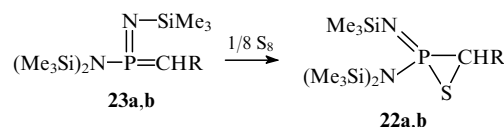


One might also expect the formation of two geometric isomers for the aforementioned 3-trimethylsilyl-2-bis(trimethylsilyl)amino-2-thioxo-1,2λ⁵-thiaphosphirane (**3**),³⁰ and for λ⁵-thiaphosphirane **20**, which is the reaction product of 1-[bis(trimethylsilyl)amino]phosphadiene (**21**) with sulfur.³⁹



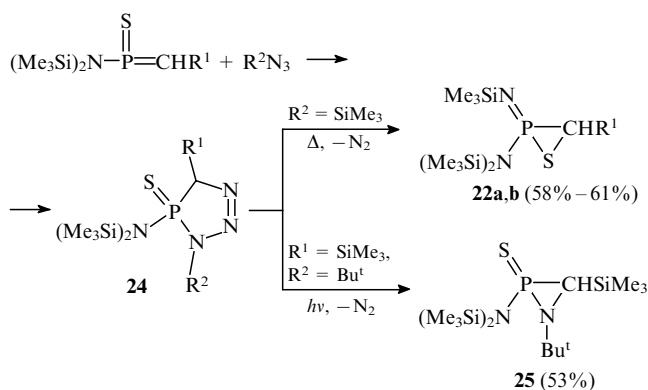
Nevertheless, in these cases the products were isolated as single isomers; their configurations were not discussed by the authors. Evidently, cycloaddition of sulfur to the intermediate methylenethio(phosphorane) is the step determining the type of the λ⁵-thiaphosphirane isomer formed. Most likely, this process is stereoselective and results in the sterically least hindered product.

2-Imino-1,2λ⁵-thiaphosphiranes **22** are also available by [1 + 2]-cycloaddition of sulfur to methylenethio(phosphorane) **23**.⁴⁰



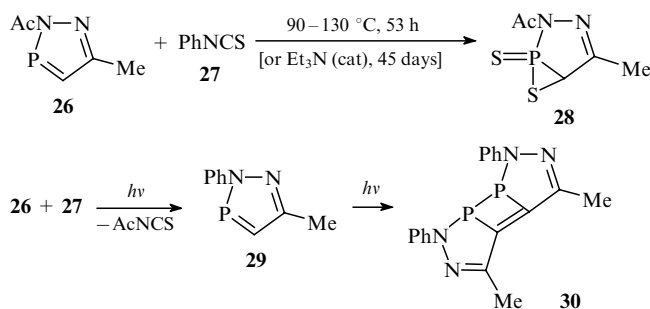
R = SiMe₃ (**a**, 72%), Bu^t (**b**, 77%).

Compounds **22** were also obtained starting from methylenethio(phosphorane) by independent synthesis, which involved the addition of trimethylsilyl azide followed by the thermal decomposition of the Δ¹-triazaphospholene **24** (R² = SiMe₃) formed.⁴⁰ It is noteworthy that the photochemical decomposition of the adduct **24** (R² = Bu^t) yields 2-thioxo-λ⁵-azaphosphirane **25**.



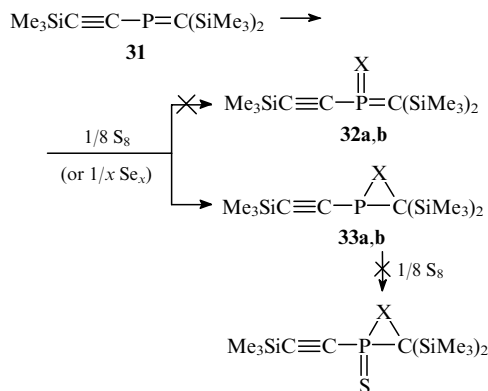
R¹, R² = SiMe₃, Bu^t.

An unusual reaction of 2-acetyl-5-methyl-1,2,3-diazaphosphole (**26**) with phenyl isothiocyanate (**27**) afforded a fused 2-thioxo-1,2λ⁵-thiaphosphirane **28**.⁴¹ The latter can be obtained either upon prolonged heating of the equimolar mixture of reactants or in the presence of a catalytic amount of triethylamine. Changing the reaction conditions (UV-irradiation) causes a change in its direction: the acetyl group at N(2) atom of the starting phosphole is substituted for the phenyl group of phenyl isothiocyanate, giving the product **29**, which is partially dimerised during the reaction affording compound **30**.



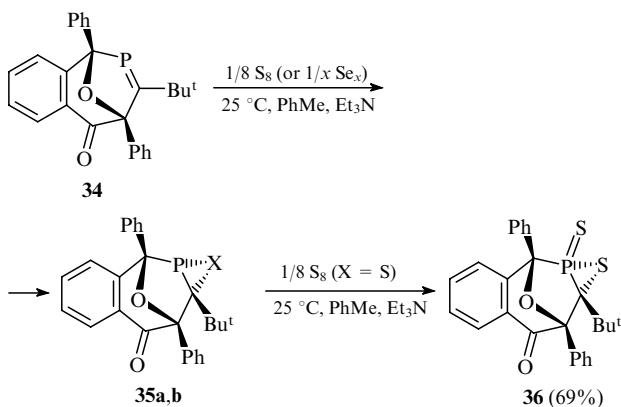
2. Synthesis of 1,2λ³-thiaphosphiranes

As was mentioned above, the addition of one equivalent of sulfur to methylenephosphine usually gives rise to methylenethio(phosphorane) rather than to thiaphosphirane or to their mixture with the former predominating. Nevertheless, exceptions from this rule are documented. Thus the reactions of ethynylphosphaalkene **31** with sulfur and selenium do not result in methylenethio(phosphorane) (**32a**) and methylenethio(selenophosphorane) (**32b**), but occur as a [2 + 1]-cycloaddition yielding 1,2λ³-thiaphosphirane (**33a**) and 1,2λ³-selenaphosphirane (**33b**);⁴² the latter do not react with the second equivalent of sulfur.



X = S (**33a**, 55%), Se (**33b**, 50%).

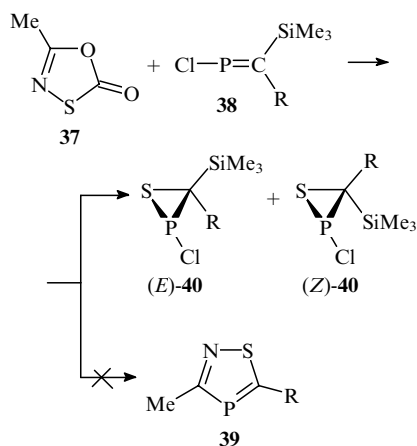
Analogously, in the reaction of tricyclic phosphalkene **34** with sulfur (or selenium)⁴³ the sulfur (or selenium) atom adds stereoselectively to the P=C bond with the formation of tetracyclic λ^3 -thiaphosphirane (**35a**) [(or λ^3 -selenaphosphirane (**35b**)] where the sulfur (or selenium) atom is located *trans* relative to the bridging oxygen atom. However, in this case treatment of the sulfur-containing λ^3 -thiaphosphirane with the second equivalent of sulfur under the same conditions readily gives the corresponding 2-thioxo derivative **36**.



X = S (**35a**), Se (**35b**).

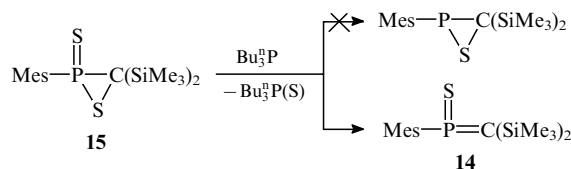
It should be noted that the use of a base (Et₃N) enables one to perform the above reaction under very mild conditions.

The reaction of 5-methyl-1,3,4-oxathiazol-2-one (**37**) with *P*-chloromethylidene phosphine **38** afforded, instead of the expected thiazaphospholenes **39**, a mixture of *E*- and *Z*-isomers of 2-chloro-1,2 λ^3 -thiaphosphiranes **40** (it is of note, that the interaction of 5-aryl-substituted oxathiazole with phosphines **38** yielded the corresponding thiazaphospholene).⁴⁴

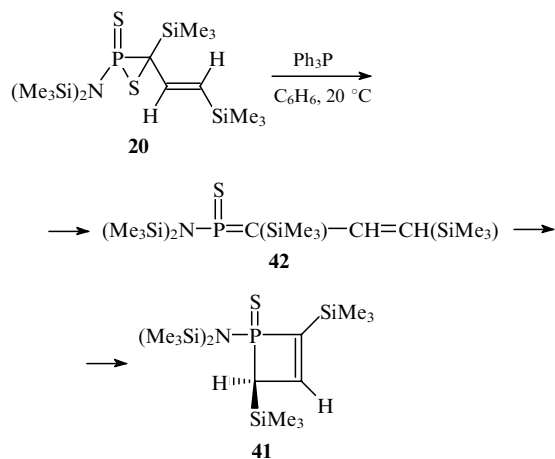


R = Ph (total yield 32%, *E* : *Z* = 75 : 25), SiMe₃ (22%).

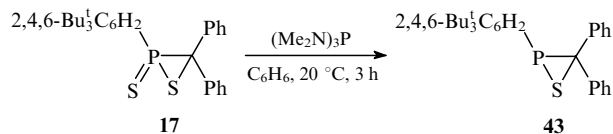
With general considerations in mind, one could suggest desulfurisation of the corresponding 2-thioxo-1,2 λ^5 -thiaphosphiranes as a possible approach to 1,2 λ^3 -thiaphosphiranes. However, 2-mesityl-3,3-bis(trimethylsilyl)-2-thioxo-1,2 λ^5 -thiaphosphirane (**15**) yields the corresponding methylenethiophosphorane **14** rather than the expected λ^3 -thiaphosphirane under the action of tributylphosphine.^{34,35}



Desulfurisation of 2-thioxo-1,2 λ^5 -thiaphosphirane **20** obtained from 1-phosphadiene **21** (see above) with triphenylphosphine affords phosphacyclobutene **41**,³⁹ which is the intramolecular cyclisation product involving C=C and P=C bonds in the intermediate methylenethiophosphorane **42**. The formation of the latter in the reaction was confirmed by ³¹P NMR spectroscopy.

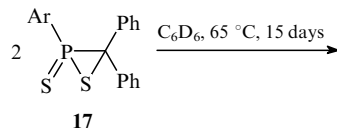


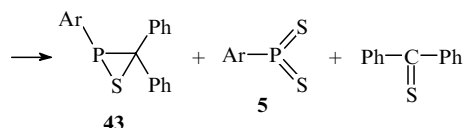
At the same time, 2-thioxo-2-(2,4,6-*tert*-butylphenyl)-3,3-diphenyl-1,2 λ^5 -thiaphosphirane (**17**) is desulfurised readily giving the corresponding 1,2 λ^3 -thiaphosphirane **43**.^{36,37} Different phosphines were tested as desulfurisation agents; tris(dimethylamino)-phosphine proved to be the most efficient.



It is believed³⁷ that the distinction in the results of the reaction of different 2-thioxo-1,2 λ^5 -thiaphosphiranes suggests that the desulfurisation affording 1,2 λ^3 -thiaphosphirane^{36,37} is governed by kinetic control, while the reaction giving more stable methylenethiophosphorane^{34,35} is governed by thermodynamic control.

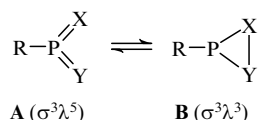
It should be noted that triaryl-substituted 2-thioxo-1,2 λ^5 -thiaphosphirane **17** is unstable and decomposes in deuterated benzene yielding arylmetadithiophosphonate **5**, thiobenzophenone and the corresponding λ^3 -thiaphosphirane **43**.³⁶





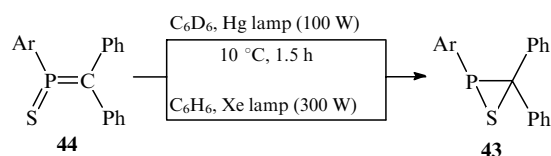
Ar = 2,4,6-Bu₃C₆H₂.

In many respects, the special interest in 1,2λ³-thiaphosphiranes is caused by the existence of valence isomerism between σ³λ⁵-phosphoranes (**A**) and σ³λ³-phosphiranes (**B**).



Thus thermodynamic conversion of methyldene(imino)phosphorane Pr₂NP(=CHBu^t)(=NBu^t) (< 110 °C) and dimethyldene-phosphorane (Me₃Si)₂NP(=CHSiMe₃)₂ (190 °C) to the corresponding azaphosphirane⁴⁵ and phosphirane⁴⁶ as well as the reverse transition of diazaphosphiranes (R = Pr₂N, Bu₂N; X = Y = NBu^t; 50 °C) to diiminophosphorane⁴⁷ have been reported earlier. Thermal or photoinduced isomerisation of sterically hindered diphosphene-*P*-sulfide (R = 2,4,6-Bu₃C₆H₂; X = S, Y = 2,4,6-Bu₃C₆H₂P) to λ³σ³-thiadiphosphirane has been described earlier.^{48,49}

Yoshifuji and co-workers^{36,37} were the first to obtain both valence isomers **A**(σ³λ⁵) and **B**(σ³λ³) in the individual state and to investigate in detail interconversions of 2,4,6-tri-*tert*-butyl-phenyl(dimethyldene)(thioxo)phosphorane (**44**) and the corresponding 1,2λ³-thiaphosphirane **43**. Being irradiated by the light of a mercury³⁶ or xenon³⁷ lamp, phosphorane **44** gave λ³-thiaphosphirane **43** as the main reaction product.

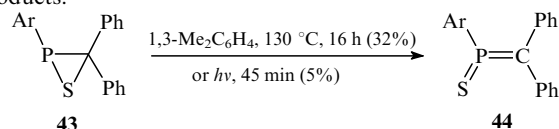


Ar = 2,4,6-Bu₃C₆H₂.

Irradiation by the Hg lamp (followed by flash chromatography and recrystallisation) and the Xe lamp, yielded 35% and 86% of compound **43** respectively.

The thermal transition of the linear form **44** to the cyclic form **43** for such a type of σ³λ⁵-phosphoranes was not observed. Thus, no traces of the cyclic isomer **43** could be detected upon refluxing of methyldene(thioxo)phosphorane **44** in toluene in the absence of light for 6 days.^{36,37} On the contrary, the reverse thermally induced transition of λ³-thiaphosphirane **43** to methyldene(thioxo)phosphorane **44** did occur.

Investigation of the temperature- and time-dependent transition **43** → **44** showed that the maximum yield of phosphoranes **44** (32%) was achieved upon 16-h reflux of a solution of λ³-thiaphosphirane **43** in *m*-xylene in the dark. More prolonged heating of compound **43** under these conditions resulted in the decomposition of the methyldene(thioxo)phosphorane **44** that was formed. A decrease in the reaction temperature down to 100 °C along with a simultaneous increase in the heating time (7 days) gave no positive result: the yield of the linear isomer **44** was only 10%. Irradiation of λ³-thiaphosphirane **43** by the mercury lamp afforded methyldene(thioxo)phosphorane **44** in 5% yield or as traces in a mixture with other unidentified products.



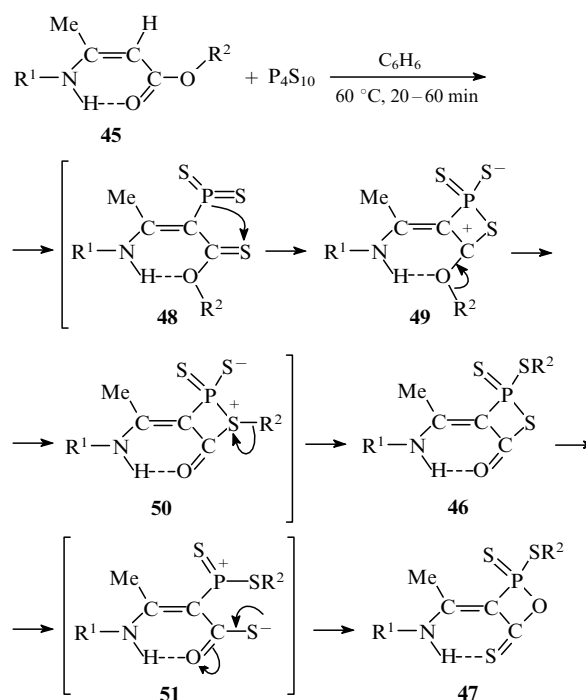
Ar = 2,4,6-Bu₃C₆H₂.

Thus, in the case of methyldene(thioxo)phosphoranes the conversion of the linear form to the cyclic one is only possible upon irradiation, while the reverse process can be both thermally and photochemically induced, though in the latter case to an considerably lesser extent.

III. 1,2-Thiaphosphetanes

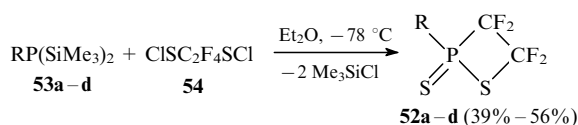
The number of publications devoted to the synthesis of 4-membered 1,2-thiaphosphacyclanes, *i.e.*, 1,2-thiaphosphetanes, is very limited, all the known methods provide only 2-thioxo-1,2λ⁵-derivatives.

Thus the reaction of alkyl aminocrotonates **45** with P₄S₁₀ gives 2-thioxo-1,2-thiaphosphetan-4-ones **46**.⁵⁰ However, being heated in benzene (for more than 30 min) or upon chromatographic purification on silica gel the latter rearrange spontaneously to the isomeric oxaphosphetanes **47**. The authors suggested that the possible reaction mechanism involves the addition of a PS₂ fragment and substitution of sulfur for the carbonyl oxygen (intermediate **48**), electrophilic attack by the phosphorus atom of the PS₂ group on the thiocarbonyl sulfur atom with the closure of the P,S-heterocycle **49** and a series of successive rearrangements resulting in migration of the alkyl radical from the oxygen atom to sulfur (intermediates **50**, **51**). Taking into account data from IR spectroscopy (using deuterium exchange), which show that the intramolecular hydrogen bond stabilizing the isomeric heterocycles formed is stronger by far in the thiocarbonyl product **47**, it was proposed that the thiaphosphetane **46** represents a product of kinetic reaction control and the isomeric oxaphosphetane **47**, of thermodynamic control. It should be noted that this method cannot be considered as a preparative one, since the product yields are only 1%–4%.

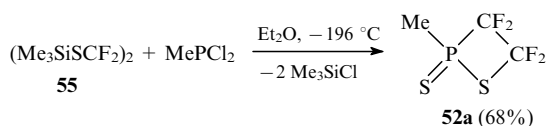


R¹ = Me, Prⁿ; R² = Me, Et.

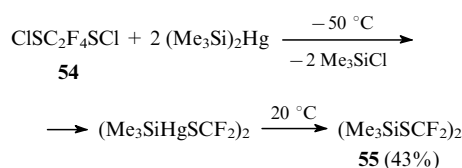
Two approaches to the synthesis of tetrafluoro-1,2-thiaphosphetanes **52** are described.⁵¹ One of them is based on the reaction of [bis(trimethylsilyl)]phosphines **53** with 1,1,2,2-tetrafluoroethane-1,2-bisulfenyl chloride (**54**), which has found application in the preparation of partially fluorinated heterocycles,^{52–54} and the second one makes use of the reaction of dichloro(methyl)phosphine with 4,4,5,5-tetrafluoro-2,2,7,7-tetramethyl-3,6-dithia-2,7-disilaoctane (**55**).



R = Me (**a**), Bu^t (**b**), Ph (**c**), 2,4,6-Bu^t₃C₆H₂ (**d**).

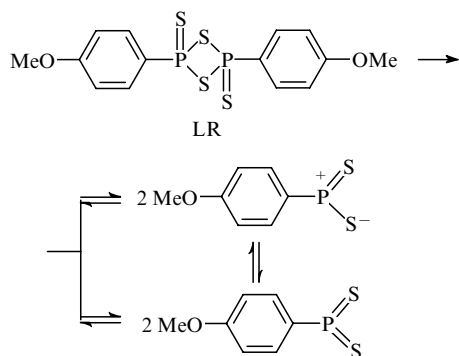


The latter reaction proceeds extremely readily at low temperature and results in the desired heterocycle **52a** in 68% yield, but since the fluorinated agent **55** used in this reaction was obtained in turn from 1,1,2,2-tetrafluoroethane-1,2-bisulfenyl chloride (**54**),⁵¹ the overall yield of the perfluorinated heterocycle **52a** according to this procedure is somewhat lower.

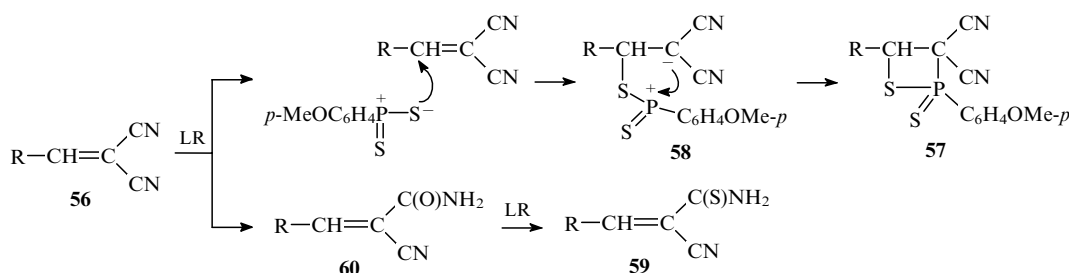


The application of the Lawesson reagent for the synthesis of unsaturated 5- and 6-membered P,S-heterocycles has already been mentioned. This is based on the reactions of the LR with alkenes,²⁰ the simplest 1,3-dienes^{55–58} and α,β-unsaturated ketones.^{27, 59}

The ability of the LR to enter into cycloaddition reactions with multiple bonds of different types is believed to be connected with its existence in solution^{60, 61} or at elevated temperatures^{28, 31} (and all the above reactions take place under rather drastic conditions) in an equilibrium with metadithiophosphonate.^{31, 32, 62} The latter is often referred to as dipolar dithiophosphonium ylide, since its reactivity is similar to that of the Wittig reagents.



The addition of the Lawesson reagent to the double bond of dicyanomethylidene compounds **56** aiming at obtaining 2-thioxo-1,2-thiaphosphetanes **57** was investigated.⁶³ This was the first example of the application of LR for such a purpose. The putative

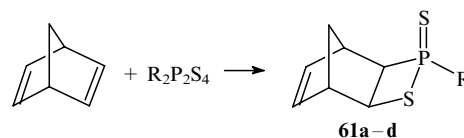


R = C₆H₄OH-*o*, C₆H₄OMe-*p*, C₆H₄NO₂-*p*, 2-thienyl.

reaction mechanism involves nucleophilic attack by the monomeric LR fragment on the sp²-carbon atom resulting in the intermediate **58**, which undergoes intramolecular cyclisation (Scheme 2).

Unsaturated thioamides **59** are formed in this reaction in parallel (as a result of partial hydrolysis of one cyano group in compound **56** under the reaction conditions followed by the substitution of sulfur for the oxygen atom in compound **60** under the action of LR). In the case of benzyldenemalonodinitrile (**56**, R = Ph), the latter reaction pathway is the only one (see Scheme 2).

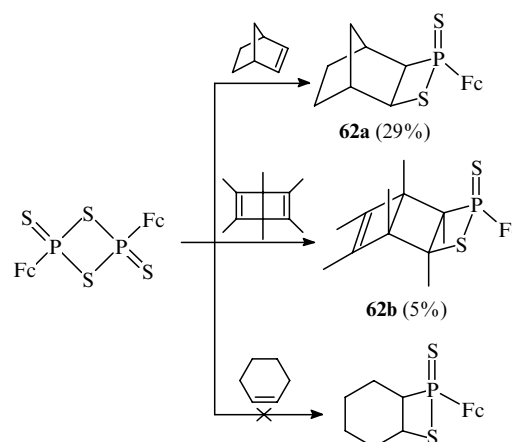
An effective straightforward synthesis of fused 2-thioxo-1,2-thiaphosphetanes has been proposed⁵⁸ based on the addition of dithiaphosphetane disulfides R₂P₂S₄ to sterically hindered alkenes. Thus exo-[2+2]-cycloaddition of R₂P₂S₄ to the multiple bond of norbornadiene (NBD) results in a series of stable tricyclic 2-thioxo-1,2-thiaphosphetanes **61**.



R = 4-MeOC₆H₄ (**a**), 3-Bu^t-4-OBu^tC₆H₃ (**b**), (C₅H₅)Fe(C₅H₄) ≡ Fc (**c**), (C₅H₄Me)Fe(C₅H₃Me) (**d**).

The rate of this reaction is determined mostly by the solubility of the starting dithiaphosphetane. Thus bis(methylferrocenyl)dithiaphosphetane — [(C₅H₄Me)Fe(C₅H₃Me)]₂P₂S₄ reacts with NBD at room temperature to give the [2+2] adduct **61d** in virtually quantitative yield in 14 h (CDCl₃, NMR experiment). The ferrocenyl derivative **61c** is obtained upon heating the reactants in the absence of a solvent at 80 °C for 16 h (the product yield is 69%). The reactions of bis(3-*tert*-butyl-4-*tert*-butoxyphenyl)dithiaphosphetane and the Lawesson reagent itself with NBD afford the target tricyclic compounds **61b** and **61a** in 44% and 13% yields, respectively.

Using Fc₂P₂S₄ as an example, an attempt was undertaken to evaluate the scope of the method proposed. The cycloaddition of Fc₂P₂S₄ to cyclohexene, norbornene and hexamethylbi-



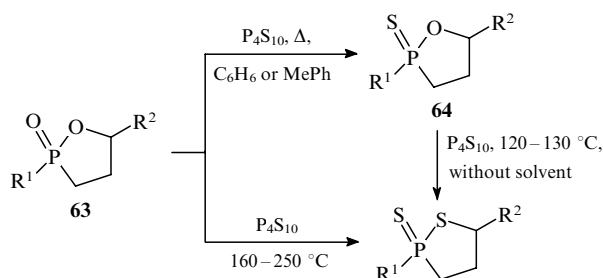
Scheme 2

cyclo[2.2.0]hexa-2,5-diene was investigated.⁵⁸ As cyclohexene did not react with $\text{Fc}_2\text{P}_2\text{S}_4$, the authors supposed that only sterically strained alkenes are able to react according to the cycloaddition scheme under such mild conditions giving products of the type **62**.

In conclusion it should be mentioned that the main methods for obtaining 1,2-thiaphosphetanes, excluding the perfluorinated rings, involve the addition of phosphorus pentasulfide and the Lawesson reagent to various unsaturated substrates.

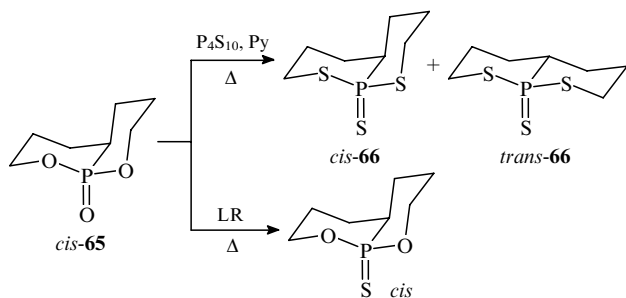
IV. 1,2-Thiaphospholanes and 1,2-thiaphosphinanes

The first representatives of the 5- and 6-membered saturated 1,2-thiaphosphacyclane family have been obtained upon exhaustive replacement of oxygen atoms by sulfur in the well-known 2-oxo-1,2-oxaphosphacyclanes.^{24, 64, 65} Such a replacement occurs under the action of an excess of phosphorus pentasulfide on the parent compounds, *e.g.*, 2-oxo-1,2-oxaphospholanes **63**, under drastic conditions (at 160–250 °C). Under milder conditions (reflux in benzene⁶⁴ or toluene^{24, 65}), only the phosphoryl oxygen atom is replaced affording 2-thioxo-1,2-oxaphospholanes **64**. Their yields range from 17% to 58% depending on the substituent R^1 at the phosphorus atom. The intermediate 2-thioxo-1,2-oxaphospholanes **64** are thermally stable,⁶⁴ in particular, upon distillation (80–130 °C) they do not undergo thione–thiol rearrangement, which would result in the migration of the sulfur atom into the ring. Replacement of the oxygen atom in the oxaphospholane ring by sulfur requires heating of compounds **64** with P_4S_{10} either at 120–130 °C (2 h without a solvent,⁶⁴ 6 h in chlorobenzene⁶⁵) or in an autoclave at 250 °C (in toluene).²⁴



$\text{R}^1 = \text{Me, Et, Ph}; \text{R}^2 = \text{H, Me}.$

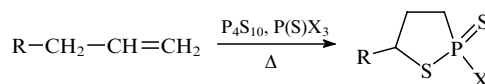
Using this procedure, Polozov and Cremer⁶⁶ have performed exhaustive replacement of oxygen atoms by sulfur in both fused 1,2-oxaphospholane rings of the *cis*-isomer of 2,10-dioxaphosphabicyclo[4.4.0]decane 1-oxide **65** (P_4S_{10} , pyridine, reflux).



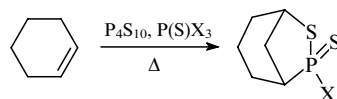
It was found that the stereochemistry of the starting bicycle can be changed during the reaction; the corresponding trithio derivative **66** was obtained as a mixture of *cis*- and *trans*-isomers in a 1.6 : 1 ratio. A milder thiylating agent, LR, enables only a partial replacement of the oxygen atoms in the substrate **65**, and the configuration of the initial *cis*-isomer is retained.

Numerous methods to obtain various 5- and 6-membered 2-oxo-1,2-oxaphospholanes is described in the literature. Evidently, the corresponding 2-thioxo-1,2-thia derivatives may be synthesised from them using phosphorus pentasulfide.

A method different in principle to obtain 2-thioxo-1,2-thiaphospholanes was proposed by Wing.^{21, 67} It is based on direct reaction of an unsaturated hydrocarbon, phosphorus pentasulfide and thiophosphoric acid halide under drastic conditions (autoclave, 150–200 °C, 10–18 h). When cyclic alkenes (*e.g.*, cyclohexene) are used as the starting substrates, bicyclic compounds are formed with one of the rings representing 1,2-thiaphospholane. These reaction products are used as antioxidant additives for motor oils, polymers and agrochemicals.

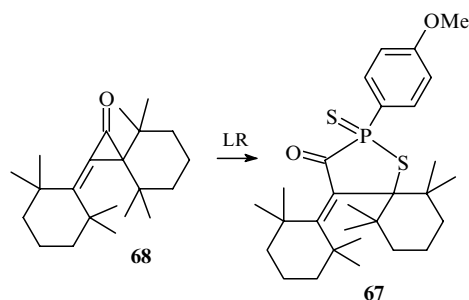


$\text{R} = \text{H, Me, Et}; \text{X} = \text{Cl, Br}.$

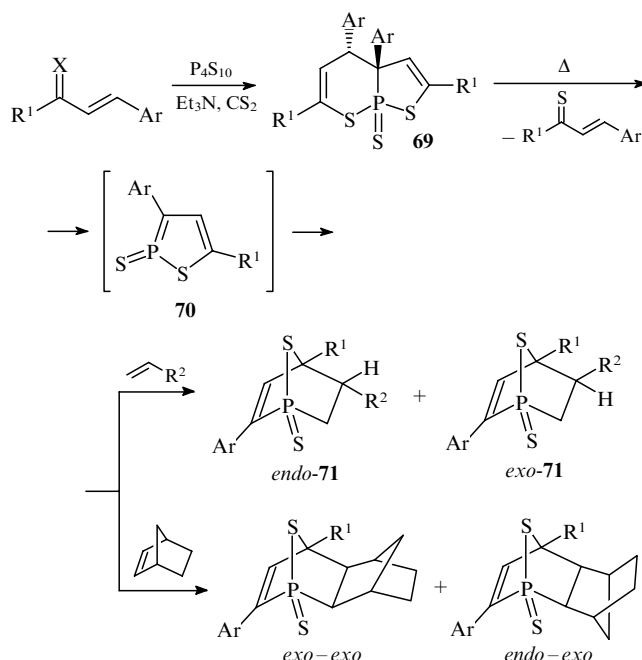


$\text{X} = \text{Cl, Br}.$

Conjugated 2-thioxo-1,2-thiaphospholanes **67** substituted in the ring were obtained by the reaction of the Lawesson reagent with a sterically crowded cyclohexyldienecyclopropanone **68**.⁶⁸ Nominally, this reaction may be considered as the insertion of the LR monomeric fragment (dithiophosphonium ylide) into the strained C–C bond of the starting cyclopropanone.



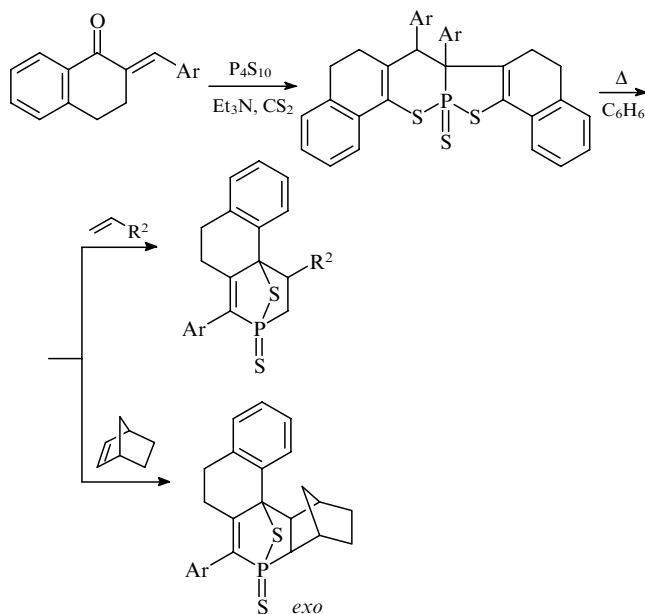
2,9-Dithia-1-thioxophosphabicyclo[4.3.0]nona-3,7-dienes **69** should be mentioned as precursors of another type of fused 2-thioxo-1,2-thiaphospholanes; these are formed in the reaction of α,β -unsaturated ketones with P_4S_{10} in the presence of



$\text{X} = \text{O, S}; \text{Ar} = \text{Ph, 4-ClC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4; \text{R}^1 = \text{Bu}^t, \text{Ph, 4-ClC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4; \text{R}^2 = \text{CN, Ph, OBU}.$

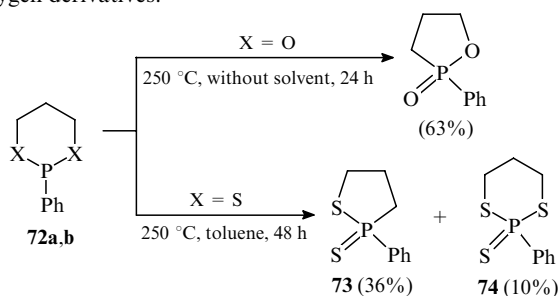
Et_3N .^{69–71} Thermolysis of such compounds in benzene occurs with the generation of 2-thioxo-1,2-thiaphospholes **70**, which act as cyclic heterodienes in [4 + 2]cycloaddition reactions with acrylonitrile,^{69, 70} styrene,⁷⁰ butyl vinyl ether⁷⁰ and norbornene.⁷⁰ In most cases, the cycloaddition products are obtained as mixtures of *exo*- and *endo*-isomers **71** or *exo-exo*- and *endo-exo*-isomers (in the case of norbornene), usually with the *endo*-isomer (when $\text{R}^2 = \text{CN}, \text{Ph}$) and *exo-exo*-isomer for the norbornene derivative predominating. The configuration of these compounds was established using NMR spectroscopy^{69, 70} and X-ray diffraction analysis.⁷¹ For butoxy-substituted polycarbocycles, it was not possible to establish the geometry of the molecule.

(*E*)-Arylmethylidene-1,2,3,4-tetrahydronaphthalen-1-one can be used as an α, β -unsaturated ketone, too.⁷⁰



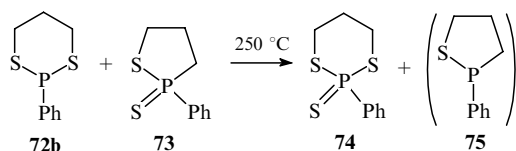
$\text{Ar} = \text{Ph}, 4\text{-ClC}_6\text{H}_4, 4\text{-MeOC}_6\text{H}_4$.

Some processes can be applied for the preparation of both 1,2-oxaphosphacyclanes and their 1,2-thia analogues. Thus an intramolecular thermal isomerisation of the Arbuzov rearrangement type is characteristic of 1,3,2 λ^3 -diheterophosphacyclanes **72** ($\text{X} = \text{O}, \text{S}$); this occurs with a ring contraction.^{24, 63} The reaction occurs more readily and in higher yields for the corresponding oxygen derivatives.



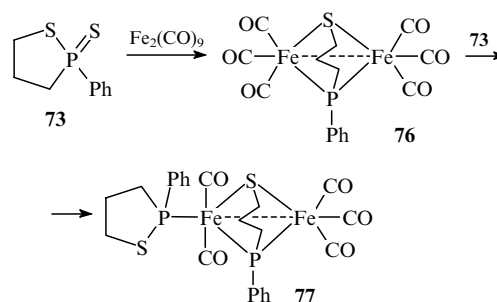
$\text{X} = \text{O}$ (**72a**), S (**72b**).

In the case of 1,3,2 λ^3 -dithiaphosphinane **72b** ($\text{X} = \text{S}$), both 2-thioxo-1,2-thiaphospholane (**73**) and 2-thioxo-1,3,2-dithia-



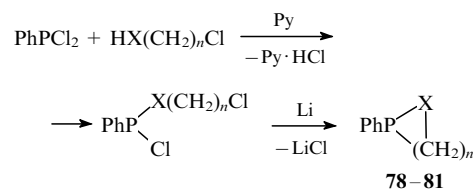
phosphinane (**74**) are formed, the latter being the addition product of sulfur to the substrate. This result is explained by the possible reaction of 1,3,2 λ^3 -dithiaphosphinane **72b** with 2-thioxo-1,2 λ^5 -thiaphospholane **73** under drastic reaction conditions.

However, the second reaction product, viz., 2-phenyl-1,2 λ^3 -thiaphospholane (**75**), was not isolated and the authors failed to detect it by spectroscopic methods. Nevertheless, in the reaction of 2-thioxo-1,2 λ^5 -thiaphospholane **73** with $\text{Fe}_2(\text{CO})_9$ such a P(III) heterocycle was obtained as a ligand bound to the iron atom. The reaction proceeds in two steps. First, the complex **76** is formed having bridging $\text{Fe}-\text{S}-\text{Fe}$ and $\text{Fe}-\text{P}-\text{Fe}$ bonds, which then reacts with the second molecule of 1,2 λ^5 -thiaphospholane **73**. As a result of selective reduction of the $\text{P}=\text{S}$ group in compound **73**, the complex **77** is formed comprising the 1,2-thiaphospholane ligand.⁷²



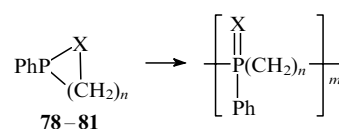
It should be emphasised that the aforementioned synthetic routes to 5- and 6-membered 1,2-thiaphosphacyclanes are limited by the possibility of obtaining products with only a thiophosphoryl group.

An alternative general method for the formation of 1,2-heterophosphacyclic structure has been proposed by Kobayashi and co-workers^{23, 73} who obtained P,O- and P,S-heterocycles **78–81** bearing a three-valent phosphorus atom. This method involves the synthesis of *O*- or *S*-(ω -chloroalkyl) phenylphosphonochloridites followed by their intramolecular cyclisation under the action of metallic lithium.



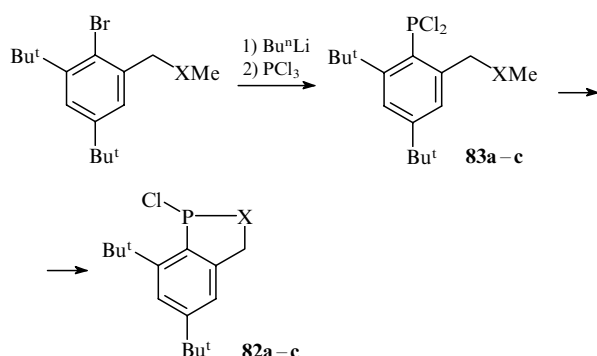
Compound	X	n	Yield (%)
78	O	3	37
79	O	4	18
80	S	3	10
81	S	4	5

Independent of the nature of the X atom, 1,2-heterophospholanes ($n = 3$) are formed in higher yields than 1,2-heterophosphinanes ($n = 4$); in each class of compounds the yields of oxygen derivatives are higher than those of the sulfur-containing ones. Though in general the yields of both 1,2 λ^3 -oxaphosphacyclanes **78, 79** and 1,2 λ^3 -thiaphosphacyclanes **80, 81** in this reaction are moderate, the reaction is rather simple to perform. Compounds **78–81** were used as monomers in polymerisation.^{23, 74} The polymerisation occurs upon either the action of cationic initiators or heating and is accompanied by ring-opening.



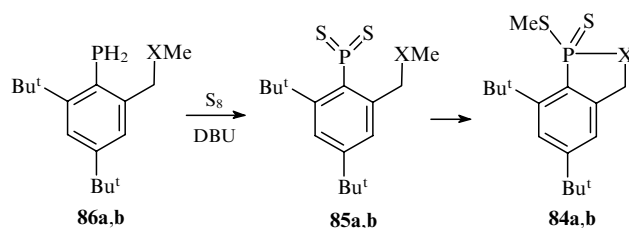
The poly(phosphine oxides) and poly(phosphine sulfides) obtained possess good chelate-forming properties including high extraction capacity towards the ions of some heavy metals.²³ Poly(phosphine sulfides) extract Pd^{2+} and Hg^{2+} cations quantitatively from solutions in a wide range of pH, Cu^{2+} ions are extracted more efficiently in weakly alkaline media. The chelating capacity of poly(phosphine sulfides) exceeds that of the corresponding poly(phosphine oxides) towards Pd^{2+} and Hg^{2+} ions and is comparable for Hg^{2+} ions and significantly lower for uranyl ions UO_2^{2+} .

Fused 2-chloro-1,2 λ^3 -heterophospholanes **82a–c** ($\text{X} = \text{O}, \text{S}, \text{Se}$) are formed as a result of the intramolecular cyclisation of 2,4-di-*tert*-butyl-6-(methylheteromethyl)phenyldichlorophosphines **83a–c**.⁷⁵ It should be noted that the ease of formation of such heterocyclic compounds decreases in the order $\text{Se} > \text{O} \gg \text{S}$.



Compound	X	Cyclisation conditions	
		$T/^\circ\text{C}$	t/h
82a	O	25	10
82b	S	25	144
		66	3
82c	Se	< 0	—

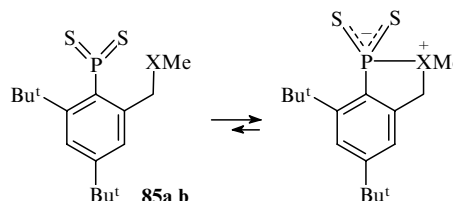
2-Thioxo-1,2 λ^5 -analogues of such fused heterocycles (compounds **84a,b**) were obtained by an intramolecular rearrangement of $\sigma^3\lambda^5$ -metadithiophosphonates **85a,b**, obtained in turn by sulfur addition to the corresponding primary phosphines **86a,b** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene.[‡]



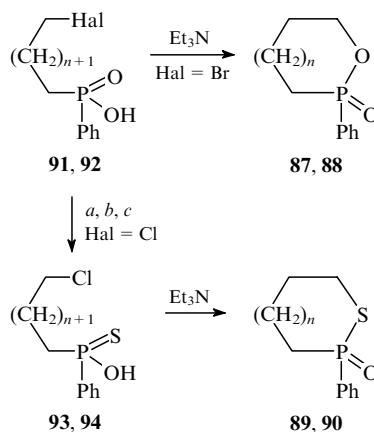
$\text{X} = \text{S}$ (a), Se (b).

In this case, too, the cyclisation rate of methylselenomethyl-substituted derivative **85b** was much higher than for its sulfur analogue **85a**. The same applies to the formation of compounds **85a,b**. Thus the reaction of the phosphine **86b** with sulfur proceeds within 1 day at ambient temperature resulting in 2-thioxo-1,2-selenaphospholane **84b** in virtually quantitative yield. The formation of dithioxophosphorane **85b** could be observed only by NMR spectroscopy due to its rapid cyclisation. In the preparation of the corresponding 1,2 λ^5 -thiaphospholane **84a**, the intermediate stable metadithiophosphonate **85a** was isolated in the pure state and its cyclisation proceeded either upon heating of the solution in toluene in a sealed tube for 1 h or on heating without the solvent

for 1 min at 180 $^\circ\text{C}$ (above the melting point of 171–173 $^\circ\text{C}$). As the chemical shifts of metadithiophosphonates **85** [$\delta_{\text{P}} = 159.9$ ($\text{X} = \text{Se}$) and 161.8 ($\text{X} = \text{S}$) in CDCl_3] in ^{31}P NMR spectra are significantly shifted upfield in comparison with the signal of the 2,4,6-tri-*tert*-butylphenyl analogue, 2,4,6- $\text{Bu}_3^t\text{C}_6\text{H}_2\text{PS}_2$ ($\delta_{\text{P}} = 298.2$ in CDCl_3), the authors suggested the existence of a strong interaction between phosphorus and chalcogen atoms in the methylthio(seleno)methyl substituent as shown below.



To obtain 2-oxo-1,2 λ^5 - (**87, 88**) or 2-oxo-1,2 λ^5 -thiaphosphacyclanes (**89, 90**), one may use an intramolecular alkylation of ω -chloroalkylphosphinous (**91, 92**) and -thiophosphinous acids occurring in the presence of triethylamine.^{76, 77} Virtually no side products are formed during this cyclisation and the reaction kinetics is approximately first order. In this case, too, the five-membered heterocyclic products were formed more rapidly than their six-membered analogues: the ratio of the rate constants for 5- and 6-membered heterocycle formation ($k^5:k^6$) is 4.3 (for the phosphinate anion) and 30 (for the thiophosphinate anion). It should be noted that despite cyclisation of thiophosphinous acids proceeding under mild conditions and 2-oxo-1,2-thiaphosphacyclanes **89, 90** being formed in fairly high yields (85%–90%), the starting thioacids **93, 94** as such were obtained by multi-step procedures complicated by numerous side reactions from the corresponding phosphoryl analogues **91, 92** in low yields and of 90%–95% purity only.



$\text{Hal} = \text{Cl}, \text{Br}; n = 0$ (**87, 89, 91, 93**), 1 (**88, 90, 92, 94**);

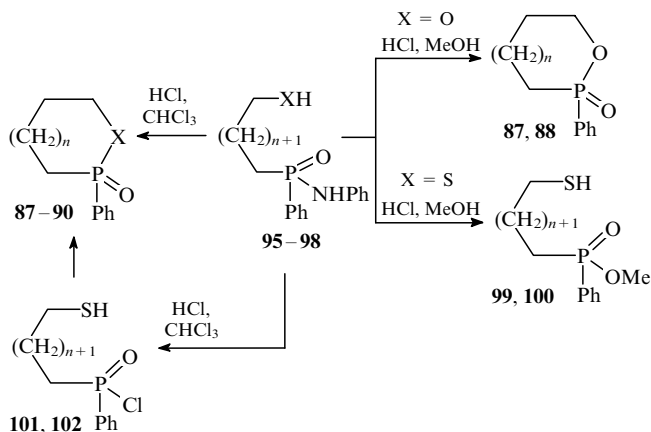
(a) $(\text{COCl})_2$; (b) P_4S_{10} , HCONMe_2 (Cat.), dioxane, reflux;

(c) H_2O , acetone.

Harger and co-workers^{78, 79} carried out the comparative investigation of acid-catalysed cyclisation of ω -hydroxy- (**95, 96**)⁷⁸ and ω -mercaptoalkylphenylphosphinous (**97, 98**) acid anilides.⁷⁹ In this case, the sharp distinction in reactivities of HS and HO groups was observed. Thus oxaphospholanes (**87**) and oxaphosphinanes (**88**) were readily formed in both methanol and chloroform [$k^5:k^6 = 70$ (in CHCl_3) and 50 (in MeOH), at 20 $^\circ\text{C}$, the cyclisation time for the anilide **95** is 1 min and 15 min for the anilide **96**]. At the same time, in MeOH the anilides **97, 98** were converted into the corresponding esters **99, 100** due to the nucleophilic substitution of the methoxy group for the anilide residue. In CHCl_3 in the presence of gaseous HCl , the cyclisation of anilides **97, 98** leading to 1,2-thiaphospholane **89** (yield $\sim 75\%$) and 1,2-thiaphosphinane **90** (yield $\sim 2\%$) takes place. It should be noted, that such a cyclisation proceeds *via* the intermediate

[‡] Phosphines **86a,b** were obtained by reduction of the corresponding aryldichlorophosphines **83** or *O*-ethyl aryldichlorophosphinates with LiAlH_4 .

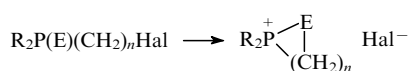
formation of phosphinic chlorides **101**, **102**, which were detected in the reaction mixtures by NMR spectroscopy.



X = O: $n = 0$ (**87**, **95**), 1 (**88**, **96**);

X = S: $n = 0$ (**89**, **97**, **99**, **101**), 1 (**90**, **98**, **100**, **102**).

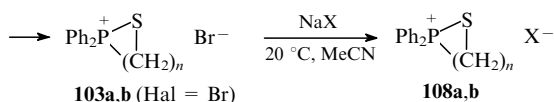
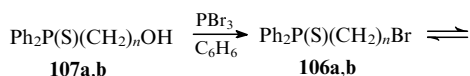
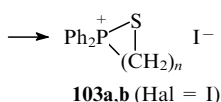
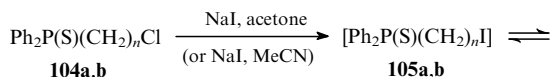
Extensive research to the development of a general approach to 1,2-monoheterophosphacyclanes of diverse structures has been performed by Mastryukova and co-workers in recent years. The method is based on the intramolecular E-alkylation of ω -halogenoalkyl-substituted compounds of tetracoordinate phosphorus bearing a P = E group.



R = Alk, Ar; E = S, O, NR'; Hal = Cl, Br, I; $n = 3, 4$.

For the first time, this reaction has been employed for the synthesis of 2,2-diphenyl-1,2,4⁴-thiaphosphacyclanium iodides **103a,b** (E = S, $n = 3, 4$; Hal = I), which were obtained by refluxing solutions of the thermally stable ω -chloroalkyldiphenylphosphine sulfides **104a,b** in either acetone or acetonitrile with NaI.⁸⁰ The reaction proceeds *via* the formation of the corresponding ω -iodoalkyldiphenylphosphine sulfides **105a,b**, which was confirmed by ³¹P NMR spectroscopy. In contrast to ω -chloro-substituted derivatives **104a,b**, ω -bromoalkylphosphine sulfides **106a,b**, obtained from the corresponding hydroxy derivatives **107a,b** and isolated in a pure state, underwent rather easy transformations into cyclic thiaphosphacyclanium bromides **103a,b** (Hal = Br) (heating at 100 °C without a solvent).^{81, 82} Starting from these compounds, one could prepare the corresponding perchlorates and tetrafluoroborates **108a,b** by an exchange reaction.⁸³

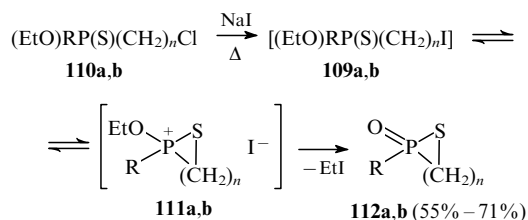
The ease of formation of the cyclic salts **103a,b** (Hal = Cl, Br, I) is determined first of all by the nature of the halogen atom and



$n = 3$ (**a**), 4 (**b**); X = ClO₄, BF₄.

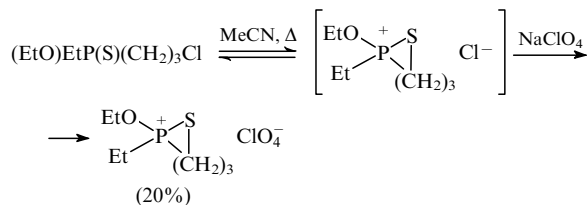
the length of the alkyl chain in the linear starting compound. Thus other conditions being equal, the iodides **105a,b** undergo cyclisation more rapidly than bromides **106a,b**, whereas chlorides **104a,b** do not undergo the intramolecular S-alkylation upon either refluxing in acetone or on heating in the absence of a solvent (140 °C, 1.5 h). The 1,2-thiaphospholanium salts (**103a**, $n = 3$) are formed more rapidly than 1,2-thiaphosphinanium salts (**103b**, $n = 4$). It should be noted that a tautomeric equilibrium between the cyclic form and the starting linear compound is established in solutions of 1,2-thiaphosphacyclanium salts, which is a rare case of ring-chain halogenotropic tautomerism (see below).

Intramolecular S-alkylation of ω -iodoalkyl-substituted thiophosphoryl compounds bearing an alkoxy group at the phosphorus atom **109a,b** obtained *in situ* from the corresponding chloro derivatives **110a,b**,[§] dealkylation of the quazi-phosphonium salt formed takes place according to the second step of the Arbuzov rearrangement resulting in 2-oxo-1,2-thiaphosphacyclanes **112a,b**.^{83–85} In this case, too, five-membered heterocyclic compounds ($n = 3$) are formed more rapidly than the six-membered ones ($n = 4$) ($k^5 : k^6 \approx 2$). In addition to the alkyl chain length, the solvent used influences the cyclisation rate: the reaction is faster in acetonitrile than in acetone, which may be connected with both the higher polarity and higher boiling point of MeCN. The nature of the substituent R at the phosphorus atom influences the cyclisation rate to a lesser extent (it decreases in the order Et > Ph > OEt). The yield of 1,2-thiaphosphacyclanes **112a,b** is 82%–96% (according to the ³¹P NMR data obtained for the reaction mixture) and 55%–71% (after isolation by chromatography or recrystallisation).



$n = 3$ (**a**), 4 (**b**); R = Et, Ph, OEt, NEt₂.

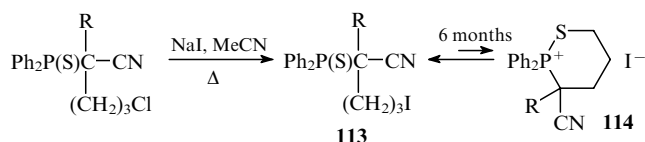
The mechanism of the reaction was established quite reliably as the authors succeeded in isolating the intermediate quazi-phosphonium salt bearing the ethoxy group starting from compound (EtO)EtP(S)(CH₂)₃Cl if the nucleophilic chloride anion is replaced by the perchlorate anion.^{84, 85} It should be noted that this is the first case where the intermediate product of the thione–thiol rearrangement of a phosphorus thioacid ester was isolated as an individual compound.



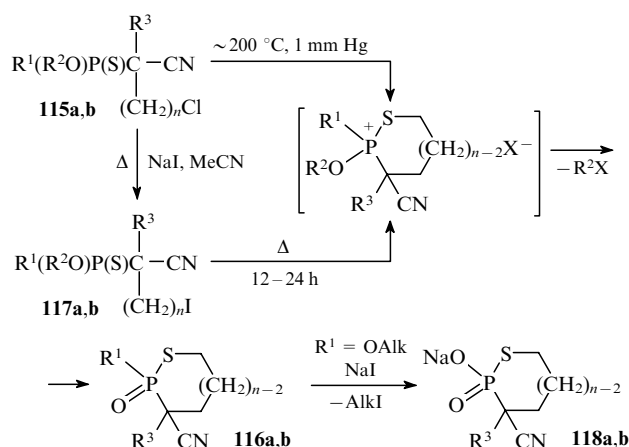
Thus, intramolecular S-alkylation represents a general method for the preparation of thiaphosphacyclanes. A wide range of thiophosphoryl compounds bearing a ω -halogenoalkyl moiety in the molecule undergo the above-mentioned intramolecular transformation. In particular, cyano-substituted mono- and bicyclic 1,2-thiaphosphacyclanes were obtained from ω -halogeno-

§ Chloroalkyl-substituted thiophosphinates and thiophosphonates **110** are thermally stable liquids that can easily be distilled (b.p. = 105–165 °C/2–3 Torr). 3-Chloropropyl(phenyl)thiophosphinate (R = Ph, $n = 3$) is the only exception, it undergoes the intramolecular thione–thiol rearrangement into 2-oxo-2-phenyl-1,2-thiaphospholane upon distillation *in vacuo* (160–170 °C/2 Torr).

As one would expect, the introduction of an electron-withdrawing cyano group at the α -position with respect to the phosphorus atom results in a decrease in the nucleophilicity of the thione sulfur atom and an increase in the stability of the linear form of cyano-substituted ω -halogenoalkyl sulfides (even the ones with a terminal iodine atom). Thus if non-functionalised ω -iodoalkylphosphine sulfides **105** undergo cyclisation *in status nascendi* under the action of NaI on chloro derivatives **104**, the cyano-substituted analogues **113** cyclise very slowly and in the equilibrium position the proportion of the corresponding phosphacyclanium salt **114** does not exceed 15%.⁸⁹



However, the α -CN group favours subsequent dealkylation in the phosphacyclanium salts formed (the intramolecular thione–thiol rearrangement) with at least one alkoxy substituent at the phosphorus atom. Thus, ω -chloroalkyl derivatives **115a,b** undergo cyclisation to the 3-cyano-2-oxo-1,2-thiaphosphacyclanes **116a,b** upon distillation *in vacuo*.^{86–90,93} Under these conditions, the cyano-substituted thiaphospholanes **116a** were formed faster and in higher yields than thiaphosphinanes **116b**. It should be noted, that the radical R^3 at the carbon atom influences sufficiently the yields of the target products (if $R^3 = \text{Alk}$, the yields decrease drastically), while the radical R^1 at the phosphorus atom virtually has no influence on the product yields. The cyclisation of the corresponding ω -iodoalkyl-substituted thiaphosphorylacetonitriles **117a,b**, formed *in situ* from the chloro derivatives proceeds under milder conditions. The yields of 3-cyano-2-oxo-1,2-thiaphosphacyclanes obtained in this way are usually higher than those of the same compounds prepared by distillation. If the starting substrate represents the thiophosphonate ($R^1 = \text{OAlk}$), the cyclisation of chloro derivatives **115a,b** carried out in the presence of an excess of NaI is accompanied by dealkylation of both alkoxy groups at the phosphorus atom and leads to the formation of sodium salts of the corresponding cyclic acid **118a,b** in virtually quantitative yields.^{89,93}

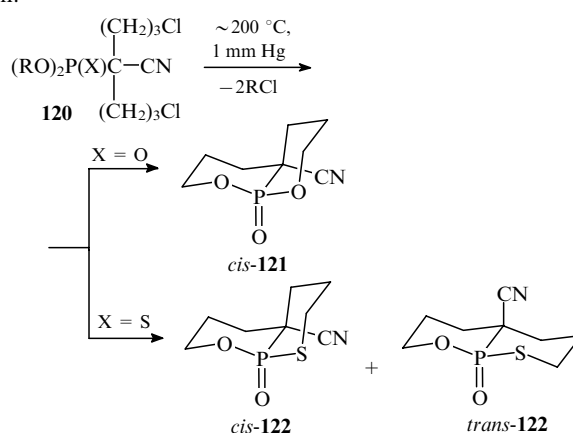


Cyano-substituted thiaphosphacyclanes **116a,b** were formed as mixtures of two stereoisomers differing in the mutual disposition of the cyano group and the phosphoryl oxygen atom relative to the ring plane (*cis*- $R_P^*R_{C^*}$ and *trans*- $R_P^*S_{C^*}$). The isomer ratio varies from 7 : 3 to 3 : 7 depending on the cyclisation method.⁸⁹ In most cases, the mixtures were separated into individual isomers

The reversible diastereomeric transformations were found to be a characteristic feature of 3-cyano-2-oxo-1,2λ⁵-thiaphosphinanes **116b** where R³ = H. Thus, the isomeric mixture obtained upon cyclisation transforms with time into a single isomer with the most favourable arrangement of the substituents as regards the general anomeric effect (*cis*-isomer for R¹ = OAlk and *trans*-isomer for R¹ = Me). In benzene solution, the isomer isolated in the pure state gradually transforms into an equilibrium mixture of both isomers.⁸⁶ Since no transformation of an isomeric mixture of **116b** R³ = Alk into an individual isomer and the reverse transformation of any individual isomer into an equilibrium mixture were observed, a carbanion mechanism was suggested for such diastereomeric transformations.^{88,90,93} It is believed that the process involves dissociation of a rather acidic hydrogen atom at position 3, the formation of a flattened carbanion and subsequent proton addition with the inversion of configuration of the asymmetric carbon atom in the ring.

$$\begin{array}{ccc} \begin{array}{c} \text{O} \\ \parallel \\ \text{R}^1-\text{P}-\text{S} \\ | \quad | \\ \text{R}^3 \quad \text{CN} \\ | \\ (\text{CH}_2)_{n-2} \end{array} & \xrightarrow[\text{C}_6\text{H}_6, \Delta]{\text{HSiCl}_3} & \begin{array}{c} \text{O} \\ \parallel \\ \text{R}^1-\text{P}-\text{S} \\ | \quad | \\ \text{R}^3 \quad \text{CN} \\ | \\ (\text{CH}_2)_{n-2} \end{array} \end{array}$$

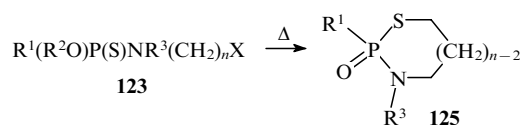
An efficient route to 6-cyano-2-oxa-10-thia(oxa)phosphabicyclodecane 1-oxides, which were previously accessible with difficulty, was elaborated based on thermal cyclisation of bis(3-chloropropyl)phosphoryl- and -thiophosphorylacetonitriles **120**. This proceeded by an intramolecular P=E alkylation (E = O, S) mechanism.^{90–93} 6-Cyano-2,10-dioxaphosphabicyclodecane 1-oxide (**121**) was obtained as a single *cis*-isomer,⁹¹ while its thio analogue with two different cyclic moieties **122** formed as a mixture of *cis*- and *trans*-isomers in a 2.3 : 1 ratio.⁹² Both isomers of 6-cyano-2-oxa-10-thia(oxa)phosphabicyclodecane 1-oxide **122** were found to be conglomerates (racemic mixture of homochiral crystals) undergoing spontaneous resolution[¶] upon crystallisation.⁹²



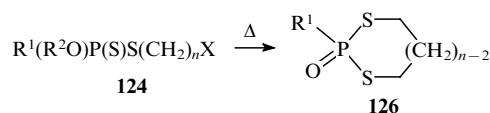
It should be mentioned, that the intramolecular P=S alkylation (followed by dealkylation of the alkoxy group at the phosphorus atom) proceeds also in the series of *N*-(ω -halogenoalkyl)thiophosphonamidates **123**^{94–100} and *S*-(ω -halogenoalkyl)

¶ Crystals are formed enriched in one enantiomer.

dithiophosphorates and -phosphonates **124**,¹⁰¹ to give 1,3,2-diheterophosphacyclanes **125** and **126**, respectively.



$n = 2, 3$; $\text{R}^1 = \text{Me, Ph}$; $\text{R}^2 = \text{Me, Et, Pr, Bu}$; $\text{R}^3 = \text{Me, Et, Ph}$.

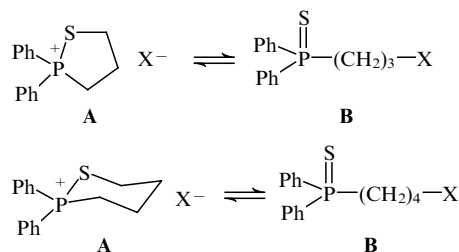


$n = 2, 3$; $\text{R}^1 = \text{Me, OPr}$; $\text{R}^2 = \text{Et, Pr}$.

Thus, the intramolecular *S*-alkylation is apparently inherent in various types of thiophosphoryl compounds with an ω -halogenoalkyl fragment. Therefore, there is good reason to believe that the method for the preparation of 2-oxo-1,2-thiaphosphacyclanes by the intramolecular thione–thiol rearrangement is the most common and is of practical importance.

V. Ring-chain tautomerism in the series of 1,2-thiaphosphacyclanes

It was reported,^{80–84} that cyclic phosphonium salts **103a,b**, called 1,2 λ^4 -thiaphosphacyclanium salts, exist in solutions as equilibrium mixtures of a cyclic form (**A**) and a linear ω -halogenoalkylphosphine sulfide (**B**). Such a tautomeric equilibrium belongs to a type of ring-chain anionotropic tautomerism, which occurs in organic chemistry much more rarely than the prototropic one.¹⁰² Moreover, even in cases where both tautomers could be isolated in the individual state, the tautomeric equilibrium in solution is rarely observed especially in the absence of a catalyst.¹⁰²



$\text{X} = \text{Cl, Br, I}$.

For the first time, the existence of such a tautomeric equilibrium $\text{A} \rightleftharpoons \text{B}$ was detected for 2,2-diphenyl-1,2 λ^4 -thiaphospholanium iodides (**103a**, $\text{Hal} = \text{I}$) and 2,2-diphenyl-1,2 λ^4 -thiaphosphinanium iodides (**103b**, $\text{Hal} = \text{I}$).⁸⁰ However, halogenotropic tautomerism in the series of 1,2-thiaphosphacyclanium salts was investigated in more detail by the example of the corresponding bromides, both the linear (**106a,b**) and the cyclic (**103a,b**) tautomers of which ($\text{Hal} = \text{Br}$) were isolated in the pure state and investigated by X-ray diffraction analysis.^{80,81} It was shown that the equilibrium position is attained starting from either the linear or cyclic tautomer. Thus, according to the ³¹P NMR data, keeping a solution of a five-membered cyclic bromide **103a** ($\text{Hal} = \text{Br}$) (or its linear tautomer **106a**) in CH_2Cl_2 at 20 °C yields an equilibrium mixture of the same composition comprising 38% of the cyclic (**A**) and 62% of the linear (**B**) tautomer. In the case of the six-membered bromide **103b** ($\text{Hal} = \text{Br}$) (or its linear tautomer **106b**), it takes *ca.* 25 days for the equilibrium to be attained in CH_2Cl_2 and the equilibrium mixture contains 48% of the cyclic (**A**) and 52% of the linear (**B**) tautomers. Thus, with the other conditions being the same (the solvent and temperature), the equilibrium is established faster for five-membered heterocyclic compounds than for the six-membered ones.

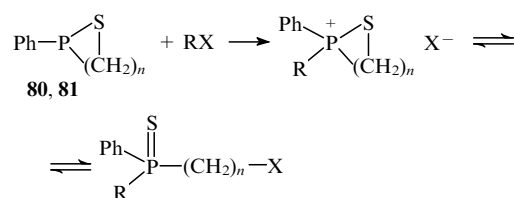
The effect of solvent polarity, ring size and the nature of the anion on the position of the tautomeric equilibrium $\text{A} \rightleftharpoons \text{B}$ was investigated in detail.⁸¹ As is evident from the data in Table 1, the position of the equilibrium shifts from the linear form to the cyclic one in going from Cl to Br and I. Thus only minor amounts of the cyclic form **A** were determined in acetonitrile solutions of ω -chloroalkyldiphenylphosphine sulfides **104a,b** after storage for 6 months, while only the cyclic form **B** was found after keeping the solutions of the corresponding iodides **105a,b** in the same solvent. As would be expected for perchlorates, the equilibrium is completely shifted to the cyclic tautomer **A** independent of the solvent polarity. Under the same conditions (solvent, temperature, time), usually an increase in the content of the form **A** is observed in equilibrium mixtures on going from the 1,2-thiaphospholanium salts to 1,2-thiaphosphinanium salts. This fact was explained^{80–82} by the higher strain in the five-membered ring.

Table 1. The content of the cyclic form **A** (%) in solutions of 1,2 λ^4 -thiaphosphacyclanium salts **103a,b** ($\text{Hal} = \text{Cl, Br, I}$) and **108a,b** ($\text{X} = \text{ClO}_4$) according to ³¹P NMR data.

Solvent	Hal = Cl		Hal = Br		Hal = I		X = ClO ₄	
	$n = 3$	$n = 4$	$n = 3$	$n = 4$	$n = 3$	$n = 4$	$n = 3$	$n = 4$
CH_2Cl_2	0	0	38	48	70	85	100	100
CHCl_3	0	0	65	85	87	92	100	100
MeCN	9	3	82	82	100	100	—	—

It was also established that the proportion of the cyclic tautomer **A** increases with a decrease in temperature,^{80,81} *i.e.*, as in other ring-chain tautomeric systems,¹⁰² the transition of a cyclic form into the linear one is an endothermic process.

A similar equilibrium was described by Kobayashi *et al.*,²³ who studied the mechanism of polymerisation of 1,2 λ^3 -thiaphosphacyclanes, where the initiation step involves the reaction of the latter with RX .



$n = 3$ (**80**), 4 (**81**); $\text{RX} = \text{MeOTf, MeI, BnBr}$.

A mixture of the starting monomer with an equimolar amount of MeOTf, MeI or BnBr in CDCl_3 was monitored by ³¹P NMR and the formation of the corresponding linear form at 80 °C was observed in the cases where halide serves as a counterion. At lower temperature (35 °C), the linear form was not detected. However neither regularities of this process were investigated nor the corresponding tautomers were isolated.

As mentioned above, the decrease in the nucleophilicity of the sulfur atom in linear ω -halogenoalkyl-substituted phosphine sulfides due to the introduction of an electron-withdrawing substituent (*e.g.*, the cyano group) into the α -position relative to the phosphorus atom resulted in the deceleration of the cyclisation, the proportion of the product **114** in the equilibrium mixture not exceeding 15%.⁸⁹

VI. Structural features of 1,2-thiaphosphacyclanes

In a number of papers devoted to 1,2-thiaphosphacyclanes having different ring sizes their structural features revealed from X-ray studies are discussed in detail. Therefore we considered it reasonable to summarise these data. Table 2 presents the principal geometric parameters of 1,2-thiaphosphacyclanes as obtained from X-ray data.

Table 2. The principal bond lengths and bond angles for 1,2-thiaphosphacyclanes according to the literature data.

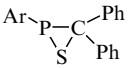
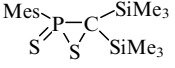
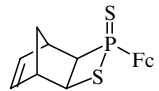
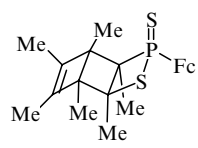
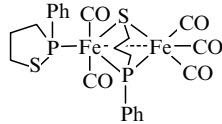
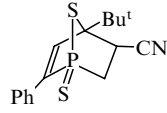
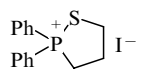
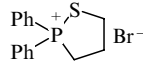
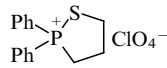
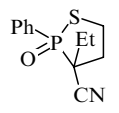
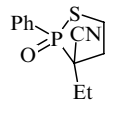
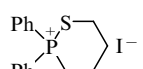
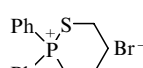
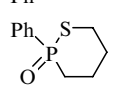
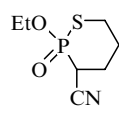
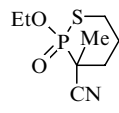
Compound	Structure	Bond lengths /Å				Bond angles /deg		Ref.
		P–S	P–C	S–C	P=X (X = S, O)	P–S–C	S–P–C	
43	 Ar = 2,4,6-Bu ₃ C ₆ H ₂	2.113(1)	1.878(2)	1.845(2)		56.18(8)	54.69(7)	36, 37
15		2.049(3)	1.795(7)	1.918(8)	1.932(3)	53.7(2)	59.4(2)	34
61c		2.102(2)	1.844(4)	1.850(6)	1.940(2)	80.1	83.8	58, 103
62b		2.095(1)	1.847(6)	1.880(3)	1.931(1)	79.9(1)	83.7(1)	58, 103
77		2.087(2)	1.907	1.832		97.2	95.3	72
71 (Ar = Ph, R ¹ = Bu ^t , R ² = CN) ^a		2.088(3) 2.073(2)	1.827(8) 1.829(7)	1.860(7) 1.866(6)	1.923(3) 1.929(3)	82.3(2) 82.6(2)	93.0(3) 94.4(2)	104
103a (Hal = I)		2.068(2)	1.805(4)	1.850(6)		93.0(2)	101.1(1)	80
103a (Hal = Br)		2.062(2)	1.818(5)	1.842(7)		93.3(2)	100.3(2)	81
108a (X = ClO ₄)		2.052(2)	1.812(5)	1.844(7)		93.8(2)	99.4(2)	83
<i>cis</i> - 116a (R ¹ = Ph, R ³ = Et)		2.078(1)	1.857(2)	1.827(3)	1.477(1)	95.7(1)	97.2(1)	89
<i>trans</i> - 116a (R ¹ = Ph, R ³ = Et) ^a		2.0751(4) 2.0832(4)	1.869(1) 1.873(1)	1.834(1) 1.840(1)	1.4805(8) 1.4817(8)	94.93(4) 95.20(4)	95.84(4) 97.87(3)	89
103b (Hal = I)		2.051(2)	1.778(5)	1.837(5)		97.6(1)	107.6(1)	80
103b (Hal = Br)		2.048(2)	1.790(5)	1.833(5)		97.3(1)	108.1(2)	81
112b (R = Ph)		2.082(1)	1.790(3)	1.828(3)	1.474(2)	96.8(2)	103.4(1)	84
<i>cis</i> - 116b (R ¹ = OEt, R ³ = H)		2.044(1)	1.817(4)	1.807(6)	1.456(3)	99.2(1)	105.5(1)	86
<i>cis</i> - 116b (R ¹ = OEt, R ³ = Me)		2.056(1)	1.836(1)	1.832(2)	1.469(1)	99.54(8)	105.8(1)	88

Table 2 (continued).

Compound	Structure	Bond lengths /Å				Bond angles /deg		Ref.
		P—S	P—C	S—C	P=X (X = S, O)	P—S—C	S—P—C	
<i>trans</i> - 116b (R ¹ = Me, R ³ = H)		2.062(2)	1.838(3)	1.835(3)	1.488(2)	97.9(2)	103.9(1)	86
<i>cis</i> - 116b (R ¹ = Me, R ³ = H)		2.065(2)	1.833(2)	1.845(3)	1.484(2)	100.13(7)	113.13(8)	89
<i>cis</i> - 116b (R ¹ = Me, R ³ = Me)		2.054(2)	1.836(2)	1.832(2)	1.470(4)	99.54(8)	105.79(5)	89
<i>trans</i> - 116b (R ¹ = Ph, R ³ = H) ^a		2.059(1)	1.839(2)	1.827(2)	1.477(2)	99.1(1)	103.45	89
		2.061(1)	1.832(2)	1.838(2)	1.479(1)	97.96(9)	103.56	
<i>trans</i> - 122 (see ^{a, b})		2.04(1)	1.824(2)	—	1.471(6)	93(1)	—	89
		2.076(9)	—	—	—	98(1)	—	
<i>cis</i> - 122 (see ^b)		2.020(1)	1.823(2)	1.821(4)	1.463(2)	96.2(2)	105.46(8)	89

^a Parameters for two independent molecules. ^b The compounds represent conglomerates, which undergo crystal-induced spontaneous resolution (data for the major enantiomer are shown). The structures are disordered due to superposition of two enantiomers (7 : 3 for *trans*-**122** and 17 : 3 for *cis*-**122**).

The structures of two 1,2-thiaphosphiranes **43** and **15**, with a tri-^{36,37} and tetracoordinate³⁴ phosphorus atom, respectively, were investigated by X-ray diffraction analysis. In λ^5 -derivative **15** with the phosphine sulfide group, the P—C and P—S bond lengths in the three-membered ring are somewhat shorter than in the λ^3 -derivative **43**, which results in the corresponding elongation of the S—C bond in compound **15**. Presumably, this is connected with the presence of bulky trimethylsilyl groups at the carbon atom in compound **15**. It is interesting to note that with allowance for the difference in the chemical structure, *i.e.*, with the presence of the sulfur atom in the ring, compound **15** is virtually isostructural with its precursor, methylidene(thioxo)phosphorane **14** Mes—P(S)=C(SiMe₃)₂.³⁴

In the series of 1,2-thiaphosphetanes, the representatives of the smallest group of 1,2-thiaphosphacyclanes, only for two ferrocenyl-substituted thiophosphoryl compounds **61c** and **62b**^{58,103} are X-ray data available. In these compounds, the four-membered ring is part of a fused cage system, both compounds being represented by *exo*-isomers. The four-membered ring in both compounds is flattened (the maximum deviation from the plane PCCS is 0.05 and 0.14 Å for **61c** and **62b** respectively). The minor deviation from planarity in compound **62b** is caused by steric hindrance due to methyl substituents. The increase in the S=P—C angle in **62b** is evidence for this fact.

X-Ray diffraction studies of the iron complex **77** with the 1,2,3-thiaphospholane P-monodentate ligand was carried out.⁷² The ligand is characterised by the longest P—C_{cyclo} bond (1.907 Å) of all the 1,2-thiaphosphacyclanes shown in Table 2. In addition, the P—S bond length in this compound (2.087 Å) also exceeds the analogous bond lengths in other 1,2-thiaphospholanes with the exception of compound **71** (Ar = Ph, R¹ = Bu^t, R² = CN)¹⁰⁴ having a norbornene structure, where the five-membered ring may be considered as a 1,2-thiaphospholane only formally (the sulfur atom serves as a bridge between the bridgehead phosphorus and carbon atoms). The parameters of the 1,2-thiaphospholane ring in

compound **71** are similar to the expected values with the exception of the P—S—C angle (82.3° and 82.6°) due to considerable steric strain in the bicyclic skeleton. It should be noted that in this case the values of the angle are similar to those in phosphetanes.

According to X-ray data for 5- and 6-membered 1,2-thiaphosphacyclanium salts **103a** (Hal = I, Br), **108a** (X = ClO₄) and **103b** (Hal = I, Br)^{80,81,83} differing only in their anions, these compounds are isostructural. In addition, the orientation of the two phenyl rings bound to the phosphorus atom relative to the planes of both the 5- and 6-membered rings is practically the same in all compounds. Thus, their structures do not depend on the nature of the anion or packing character. In all the structures under investigation, the phosphorus atom has a slightly distorted tetrahedral configuration with an endocyclic angle reduced to 100.3(2)° and 108.1(2)° in the thiaphospholane and thiaphosphinane rings, respectively.

Five-membered rings in 1,2-thiaphosphacyclanium salts **103a** (Hal = I, Br) and **108a** (X = ClO₄) have envelope conformations with an average deviation of the C(4) atom from the plane formed by the other atoms of 0.6 Å. 1,2-Thiaphosphinanium salts **103b** (Hal = I, Br) possess chair conformations. On going from five-membered to six-membered rings contraction of the P⁺—S bonds (on average, from 2.065 to 2.050 Å) and S—C bonds (from 1.846 to 1.835 Å) is observed.

The presence of shortened contacts of the type 'cation—halide anion' (P⁺—S...Hal[−]) is a characteristic feature of these compounds, and analysis of the known structural data showed that such contacts with the halide ions in compounds containing the P⁺—S bond were previously unknown. In compounds **103a** (Hal = I, Br), **108a** (X = ClO₄) and **103b** (Hal = I, Br), the phosphorus, sulfur and halogen atoms are virtually colinear [the average value of the P—S—Hal bond angle is 175.3(1)°], which points to the directionality of the contact. Taking into account the difference in the van der Waals distances, the contact strength for the same ring is virtually independent of the nature of the halogen.

Thus the difference in the $S \cdots \text{Hal}^-$ distances in five-membered rings for the bromide **103a** ($\text{Hal} = \text{Br}$) and the iodide **103a** ($\text{Hal} = \text{I}$) (0.16 Å) almost coincides with the difference in van der Waals radii for Br and I (0.17 Å). Owing to these contacts, the sulfur atom in such structures acquires a trigonal configuration. On going from five- to six-membered thiaphosphacyclanium halides, significant contraction of the $S \cdots \text{Hal}^-$ distance is observed (this correlates with the interion contact strength) by 0.19 and 0.18 Å in iodides and bromides, respectively. Based on the correlation of the $\text{P}-\text{S}$ and $S \cdots \text{Hal}^-$ bond lengths with the ring size, it was suggested that this contact is caused by the donor–acceptor interaction of the halogen lone electron pair with the antibonding orbital of the $\text{P}-\text{S}$ bond ($n-\sigma^*$ -interaction).

Despite the similarity on the whole of the geometric parameters of five-membered phosphonium salts **103a** and **108a** with those of cyano-substituted *cis* and *trans*-2-oxo-1,2λ⁵-thiaphospholanes **116a**,⁸⁹ the elongation of the $\text{P}-\text{S}$ bond and contraction of the $\text{S}-\text{C}$ bond in the latter should be mentioned. The same regularity is observed when comparing the bond lengths in salts **103b** ($\text{Hal} = \text{I}, \text{Br}$) with those in 2-oxo-1,2λ⁵-thiaphosphinane **112b** ($\text{R} = \text{Ph}$).⁸⁴

The introduction of the cyano group in position 3 of the 2-oxo-1,2-thiaphosphinane ring^{86,88,89} resulted in the contraction of the $\text{P}-\text{S}$ bonds (*cf.* structures **112b** and **116b** with different substituents R^1 and R^3 , Table 2). At the same time, the $\text{P}-\text{S}$ bond in 3-cyano-2-oxo-1,2-thiaphosphinanes **116b** ($\text{R}^1 = \text{OEt}$, $\text{R}^3 = \text{Me}$; $\text{R}^1 = \text{Me}$; $\text{R}^3 = \text{H}$, Me ; $\text{R}^1 = \text{Ph}$, $\text{R}^3 = \text{H}$) is longer[†] than the $\text{P}-\text{S}$ bond in the corresponding thiaphosphinanium salts **103b** ($\text{Hal} = \text{I}, \text{Br}$). It should be mentioned also that in both five- and six-membered rings the presence of the cyano group leads to a significant elongation of the $\text{P}-\text{S}$ bond, especially in the case of transoid arrangement of the phosphoryl oxygen atom and the CN fragment.

According to an X-ray investigation⁹² of single crystals of *cis*- and *trans*-isomers of phosphabicyclo[4.4.0]decane 1-oxide **122**, these compounds represent conglomerates (racemic mixture of homochiral crystals) which undergo the crystal-induced spontaneous resolution. Thus in the crystals of both isomers, the superposition of two enantiomers P_R and P_S (7:3 for *trans*-**122** and 17:3 for *cis*-**122**) is observed. On the whole, the geometry of compounds obtained is similar to that of the known phosphabicyclo[4.4.0]decane 1-oxides with two symmetric 1,2-oxaphosphinane rings.^{91,105–107} The $\text{P}(\text{I})\text{O}(\text{2})\text{C}(\text{4})\text{C}(\text{8})$ torsion angles in compounds *cis*-**122** and *trans*-**122**, which characterise the mutual disposition of the phosphoryl and cyano groups, are equal to -48.4° and 179° , respectively.

In conclusion, it may be mentioned that in general the length of an ordinary $\text{P}-\text{S}$ bond in 1,2-thiaphosphacyclanes independent of the ring size and coordination number of the phosphorus atom varies within a rather narrow range 2.049–2.095 Å. The longest $\text{P}-\text{S}$ bond was detected in 1,2-thiaphosphirane **43** (2.113 Å) and phosphetane **61c** (2.102 Å), and the shortest one in phosphabicyclo[4.4.0]decane 1-oxide **122** (2.02 and 2.04 Å). The $\text{P}-\text{C}$ bond length also varies insignificantly: the shortest $\text{P}-\text{C}$ bond was found in 1,2-thiaphosphirane **15** and in five- and six-membered 1,2-thiaphosphacyclanium salts **103b** ($\text{Hal} = \text{I}, \text{Br}$) and **108a** ($\text{X} = \text{ClO}_4$). The bond angles $\text{S}-\text{P}-\text{C}$ in all compounds shown in Table 2 are in keeping with the regular values corresponding to the size of the heterocycle (in three- and four-membered cycles, the bond angles decrease in compliance with the normal tendency connected with the presence of strained small rings).

VII. Conclusion

The material presented in this review is evidence of the essential progress in the field of synthesis of 1,2-thiaphosphacyclanes having the phosphorus atom in different valence states and

coordination. Such general synthetic routes should be noted as sulfur addition to methylenephosphines resulting in 2-thioxo-1,2λ⁵-thiaphosphiranes; the addition of phosphorus pentasulfide or the Lawesson reagent to a variety of unsaturated substrates leading to 2-thioxo-1,2λ⁵-thiaphosphetanes; the reaction of phosphorus pentasulfide with available five- or six-membered 2-oxo-1,2-oxaphosphacyclanes yielding 2-thioxo-1,2λ⁵-thiaphospholanes and -thiaphosphinanes; and intramolecular *S*-alkylation of ω-halogenoalkyl-substituted thiophosphoryl compounds, which give easy access to a wide range of mono- and bicyclic 2-oxo-1,2λ⁵-thiaphosphacyclanes, including those functionalised in the ring. The existence of convenient synthetic routes may open prospects for the further use of this type of organophosphorus compounds in fine organic synthesis, agriculture and some technical areas.

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[†] With the exception of compound **116b** ($\text{R}^1 = \text{OEt}$, $\text{R}^3 = \text{H}$).

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Natural compounds in the synthesis of chiral organophosphorus ligands

A G Tolstikov, T B Khlebnikova, O V Tolstikova, G A Tolstikov

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Abstract. Methods for the synthesis of chiral organophosphorus compounds based on natural optically active compounds (hydroxy acids, amino acids and their derivatives, mono- and disaccharides, mono- and diterpenoids, steroids) are discussed. Particular attention is given to the synthesis of bisphosphines and bisphosphinites. These compounds serve as ligands for transition metal complexes, which catalyse asymmetric hydrogenation. Data on the enantioselectivity of hydrogenation of unsaturated precursors of amino acids and unsaturated prochiral acids as well as on the enantioselectivity of hydrosilylation of ketones are surveyed. The bibliography includes 77 references.

I. Introduction

Chiral organophosphorus ligands are widely used in the synthesis of metal complex catalysts. It is these transition metal complexes with mono- and bidentate chiral phosphines and phosphinites that made it possible to perform important industrial reactions such as hydrogenation of prochiral unsaturated carbonyl compounds in preparative yield and with high enantioselectivity ($\geq 90\%$).

A large number of optically active phosphorus-containing ligands have been synthesised and used for the preparation of transition metal complexes exhibiting high catalytic activities resulting in high enantioselectivities.^{1–5} Chiral organophosphorus ligands are prepared either by enantiospecific transformations of native optically pure compounds or by transformations of prochiral compounds followed by resolution of racemates. Among natural compounds, hydroxy and amino acids as well as

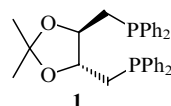
carbohydrates are most commonly used for the synthesis of such ligands (more rarely, terpenoids and steroids, are employed).

Syntheses of chiral organophosphorus ligands with the use of natural compounds have not been systematically surveyed in the literature. The aim of the present review is to close this gap.

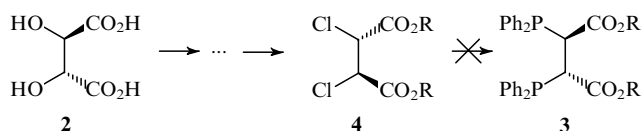
II. Organophosphorus ligands based on hydroxy acids

1. Synthesis of ligands

One of the first ligands used in asymmetric metal complex catalysis was DIOP, viz., (–)-*trans*-4,5-bis(diphenylphosphino-methyl)-2,2-dimethyl-1,3-dioxolane (**1**),

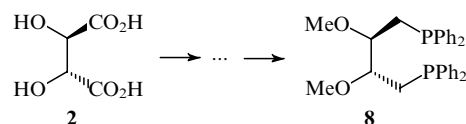


which was prepared by stereospecific transformations of (+)-(2*R*,3*R*)-tartaric acid (**2**).⁶ The synthesis of **1** was preceded by unsuccessful attempts to prepare chiral bisphosphine **3** from intermediate dichloride **4** by the reaction of the latter with nucleophilic reagents, viz., diphenylphosphine or diphenylphosphides MPPH_2 ($\text{M} = \text{Li}, \text{Na}, \text{K}$). However, in all cases only optically inactive phosphine oxide was isolated from the reaction mixtures.



An approach based on transformations of diethyl L-tartrate (**5a**) first into acetone, then into diol **6** and, finally, into ditosylate **7** appeared to be more efficient. Compound **7** was transformed into the target product (–)-DIOP (**1**) using sodium diphenylphosphide (Scheme 1).⁷

An analogous approach was used in the synthesis of dithoxybisphosphine **8**.



A G Tolstikov, O V Tolstikova Institute of Technical Chemistry, Urals Branch of the Russian Academy of Sciences, ul. Lenina 13-a, 614000 Perm, Russian Federation. Fax (7-342) 212 43 75.

Tel. (7-342) 212 62 37. E-mail: cheminst@mpm.ru (A G Tolstikov)

T B Khlebnikova G K Borekov Institute of Catalysis, Siberian Branch of the Russian Academy of Sciences, prosp. Acad. Lavrent'eva 5, 630090 Novosibirsk, Russian Federation. Fax (7-383) 234 30 56.

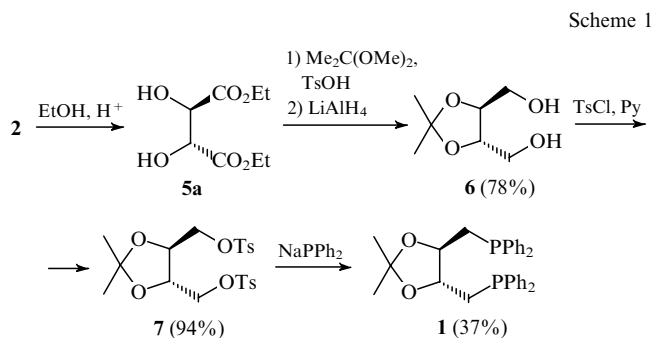
Tel. (7-383) 233 16 09. E-mail: khleb@catalysis.nsk.ru

G A Tolstikov N N Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, prosp. Akad. Lavrent'eva 9, 630090 Novosibirsk, Russian Federation. Fax (7-383) 234 47 52. Tel. (7-383) 304 49 80.

E-mail: gtolstik@nioch.nsc.ru

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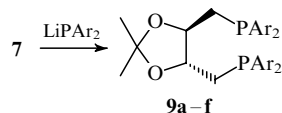


Unlike dimethoxy derivative **8**, DIOP is a crystalline compound due to which its isolation and additional purification can be substantially simplified. In addition, an essential advantage of ligand **1** over its acyclic analogue **8** is the conformational rigidity of the chelate ring formed upon its coordination to a transition metal atom due to the presence of *trans* substituents in the dioxolane ring. Metal complex catalysts thus prepared exhibit high stereoselectivity.⁷

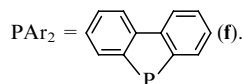
In the syntheses of chiral phosphines from natural compounds, the phosphine group is introduced by nucleophilic displacement of the toluenesulfonyl (methanesulfonyl) group or the halogen atom with alkali metal phosphides. There are two main procedures for the preparation of the latter compounds. One procedure (*in situ* synthesis of phosphides) is based on the reactions of chlorophosphines $\text{R}^1\text{R}^2\text{PCl}$ ($\text{R}^1, \text{R}^2 = \text{Ar}, \text{Alk}$) with alkali metals (Li, Na, K) in dioxane or tetrahydrofuran. Another widely used method involves the cleavage of the $\text{P}-\text{C}(\text{Ar})$ bond in tertiary phosphines by alkali metals followed by isolation of the resulting diarylphosphides.⁸ To improve the efficiency of the synthesis, one or another modification of phosphinylation is often required. Thus, high yields were achieved in all steps of the above-considered procedure for the synthesis of DIOP (see Scheme 1) except for the step of phosphinylation, which decreased the total yield of the product to 27%.⁷ Murrer *et al.*⁸ suggested that phosphinylation of ditosylate **7** should be performed with the diphenylphosphide anion, which is formed *in situ* in the reaction of triphenylphosphine with an alloy of Na and K. The use of this expedient made it possible to increase the yield in the last step of the reaction to 72% (the total yield of the ligand was 49%).

Other analogues of compound **1** were synthesised by the target replacement of substituents at the phosphorus atoms as well as by acetalisation of free hydroxy groups, which are generated upon hydrolysis of acetonide, with different carbonyl compounds.

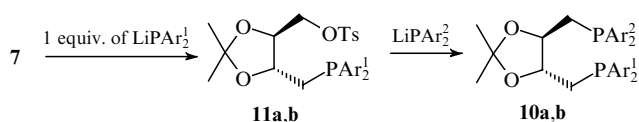
For example, the reactions of ditosylate **7** with lithium diarylphosphides afforded symmetrical bisphosphines **9a–f**.^{9–11}



$\text{Ar} = 2\text{-MeC}_6\text{H}_4$ (**a**), $4\text{-MeC}_6\text{H}_4$ (**b**), $2,5\text{-Me}_2\text{C}_6\text{H}_3$ (**c**),
 $4\text{-MeO-3,5-Me}_2\text{C}_6\text{H}_2$ (**d**), $4\text{-Me}_2\text{NC}_6\text{H}_4$ (**e**);

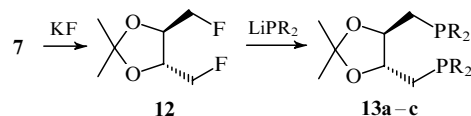


Unsymmetrical analogues of (–)-DIOP, *viz.*, compounds **10a,b** containing various aryl substituents at the phosphorus atoms, were synthesised in two steps. First, ditosylate **7** was treated with a particular lithium diarylphosphide (1 equiv.) and then the resulting monophosphines **11a,b** were treated with another diarylphosphide.¹⁰



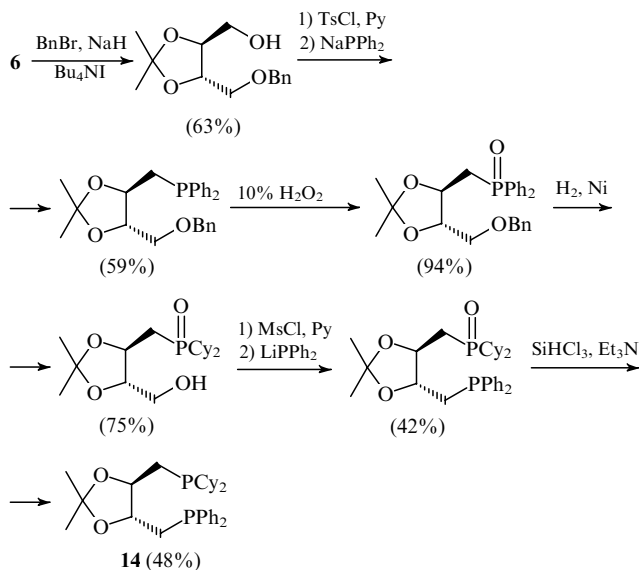
Compound	Ar ¹	Ar ²	Yield (%)
11a	Ph	—	44
11b	3-MeC ₆ H ₄	—	52
10a	Ph	4-MeNC ₆ H ₄	51
10b	3-MeC ₆ H ₄	4-MeNC ₆ H ₄	52

Alkyl derivatives of bisphosphine **1** were prepared from ditosylate **7** through intermediate difluoride **12**. The reactions of the latter with lithium dialkylphosphides afforded bisalkyl-bisphosphines, *viz.*, (–)-EtDIOP (**13a**), (–)-PrⁱDIOP (**13b**) and (–)-CyDIOP (**13c**).¹²



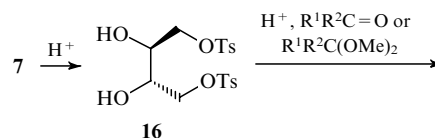
$\text{R} = \text{Et}$ (**a**, 83%), Pr^i (**b**, 34%), cyclo-C₆H₁₁ (**c**, 74%).

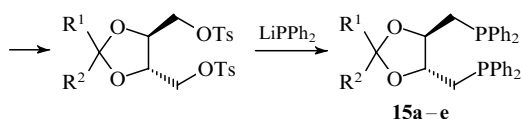
Unsymmetrical chiral bisphosphine (–)-DIOCP **14** containing cyclohexyl groups at one of the phosphorus atoms and bearing phenyl groups at another phosphorus atom was prepared from 2,3-*O*-isopropylidene-L-threitol (**6**) by the multistep synthesis.¹³



$\text{Ms} = \text{MeSO}_2$.

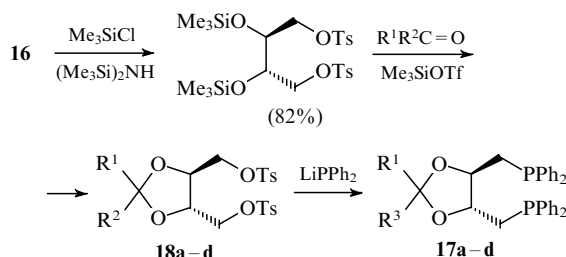
The introduction of substituents containing highly polar functional groups, which can form salts, into bisphosphine molecules gives rise to water-soluble organophosphorus ligands.¹⁴ Groups providing solubility of structural analogues of (–)-DIOP in water can be present not only in the aromatic fragments of the ligand (for example, quaternised compound **9e**) but also in the dioxolane ring. For example, among compounds **15a–e**, which were prepared from condensation products of diol **16** with various aldehydes or ketones,^{9, 15, 16} polyoxadioxolanes **15d,e** are soluble in water.





$R^1 - R^2 = (\text{CH}_2)_4$ (**a**), $(\text{CH}_2)_5$ (**b**); $R^1 = \text{H}$; $R^2 = \text{Ph}$ (**c**), $\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_5\text{Me}$ (**d**), $\text{CH}_2\text{O}(\text{CH}_2\text{CH}_2\text{O})_{16}\text{Me}$ (**e**).

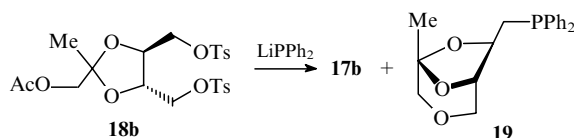
Bisphosphines **17** synthesised in the study¹⁷ are soluble in water due to the presence of hydroxy-containing substituents in the dioxolane ring.



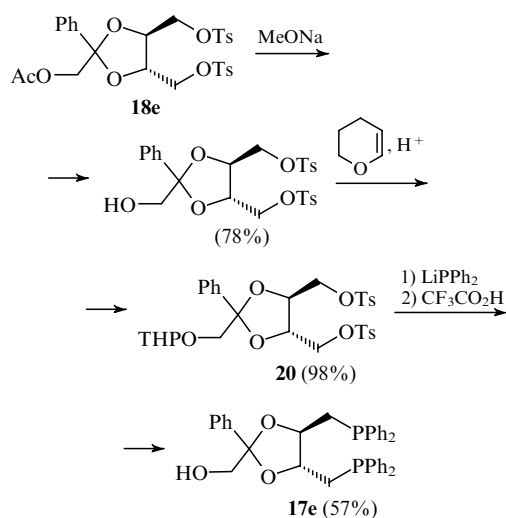
Tf = CF_3SO_2 .

Compound 17, 18	R^1	R^2	R^3	Yield (%)	
				18	17
a	Ph	Me	Me	80	79
b	Me	CH_2OAc	CH_2OH	89	52
c	H	2-AcOC ₆ H ₄	2-HOC ₆ H ₄	70	76
d	H	4-AcOC ₆ H ₄	4-HOC ₆ H ₄	73	82

Ligands **17a-d** were prepared from the corresponding ditosylates **18a-d** by the reactions with lithium diphenylphosphide, which were accompanied by elimination of acetyl groups. Phosphinylation of ditosylate **18b** afforded bisphosphine **17b** in substantially lower yield compared to those achieved in all other cases because this reaction gave rise to phosphine **17b** along with bicyclic ether ketal **19** (43%).¹⁷

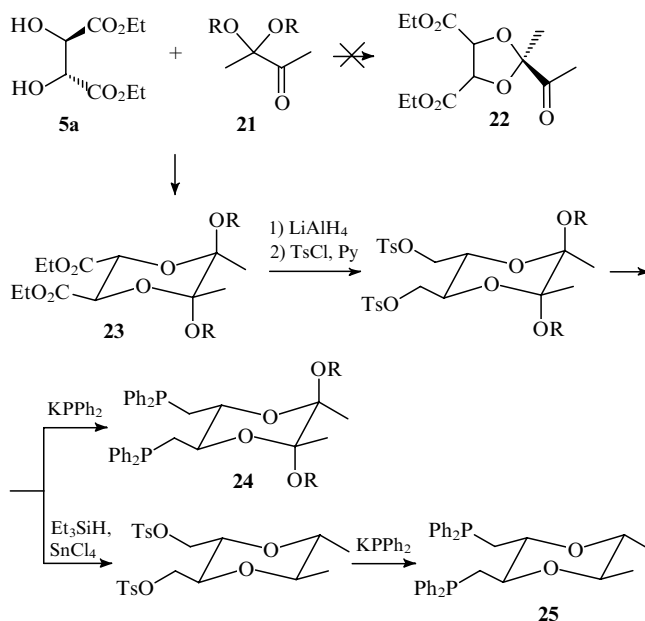


When performing analogous transformations of ditosylate **18e** ($R^1 = \text{Ph}$, $R^2 = \text{CH}_2\text{OAc}$), the acetyl group was replaced by the tetrahydropyranyl group to prevent undesired cyclisation in the final step of the synthesis. Subsequent transformations of ester **20** produced the target bisphosphine **17e**.¹⁷



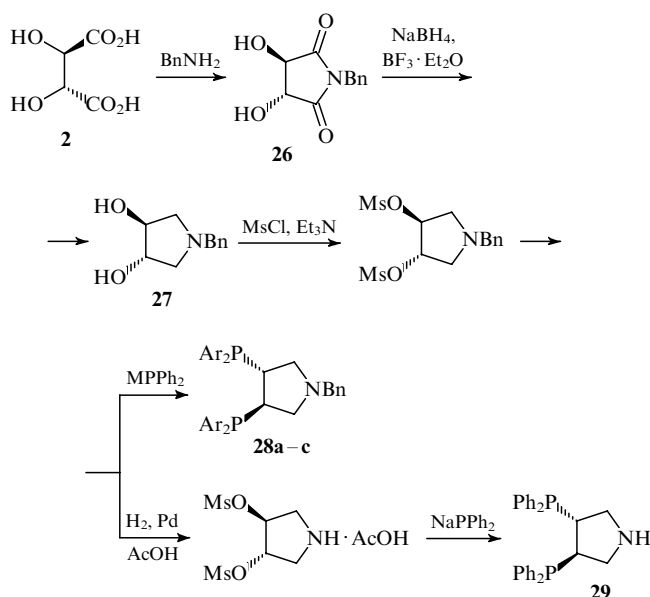
THP is tetrahydropyranyl.

Attempts to subject diethyl tartrate **5a** to acetalisation with butane-2,3-dione monoketals **21** led to the formation of 1,4-dioxane **23** instead of the expected dioxolane **22**. Compound **23** served as the starting compound for the synthesis of chiral bisphosphines of new structural types **24** and **25**.^{18, 19}



$R = \text{Me}$ (**a**), Et (**b**).

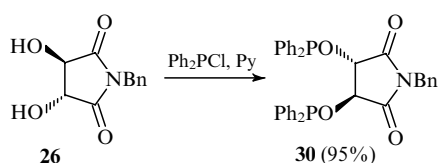
Yet another procedure for the preparation of C_2 -symmetrical ligands involves structural transformations of (+)-(-)(2*R*,3*R*)-tartaric acid (**2**) into pyrrolidine-type 1,2-bisphosphines. For example, heating of acid **2** with benzylamine afforded cyclic imide **26**, which was reduced by NaBH_4 to form dihydroxy-pyrrolidine **27**. The latter served as the starting compound for the synthesis of the DEGUPHOS ligand (**28a**), its derivatives (**28b,c**) and the PYRPHOS ligand (**29**). The presence of the amino group in these compounds substantially facilitates both their isolation from the reaction mixtures as hydrochlorides and subsequent purification.²⁰⁻²²



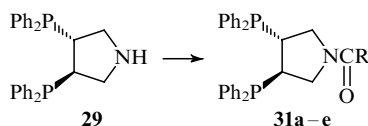
$M = \text{Na}$ (for **28a**), Li (for **28b,c**);

$\text{Ar} = \text{Ph}$ (**a**), 4-Me₂NC₆H₄ (**b**), 4-MeO-3,5-Me₂C₆H₃ (**c**).

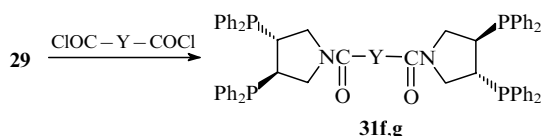
Treatment of imide **26** with chlorodiphenylphosphine in pyridine produced bisphosphinite **30**.²³



Acylation of the secondary amino group in bisphosphine **29** made it possible to prepare compounds **31a–g**, including C_2 -symmetrical ligands **31f,g**, viz., oxalic and terephthalic acid diamides.²¹

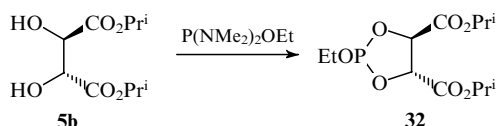


Reagent	Product	R	Yield (%)
PhCOCl	a	Ph	89
$(\text{Boc})_2\text{O}$ (Boc = $\text{Bu}^t\text{OC}(\text{O})$)	b	OBu^t	96
	c	$(\text{CH}_2)_3\text{CO}_2\text{H}$	100
$\text{MeO}(\text{CH}_2)_2\text{OCH}_2\text{COCl}$	d	$\text{CH}_2\text{O}(\text{CH}_2)_2\text{OMe}$	83
$\text{MeO}(\text{CH}_2\text{CH}_2\text{O})_3\text{CH}_2\text{COCl}$	e	$\text{CH}_2(\text{OCH}_2\text{CH}_2)_3\text{OMe}$	80



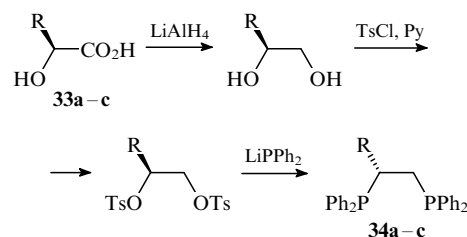
Y is a bond (**f**, 83%), C_6H_4 -*p* (**g**, 88%).

Cyclic monophosphites were synthesised based on derivatives of tartaric acid. For example, the reaction of diisopropyl tartrate **5b** with ethyl bis(dimethylamino)phosphinite produced compound **32**.²⁴

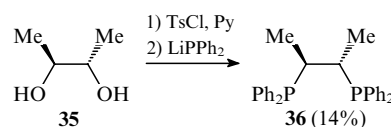


Bidentate organophosphorus ligands are derived also from natural α -hydroxycarboxylic acids. However, the general procedure for the preparation of chiral 1,2-bisphosphines based on these ligands involves the reaction of vicinal ditosylates with alkali metal organophosphides, which is difficult to reproduce. In this step of the synthesis, the $\text{S}_{\text{N}}2$ reaction is generally accompanied by competitive elimination giving rise to intermediate oxiranes. The latter are subjected to the repeated nucleophilic attack by the phosphide anion to produce a mixture of undesired hydroxy-monophosphines. Under certain conditions, the latter reaction becomes the major process, which substantially decreases the yield of the target bisphosphines. Nevertheless, bisphosphines (*R*)-PROPHOS (**34a**) and (*R*)-PHENPHOS (**34b**) were prepared from (*S*)-(+)-lactic (**33a**) and (*S*)-(+)-mandelic (**33b**) acids in 10 and 20% yields, respectively. The reaction with (2*R*,3*R*)-butanediol (**35**) afforded C_2 -symmetrical 1,2-bisphosphine (*S,S*)-CHIRAPHOS (**36**). The (*R*)-CYCPHOS ligand (**34c**) was synthesised from (*S*)-(+)-hexahydromandelic acid (**33c**), which was generated by hydrogenation of (*S*)-(+)-mandelic acid (5% $\text{Rh}/\text{Al}_2\text{O}_3$ as the catalyst). Unlike the (*R*)-PHENPHOS compound (**34b**) isolated in pure form, bisphosphines (*R*)-PROPHOS (**34a**), (*R*)-CYCPHOS (**34c**) and (*S,S*)-CHIRAPHOS (**36**) were contaminated with by-products. To purify the latter bisphosphines, they were transformed into insoluble complexes with

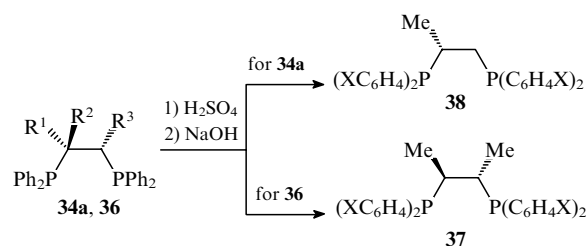
NiCl_2 and then optically pure ligands were regenerated by treatment with sodium cyanide.^{25–28}



R = Me (**a**), Ph (**b**), Cy (**c**).

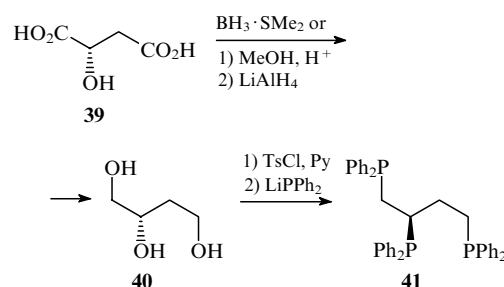


The introduction of highly polar substituents into the aromatic fragments of the (*R*)-PROPHOS (**34a**) and (*S,S*)-CHIRAPHOS (**36**) ligands gave rise to water-soluble derivatives. The reaction of chiral ligand **36** with oleum produced the tetrasulfonated analogue of (*S,S*)-CHIRAPHOS (**37**). Under the same conditions, sulfonation of bisphosphine **34a** proceeded much more slowly and with lower selectivity. The tetrasulfonated analogue of (*R*)-PROPHOS (**38**) was isolated only as a mixture with trisulfonated phosphine and phosphine oxide (in 55%, 35% and 10% yields, respectively).²⁹

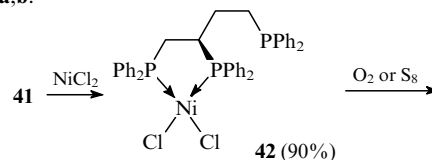


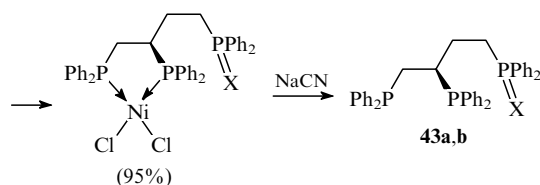
34a: $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{R}^3 = \text{H}$; **36**: $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{R}^3 = \text{Me}$; X = 3- SO_3Na .

Mono-, bi- and tridentate chiral phosphine ligands in which only one diphenylphosphine group is directly bound to the asymmetric centre were synthesised starting from L-malic acid (**39**). Reduction of acid **39** with the borane dimethyl sulfide complex followed by the two-step treatment of triol **40** with tosyl chloride and lithium diphenylphosphide afforded 1,2,4-trisphosphine **41**.³⁰



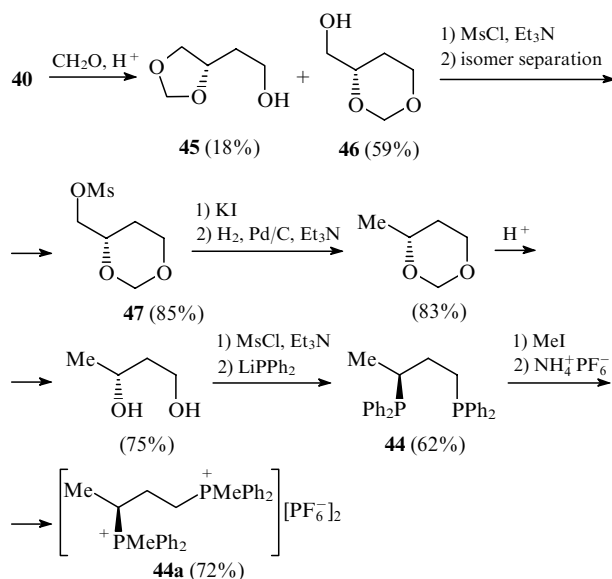
Trisphosphine **41** can selectively form nickel complex **42** involving only the vicinal phosphine groups. This made it possible to modify the remote phosphine group giving rise to ligands **43a,b**.³¹



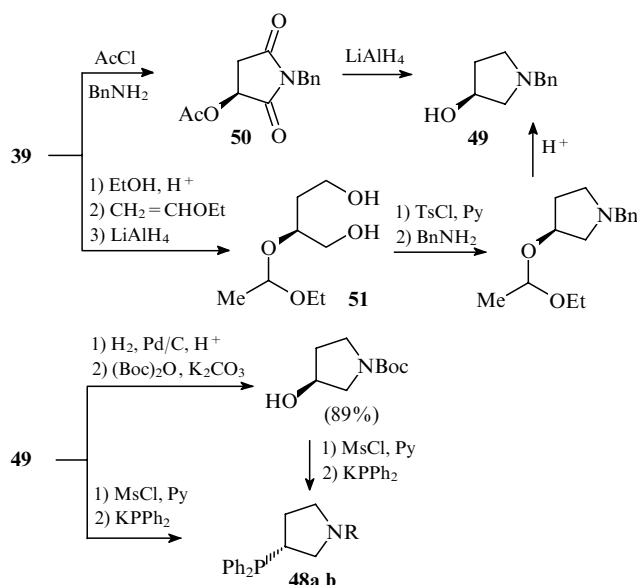


X = O (**a**, 63%), S (**b**, 77%).

Chiral 1,3-bisphosphine **44** was synthesised starting from triol **40**, which was prepared by reduction of dimethyl L-malate.³² The reaction of compound **40** with formaldehyde produced a mixture of cyclic acetals **45** and **46**. The latter was subjected to mesylation without separation. The major isomer **47**, which was isolated from the mixture of the resulting methanesulfonates, was transformed into the target bisphosphine **44** in five steps. The reaction product was characterised as the stable bisquaternary salt **44a**.



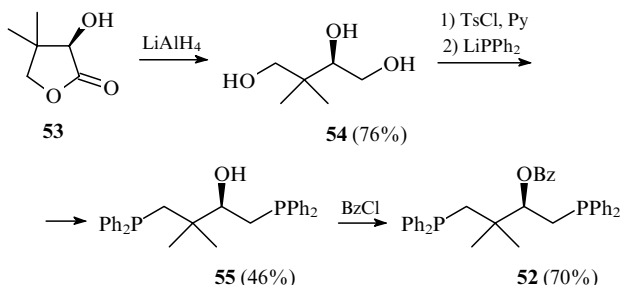
The synthesis of chiral monophosphines **48a,b** from L-malic acid (**39**) was based on transformations of intermediate hydroxypyrrolidine **49**. The latter was prepared without epimerisation of the chiral centre either by the two-step synthesis (heterocyclisation followed by reduction) through imide **50** or by the six-step



R = Bn (**a**, 75%), Boc (**b**, 70%).

synthesis (reduction followed by heterocyclisation) through protected triol **51**.³³

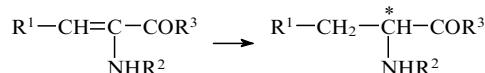
In the study,³⁰ bisphosphine **52** was synthesised starting from natural optically active pantolactone **53**. Tosylation of triol **54** followed by phosphinylation of the tosylates yielded bisphosphine **55** instead of the expected trisphosphine.



The phosphorus-containing ligands thus prepared were used for the synthesis of metal complex catalysts.

2. Use in asymmetric synthesis

The stereodifferentiating abilities of ligands and catalysts are most often estimated and compared using catalytic asymmetric hydrogenation, for example, asymmetric hydrogenation of unsaturated α -amino acids and their derivatives.



R¹ = Alk, Ar; R² = Alk, Ar, COAlk, COAr; R³ = OH, OAlk, NAlk₂.

Metal complexes with DIOP exhibit high catalytic activities in hydrogenation with enantioselectivity varying from moderate to high depending on the structure of the substrate subjected to hydrogenation. It appeared that the enantiomeric purities of the hydrogenation products of free *N*-acylaminocinnamic acids are much higher (*ee* = 25%–81%) than those of the hydrogenation products of their esters on the same catalysts (*ee* = 5%–55%).⁴

The products were obtained with an enantiomeric excess of 90%–92% by reduction of certain enamides using the cationic complex [Rh(COD)(DIOP)]⁺ClO₄[−], where COD is cyclooctadiene.³ The methyl substitution in the *meta* position of the aromatic ring of the ligand made it possible to achieve an enantiomeric purity of 88% in the asymmetric synthesis of 3-(3,4-dihydroxyphenyl)alanine derivatives.⁹

Analogues of DIOP containing electron-donating substituents at the phosphorus atom were also successfully used as catalysts for asymmetric hydrogenation of electron-deficient alkenes and carbonyl compounds. Thus, reduction of itaconic acid and its β -aryl derivatives catalysed by Rh(I) complexes with ligands **9d,e** afforded products with an enantiomeric purity of 91%–96%, whereas the enantioselectivity of reduction of these substrates in the presence of the Rh(I) complex with unmodified DIOP was at most 58%.¹¹

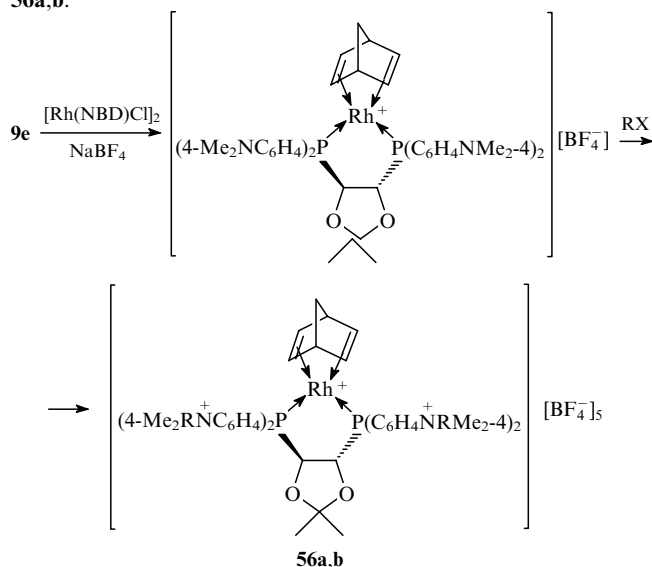
The Rh(I) complexes with chiral bisphosphines **13a–c** were successfully used in hydrogenation of α -oxo amides and *N*-oxo-acylamino acid esters. It was demonstrated that the activity and enantioselectivity of the catalyst increases as the size of the alkyl substituent at the phosphorus atom in the ligand increases. The enantiomeric excess of up to 77% was achieved in hydrogenation of *N*-benzylphenylglyoxylamide catalysed by the Rh(I) complex with CyDIOP ligand **13c**.¹² The Rh(I) complex with DIOCP ligand **14** appeared to be a better stereodifferentiating catalyst for asymmetric hydrogenation of α -ketopantolactone than the Rh(I) complexes with the DIOP and CyDIOP ligands. The enantiomeric purities of the products prepared with the use of these catalysts were 72%, 52% and 45%, respectively.¹³

Rhodium catalysts containing DIOP derivatives with dibenzophosphole groups (compound **9f**) as ligands proved to be less

enantioselective in hydrogenation of α -acetamidocinnamic acid than Rh catalysts with unmodified bisphosphine ligands (*ee* decreased from 81% to 28%). At the same time, the use of ligand **9f** in a Pd(II) complex made it possible to increase the enantiomeric purity of the product of asymmetric hydroesterification of α -methylstyrene to 44% (in the case of DIOP, *ee* = 9%).⁴

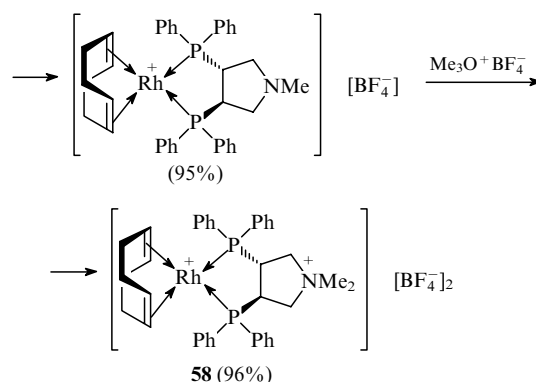
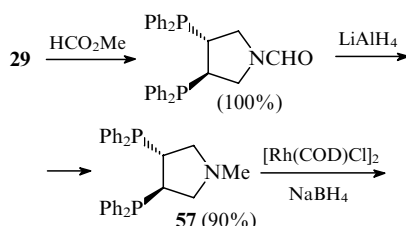
Modifications of the acetal groups of DIOP (compounds **15a–c**) do not change the structure of the coordination centre of the catalyst and, consequently, have only a slight effect on the stereoselectivity of the reaction.^{9,15} The enantioselectivity of hydrogenation of unsaturated acids catalysed by Rh(I) complexes with hydroxy-containing ligands **17b–e** is increased due, apparently, to additional interactions between the substrate and functional groups of the ligand remote from the coordination centre.¹⁷ Hydrogenation of methyl (*Z*)-2-*N*-benzamidocinnamate on Rh(I) complexes with ligands **24** and **25** proceeded with moderate enantioselectivity. The highest enantiomeric excess (54%) was obtained in hydrogenation catalysed by the Rh(I) complex with ligand **24b**.¹⁹

The synthesis of water-soluble chiral bisphosphine ligands enables one to solve some problems of homogeneous catalysis. In particular, the use of water-soluble rhodium phosphine catalysts for asymmetric hydrogenation in two-phase (aqueous–organic) systems substantially simplifies separation of the reaction products present in the organic phase from the catalyst. The rhodium phosphine complex that remains in the aqueous phase can be repeatedly used without substantial loss of efficiency. As mentioned above, water-soluble ligands are prepared by introducing highly polar functional groups into the bisphosphine structure. These groups can be present both in the phosphine and alkyl fragments of the molecule. For example, quaternisation at the nitrogen atoms of ligand **9e** [tetraamino analogue of (–)-DIOP] in the Rh complex afforded water-soluble chiral complexes **56a,b**.¹⁴



NBD is norbornadiene; R = H (**a**), Me (**b**);
RX = HBF₄ (for **a**), Me₃O⁺BF₄[–] (for **b**).

Quaternisation of the amino group of bisphosphine ligand **57** (prepared from PYRPHOS **29**) in the rhodium complex gave rise to water-soluble catalyst **58**.²⁰



However, the enantioselectivity of hydrogenation in the presence of water-soluble Rh catalysts was found to be much lower than that of hydrogenation performed with Rh catalysts based on unmodified DIOP. Besides, the use of complexes **56a,b** led to a change in the sign of asymmetric induction. These results suggest that ammonium substituents in aromatic fragments of the DIOP ligand substantially influence the conformation of the chelate ring in the catalysts.¹⁴

The use of Rh(I) catalysts with water-soluble polyoxabisphosphines **15d,e** in hydrogenation of *N*-acylaminocinnamic acids in water led to a decrease in the enantiomeric purity of the product to 30% (hydrogenation on the same catalysts in ethanol gave *ee* = 75%).¹⁶ The enantioselectivity of hydrogenation of *N*-acylaminocinnamic acids in water catalysed by the cationic Rh(I) complex with ligand **17a** was also no higher than 34%. However, the addition of sodium dodecyl sulfate as an amphiphilic agent to the reaction mixture made it possible to increase the enantioselectivity of the reaction to 77%.³⁴

Hydrogenation of (*Z*)- α -acetamidocinnamic acids on Rh(I) complexes with bis(diphenylphosphino)pyrrolidine-type ligands proceeded with high enantioselectivity [92%, 94% and 96% for ligands **29** (PYRPHOS) and **28b,c**, respectively].^{21,22} The use of catalyst **58** for hydrogenation of sodium α -acetamidocinnamate in water made it possible to prepare (*S*)-*N*-acetylphenylalanine with an enantiomeric purity of 90%.²⁰

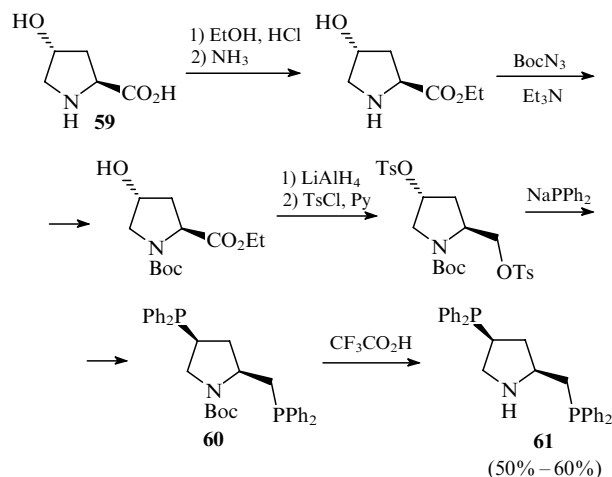
The Rh(I) complexes with the (*R*)-PROPHOS (**34a**), (*R*)-PHENPHOS (**34b**), (*R*)-CYCPHOS **34c** and (*S,S*)-CHIRAPHOS (**36**) ligands serve as highly efficient catalysts for enantioselective hydrogenation of unsaturated precursors of amino acids. The enantiomeric purities of the products prepared with the use of these catalysts were higher than 80%. The best result (*ee* = 100%) was achieved in hydrogenation of acetamidoisopropylacrylic acid catalysed by the Rh(I) complex with (*S,S*)-CHIRAPHOS.^{25–28} The Rh(I) complex with ligand **37** [water-soluble analogue of the (*S,S*)-CHIRAPHOS ligand] also showed high enantioselectivity (*ee* up to 94%) in reduction of unsaturated amino acids both in water and a two-phase aqueous-organic system.^{14,29}

The enantioselectivity of catalytic hydrogenation of precursors of amino acids catalysed by the Rh(I) complexes with ligands **41** and **44** appeared to be low. For example, reduction of (*Z*)- α -acetamidocinnamic acid using Rh(I) complexes with trisphosphine **41** afforded the target product with an enantiomeric excess of 25%.³¹ The enantiomeric purity of the reduction product prepared with the use of the Rh(I) complex with ligand **44** was no higher than 20%.³² The replacement of one phosphine group in ligand **44** by phosphine oxide or phosphine sulfide (compounds **43a,b**) led to a substantial enhancement of enantioselectivity of the catalyst. For example, the use of the Rh(I) complexes with ligands **43a,b** in the hydrogenation of (*Z*)- α -acetamidocinnamic acid made it possible to increase the enantiomeric purities of the products to 72%–74%.³¹

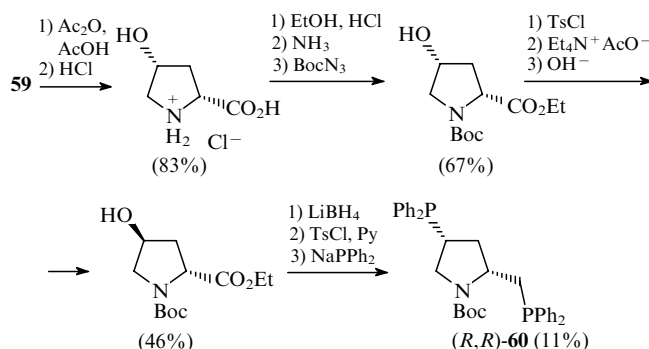
III. Organophosphorus ligands based on amino acids

1. Synthesis of ligands

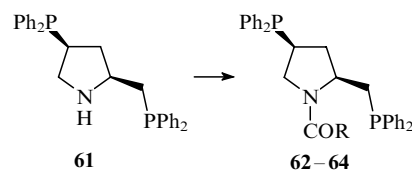
A large number of efficient chiral phosphorus-containing ligands were prepared starting from natural and synthetic amino acids. For instance, readily accessible 4-hydroxy-L-proline (**59**) can be used as the starting compound for the synthesis of the above-mentioned ligands. The first hydroxyproline derivatives to be prepared were 1,4-bisphosphines (2*S*,4*S*)-BPPM (**60**) and (2*S*,4*S*)-PPM (**61**).³⁵



The synthesis of the optical antipode of bisphosphine **60**, viz., the chiral ligand (2*R*,4*R*)-BPPM, required successive epimerisation of two chiral centres of 4-hydroxy-L-proline (**59**).³⁶



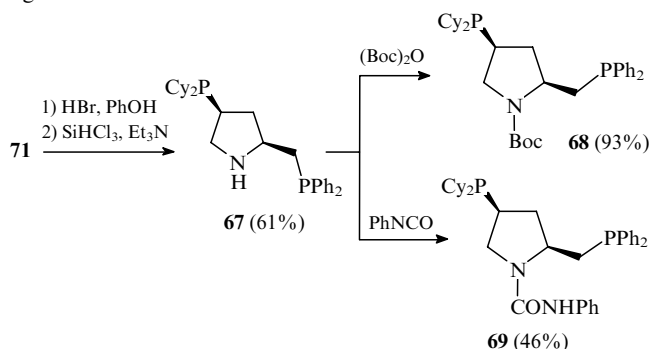
Later on, various derivatives of bisphosphinopyrrolidines **61**, viz., amides **62**, carbamides **63** and carbamates **64a,b**, were prepared.³⁷



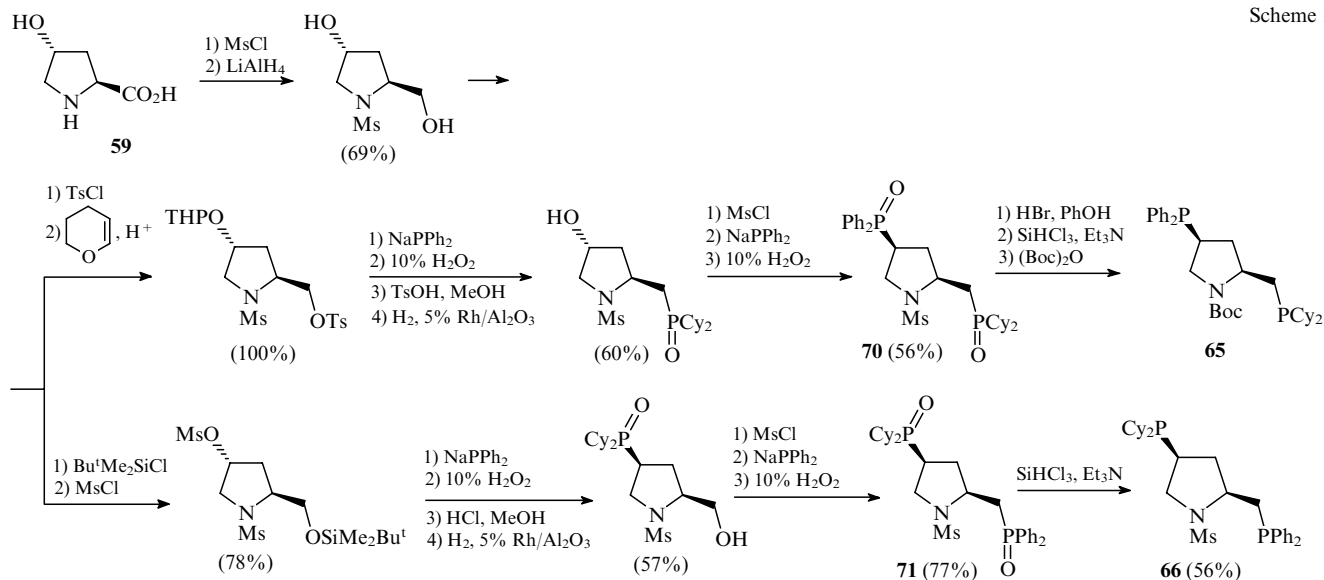
Reagent	Product	R	Yield (%)
HCO ₂ H, AcOH	62a	H	65
MeCOCl, Py (or Et ₃ N)	62b	Me	70
Bu ^t COCl, Py (or Et ₃ N)	62c	Bu ^t	75
PhCOCl, Py (or Et ₃ N)	62d	Ph	91
MeNCO	63a	MeNH	95
Bu ^t NCO	63b	Bu ^t NH	73
PhNCO	63c	PhNH	76
MeOCOCl	64a	MeO	91
PhOCOCl	64b	PhO	99

The synthesis of bisphosphines **65–69** containing various combinations of cyclohexyl and phenyl groups at the phosphorus atoms offers wide possibilities in the design of pyrrolidine-type ligands.^{38,39} Multistep transformations of 4-hydroxy-L-proline (**59**) produced phosphine oxides **70** and **71**. Bisphosphine **65** was derived from compound **70** (Scheme 2).

Phosphine oxide **71** was used for the preparation of the target ligands **66–69**.

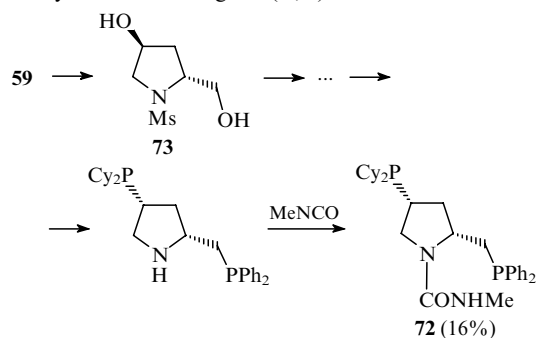


An analogous sequence of transformations was employed in the synthesis of ligand **72**, in which the stereocentres have configurations opposite to those in bisphosphine **65**. The ligand

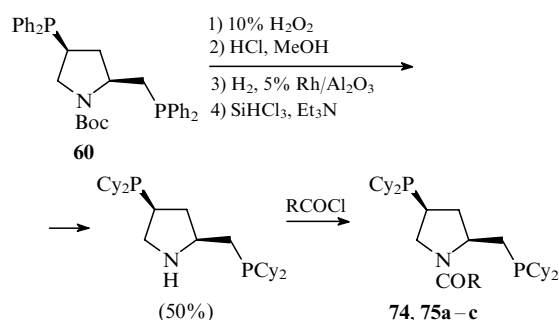


Scheme 2

72 was prepared starting from 4-hydroxy-*N*-(methylsulfonyl)-D-prolinol (**73**), which was generated by epimerisation of the chiral centres of 4-hydroxy-L-proline (**59**) according to the method used for the synthesis of the ligand (*R,R*)-**60**.⁴⁰

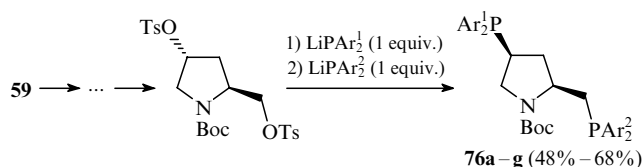


Chiral bisphosphines **74** and **75a–c** were generated from bisphosphine **60**.¹²



R = *OBu*^t (**74**, 54%), *NHPh* (**75a**, 78%), *NHCy* (**75b**, 75%), *NHBu*^t (**75c**, 89%).

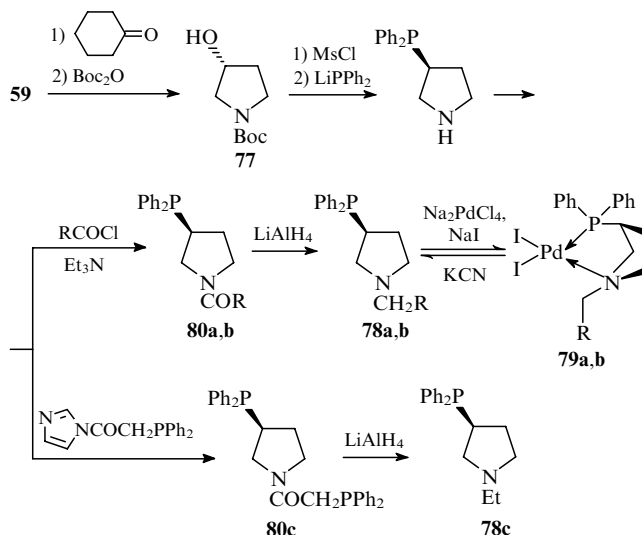
Various ligands **76a–g** containing functional substituents in aromatic rings of the bisphosphine fragments were synthesised from other analogues of (*2S,4S*)-BPPM.^{41–43}



Ar¹ = Ar² = 2-MeOC₆H₄ (**a**), 3-MeOC₆H₄ (**b**), 4-MeOC₆H₄ (**c**), 4-MeO-3,5-Me₂C₆H₂ (**d**), 4-Me₂NC₆H₄ (**e**); Ar¹ = Ph, Ar² = 4-Me₂NC₆H₄ (**f**); Ar¹ = 4-Me₂NC₆H₄, Ar² = Ph (**g**).

Alcohol **77**, which was prepared by decarboxylation of 4-hydroxy-L-proline (**59**), was transformed into chiral mono-phosphines **78a–c**. The optically pure ligands **78a,b** were isolated in the individual form after treatment of palladium complexes **79a,b** with potassium cyanide. It should be noted that reduction of

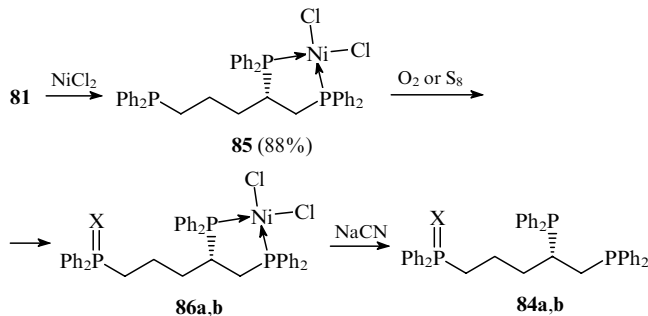
phosphine amides **80a,b** with lithium aluminium hydride giving rise to phosphine amines **78a,b** proceeded smoothly without elimination of the diphenylphosphine group at the chiral centre. By contrast, analogous reduction of bisphosphine **80c** was accompanied by elimination of the activated phosphine group to form monophosphine **78c** instead of the expected tridentate P,N,P ligand.³³



R = Ph (**a**), 4-MeC₆H₄ (**b**).

Chiral trisphosphine **81** and bisphosphine **82** were derived from L-glutamic acid **83** (Scheme 3).³⁰

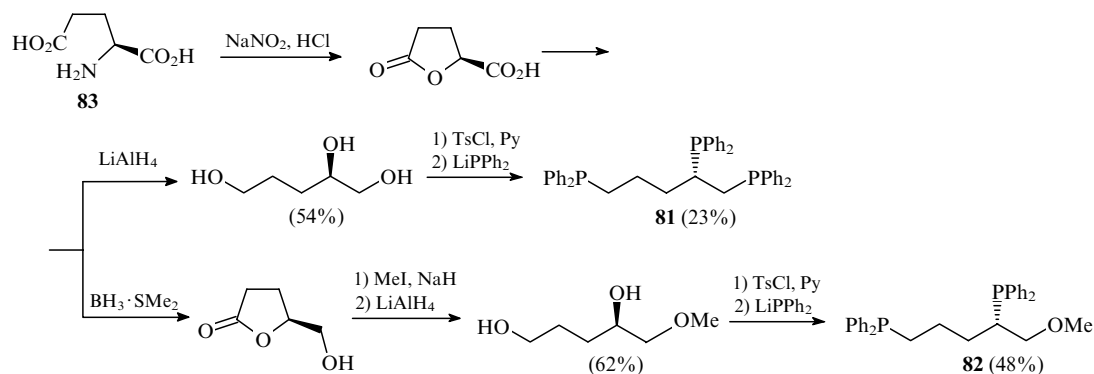
Phosphine oxide **84a** and phosphine sulfide **84b** were synthesised using a known procedure, which required the additional preparation of intermediate Ni complex **85** from trisphosphine **81**. Oxidation or sulfonation of the free phosphine group in compound **85** produced complexes **86a,b**, respectively. Regeneration with sodium cyanide completed the synthesis of the target ligands.^{30, 31}



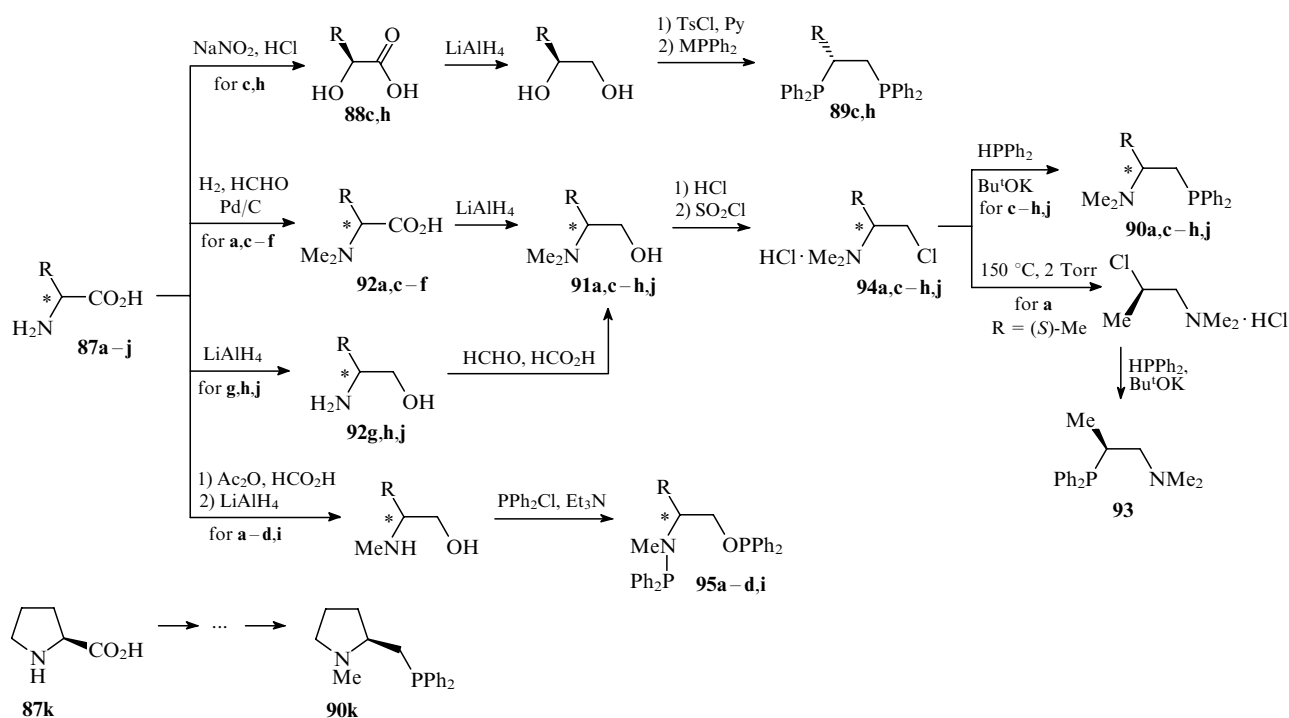
X = O (**a**, 63%), S (**b**, 31%).

Enantiospecific transformations of natural and synthetic amino acids were employed for the preparation of chiral 1,2-

Scheme 3



Scheme 4



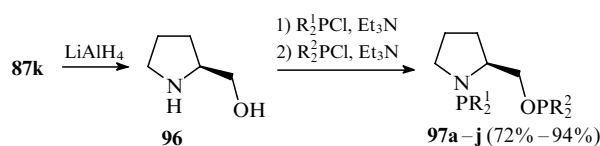
R = (S)-Me (a), (S)-Et (b), (S)-Prⁱ (c), (S)-Bu^t (d), (R)-Bu^s (e), (R)-Bu^t (f), (R)-Cy (g), (S)-Bn (h), (R)-Bn (i), (R)-Ph (j); M = Li, Na, K.

bisphosphines, aminophosphines and phosphinoaminophosphinites (Scheme 4). The synthesis of bisphosphines was preceded by the transformation of the amino group in the starting amino acid into the hydroxy group under the action of HNO₂. For example, hydroxy acids **88c,h** derived from (S)-valine (**87c**) and (S)-phenylalanine (**87h**), respectively, were transformed into chiral bisphosphines **89c,h** according to a conventional procedure.⁴⁴

Chiral ligands **90a,c-h,j,k** were synthesised starting from (S)-alanine (**87a**), (S)-valine (**87c**), (S)-leucine (**87d**), (S)-isoleucine (**87e**), (R)-tert-leucine (**87f**), (R)-cyclohexylglycine (**87g**), (S)-phenylalanine (**87h**), (R)-phenylglycine (**87j**) and (S)-proline (**87k**), respectively, by successive transformations involving N,N-dimethylation, reduction and chlorination in different orders. It should be noted that the key β-dimethylamino alcohols **91g,h,j** were synthesised in higher yields by N,N-dimethylation of amino alcohols **92g,h,j** prepared by reduction of the corresponding amino acids. Aminophosphine **93** was produced by the thermal rearrangement of chloro derivative **94a** followed by phosphinylation in the presence of potassium *tert*-butoxide.^{23, 45, 46}

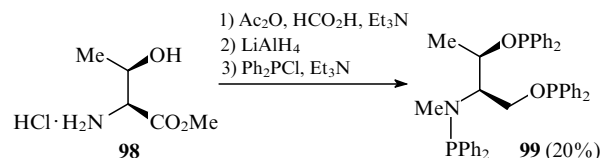
After N-formylation and reduction with LiAlH₄, amino acids **87a-d,i** were transformed into N,O-bisphosphinylaminoethanols **95a-d,i** (see Scheme 4).⁴⁷⁻⁴⁹

(S)-Prolinol (**96**) produced by reduction of (S)-proline (**87k**) was used as the starting compound for the synthesis of phosphinoaminophosphinites containing identical (**97a-d**) or different (**97e-j**) substituents at the phosphorus atoms.^{50, 51}



R¹ = R² = Prⁱ (a), cyclo-C₅H₉ (b), Cy (c), Ph (d); R¹ = Prⁱ, R² = Cp (e); R¹ = Cp; R² = Prⁱ (f), Cy (g), Ph (h); R¹ = Cy, R² = Cp (i); R¹ = Ph, R² = Cp (j).

Tridentate phosphinoaminobisphosphinite **99** was derived from (2S,3R)-threonine (**98**).⁵²



The sequence of transformations of this compound is analogous to that used for transformations of amino acids **87a-d,i** into phosphinoaminophosphinites **95a-d,i** (see Scheme 4).

2. Use in asymmetric synthesis

Catalysts based on pyrrolidine-type bisphosphines BPPM (**60**) (proline derivatives) were used in hydrogenation of various substrates. Generally, such reactions proceed at 50 atm. For hydrogenation products of α-acetamidoacrylic acids, good results were obtained (enantiomeric purity up to 91%) in the presence of Rh(I) complexes with the unmodified (2S,4S)-BPPM ligand and its optical antipode, *viz.*, (2R,4R)-BPPM.^{35, 36} The enantioselectivity of hydrogenation of (Z)-2-acetylaminocinnamic acid was increased to 98% by introducing the methoxy group in the *ortho* position of the benzene rings of this ligand (compound **76a**). The use of the Rh(I) complex with ligand **76c** containing the methoxy groups in the *para* positions of the benzene rings made it possible to increase the [substrate]:[catalyst] ratio from 10³ to 10⁴.⁴¹ Hydrogenation of derivatives of (Z)-2-acetamidoacrylic acids on the Rh catalyst with ligand **76d** afforded products with *ee* = 99% (*p*_{H2} = 20 atm, [substrate]:[catalyst] = 10⁴).⁴² These results are consistent with the assumption^{41, 42} that an increase in the enantioselectivity of the catalyst results from the steric effect of the *o*-MeO substituents in the aromatic fragments of the ligand. The electron-donating substituents in the benzene ring also substantially influence the reaction rate, the best result being achieved for compounds containing the *p*-MeO groups.^{41, 42}

Hydrogenation of ketopantolactone catalysed by the Rh(I) complexes with the BPPM ligand proceeded with an enantioselectivity of 87% (50 °C, *p*_{H2} = 50 atm).⁴ Of Rh(I) complexes with cyclohexyl analogues of the BPPM ligand, the metal complex with ligand **68** containing both the cyclohexyl and phenyl substituents

at the phosphorus atom provided the highest enantiomeric yield (*ee* up to 91%) in this reaction. The Rh(I) complexes with this bisphosphine and its analogue containing only the dicyclohexylphosphine groups (compound **74**) exhibited much higher catalytic activities in this reaction as compared to the catalyst prepared based on the unmodified BPPM ligand (the [substrate]:[catalyst] ratio increased from 10^2 to 10^4 ; see Refs 38 and 39). Hydrogenation of ketopantolactone in the presence of the Rh(I) complex with bisphosphine ligand **75c** containing the carbamoyl substituent proceeded under substantially milder conditions, *viz.*, at room temperature and under normal H_2 pressure. However, the enantioselectivity of this reaction was at most 66%.¹²

Of the three types of rhodium catalysts with *N*-substituted pyrrolidinebisphosphines **62–64**, the Rh(I) complexes with *N*-carbamoyl ligands **63a–c** proved to be most efficient in the hydrogenation of 2-methylidenesuccinamic acid. The use of these catalysts led to an increase in the enantioselectivity to 77% at normal H_2 pressure, whereas hydrogenation catalysed by the Rh(I) complexes with ligands **62a–e** and **64a,b** proceeded only under an H_2 pressure of 30 atm, the enantiomeric purities being 43%–64% and 53%–66%, respectively.³⁷

The introduction of the *p*-Me₂N group into the benzene ring of the BPPM ligand (compounds **76e–g**) led to an increase in the activity and stereoselectivity of the Rh catalyst for the hydrogenation of dimethyl itaconate. The best results (*ee* = 93%, the conversion was 100%) were achieved in the presence of the Rh(I) complex with ligand **76f** (for comparison, hydrogenation catalysed by the complex with unmodified BPPM afforded the product with an *ee* of 5% and a conversion of 36%).⁴³

The Rh(I) complexes with tris- (**81**) and bisphosphines (**82**) exhibited moderate enantioselectivity in hydrogenation of (*Z*)- α -acetylaminocinnamic acid (*ee* = 31%–36% and 54%–58%, respectively). The transformation of one of the phosphine groups into phosphine oxide (compound **84a**) or phosphine sulfide (compound **84b**) led to an increase in the enantioselectivity of the catalyst for hydrogenation of (*Z*)- α -acetylaminocinnamic acid. Thus, the enantiomeric purities of the hydrogenation product prepared in the presence of the Rh(I) complexes with ligands **84b** and **84a** were 54%–58% and 85%–89%, respectively.^{31, 32}

Rhodium complexes with bisphosphines **89c,h** were successfully used in enantioselective hydrogenation of (*Z*)- α -acylaminoacrylic acids to form the corresponding α -acylamino acids (*ee* = 85%–99%).⁴⁴ Unlike Ni(0) complexes with β -dimethylaminomethylphosphines **90a,c–h,j**, Ni(0) complexes with ligands of this type proved to be less efficient in catalytic asymmetric cross-coupling. The highest enantiomeric purity (*ee* up to 80%) of the products of this reaction was achieved with the use of Rh(I) complexes prepared based on ligands **90c,e,h,j**. It was demonstrated that an increase in the stereoselectivity of hydrogenation in the presence of catalysts containing aminophosphines of the structural type **90** as ligands is favoured by an increase in the volume of the substituent at the chiral β -carbon atom directly bound to the dimethylamino group. For example, *ee* of 25% and 38% were achieved in hydrogenation catalysed by the Ni(0) complexes with ligands **93** and **90e**, respectively.^{45, 46} In asymmetric hydrosilylation of acetophenone, Rh(I) complexes with phosphinoaminophosphinites **95a,c** showed low enantioselectivity (*ee* = 10%–26%), which depended on the structure of the silane used.⁴⁸ Hydrogenation of *N*-acetylaminocinnamic acid in the presence of the Rh(I) complex with phosphinoaminophosphinite **95i** afforded products with *ee* = 60%.⁴⁹

Cationic Rh(I) complexes based on ligands **97** were used as catalysts for asymmetric hydrogenation of activated ketones, the best results (*ee* = 85%) being achieved with the complex based on phosphinite **97j**.^{50, 51}

Asymmetric hydrovinylation of 1,3-cyclohexadiene catalysed by Ni(0) complexes with ligand **99** afforded products with *ee* = 93%, whereas the enantioselectivity of the same reaction in the presence of Ni(0) complexes with phosphinoaminophosphinites **95a,c** was no higher than 50%.⁵²

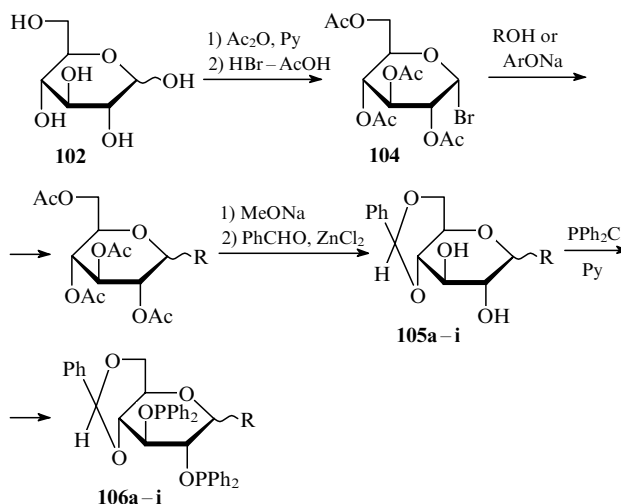
Therefore, the above-considered examples demonstrate that metal complexes with chiral organophosphorus ligands based on both natural and synthetic amino acids show promise as catalysts.

IV. Organophosphorus ligands based on carbohydrates

1. Synthesis of ligands

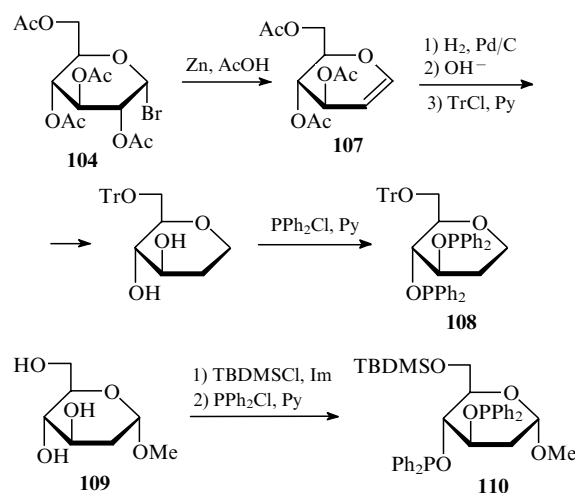
Carbohydrates and their derivatives are readily accessible, optically pure and contain several functional groups at the asymmetric centres with different configurations, which can be readily transformed. Hence, these compounds are attractive for the synthesis of chiral heteroorganic ligands. The synthesis of diastereomeric bisphosphines **100a,b** and bisphosphinites **101a,b** from α -D-glucose **102** was described in the study.⁵³ In this synthesis, 3-*O*-benzyl-1,2-*O*-cyclohexylidene- α -D-glucopyranose **103** (Scheme 5) was generated as an intermediate.

D-Glucopyranoside **102** was transformed into glucosyl bromide **104**, from which aryl- and alkyl-*O*-glucosides **105a–i** were generated. The latter compounds were used in the synthesis of chiral 2,3-bis(diphenylphosphinites) **106a–i**.



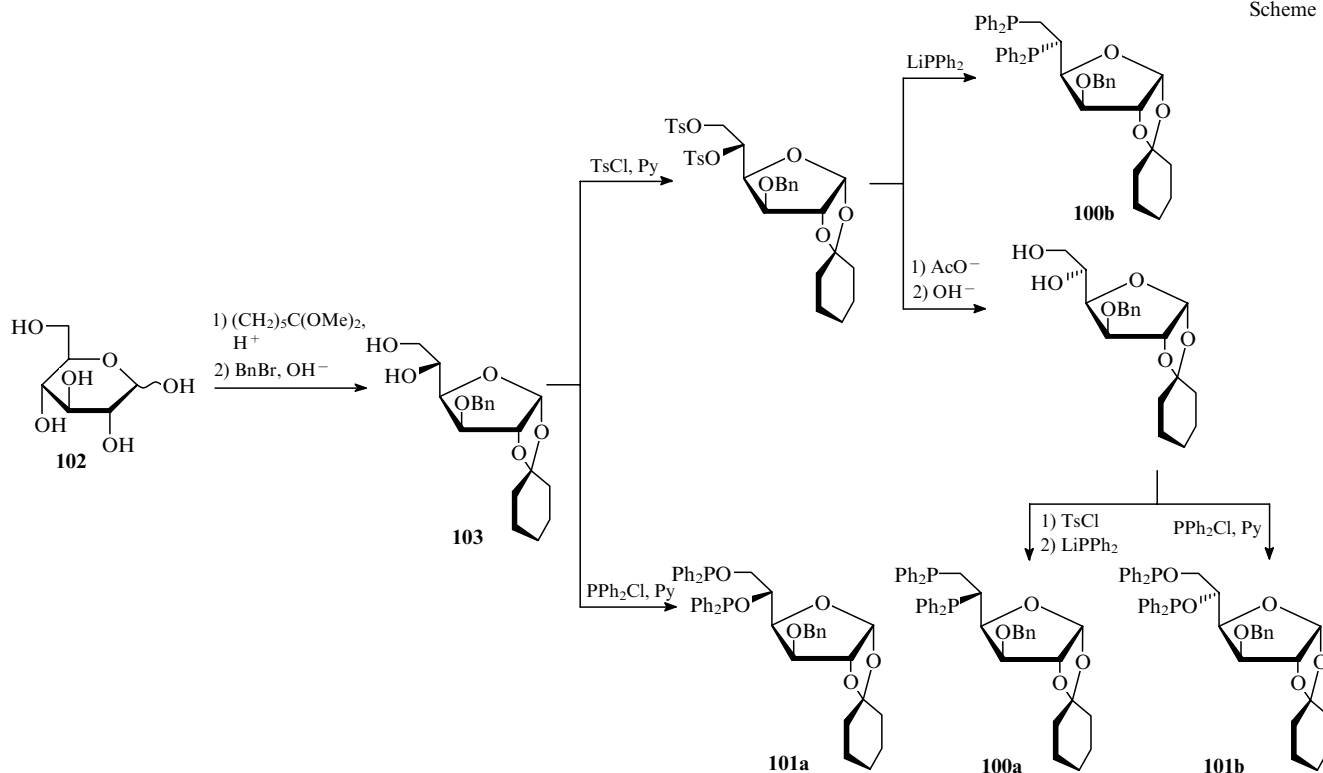
R = α -OMe (**a**), α -OPh (**b**), β -OBn (**c**), β -OPh (**d**), β -OC₆H₄Me-2 (**e**), β -OC₆H₄Me-4 (**f**), β -OC₆H₄NO₂-2 (**g**), β -OC₆H₄NO₂-4 (**h**), β -OC₁₀H₇-2 (**i**).

Treatment of 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide **104** with zinc in acetic acid afforded tri-*O*-acetyl-D-glucal **107**, which was used for the synthesis of 3,4-bisphosphinite **108**.



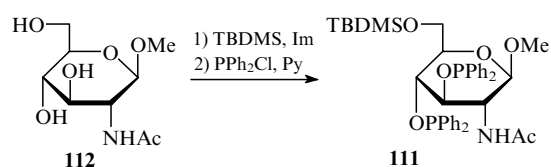
Tr is trityl, TBDMS is *tert*-butyldimethylsilyl, Im is imidazole.

Scheme 5

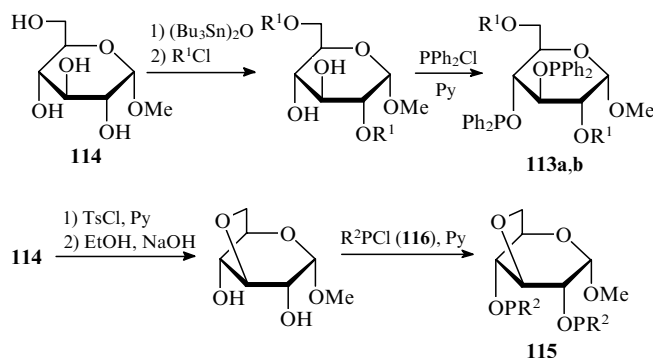


Phosphinite **110** was derived from methyl-2-deoxy- α -D-glucopyranoside **109**.⁵⁴

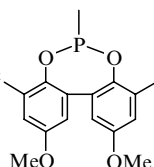
Analogous bisphosphinite **111** was generated from 2-acetyl-amino- β -methyl-2-deoxy-D-glucopyranoside **112**.⁵⁴



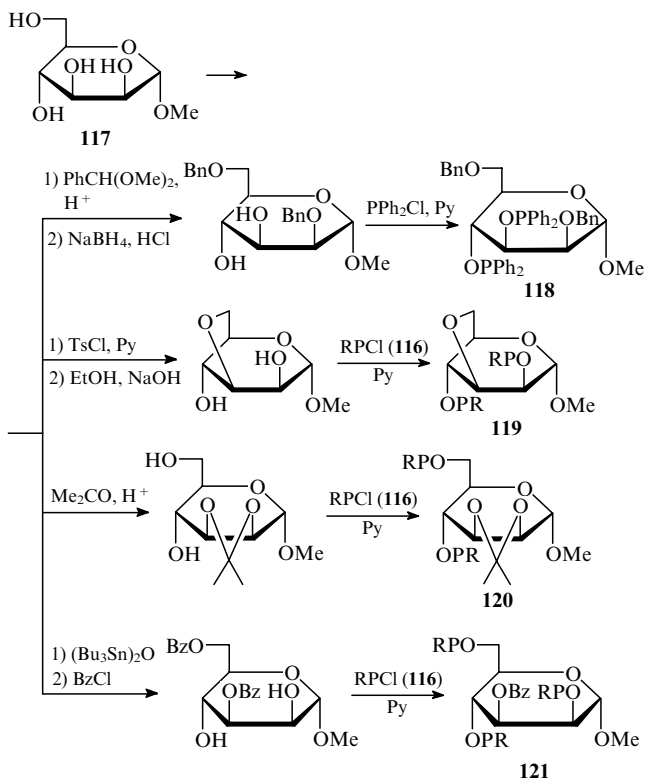
3,4-Bis(diphenylphosphinites) **113a,b** were prepared by selective acylation of methyl- α -D-glucopyranoside (**114**) followed by phosphinylation.⁵⁴ The same glycoside **114** was used for the synthesis of the 2,4-bisphosphite of 3,6-anhydroglucopyranoside **115** containing bulky substituents, viz., derivatives of *o,o'*-biphenylene **116**.⁵⁵



$\text{R}^1 = \text{COBu}^t$ (**a**), COPh (**b**); $\text{R}^2\text{P} = \text{Bu}^t$ (BMOPP).

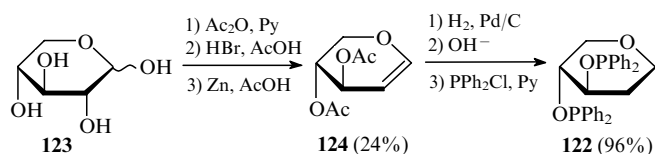


Methyl- α -D-mannopyranoside **117** was transformed into 3,4-bisphosphinite **118**, 2,4- (**119**) and 4,6-bisphosphites **120** and **121** employing different procedures for the protection of the hydroxy groups.^{54,55}

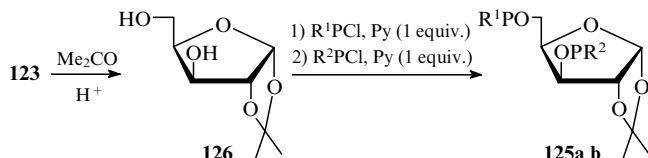


$\text{RP} = \text{BMOPP}$.

Bisphosphinite **122**, which was synthesised from D-xylopyranose **123** through di-*O*-acetyl-D-xylal **124**, was isolated as a complex with $\text{Cu}(\text{I})$ and then purified.⁵⁶

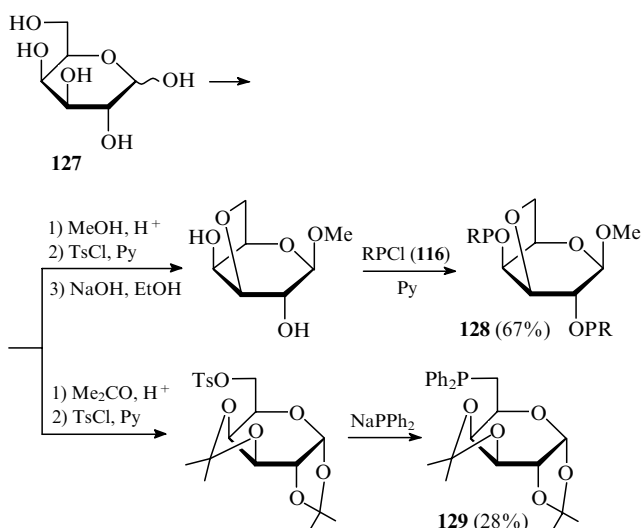


Ligands **125a,b** containing the bulky *o,o'*-biphenylene substituents were prepared by the reactions of 1,2-*O*-isopropylidene-D-xylofuranose **126** with phosphorochloridites.⁵⁵



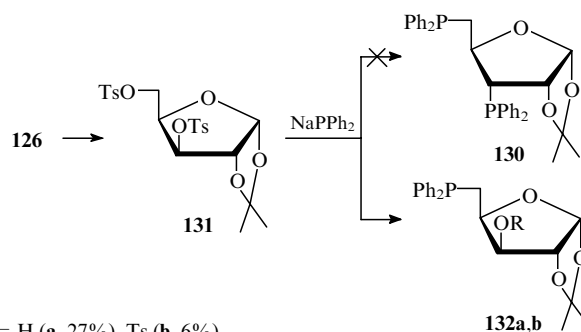
R¹P = BMOPP; R²P = R¹P (**a**, 53%), P(2-Bu¹-6-MeC₆H₃O)₂ (**b**, 27%).

Chiral 2,4-bisphosphite **128** was synthesised in several steps from D-galactose **127**.⁵⁵ The same compound was used for the preparation of monophosphine **129**.¹⁵



RP = BMOPP.

Unlike pyranosides, the synthesis of 3,5-bisphosphines based on furanosides presented difficulties. Thus, an attempt to synthesise bisphosphine **130** from 1,2-*O*-isopropylidene-D-xylofuranose **126** through ditosylate **131** led to the formation of a mixture of monophosphines **132a,b**.⁵⁷



R = H (**a**, 27%), Ts (**b**, 6%).

It was hypothesised⁶⁰ that attempts to synthesise compound **130** failed due primarily to steric overcrowding of the 1,2-*O*-isopropylidene-3,5-di-*O*-tosyl-D-xylofuranose molecule (**131**). The α -attack of the diphenylphosphide anion on the C(3) atom of the furanoside ring of compound **131** is hindered by steric effects, and the S_N2 reaction with sodium diphenylphosphide does not proceed. To relieve steric hindrances, attempts were made to synthesise bisphosphine ligands **136** from monotosylate **134** through alkene intermediates **135a,b**. The latter were prepared by the reaction of 3-oxofuranose **133** with α -cyanomethylidene-triphenylphosphorane. The reactions of isomeric nitriles **135a,b** with sodium diphenylphosphide afforded the same bicyclic product **137** instead of the corresponding bisphosphines **136**. Reduction of compound **137** with LiAlH₄ gave rise to phosphinoamine **138** (Scheme 6).⁵⁷

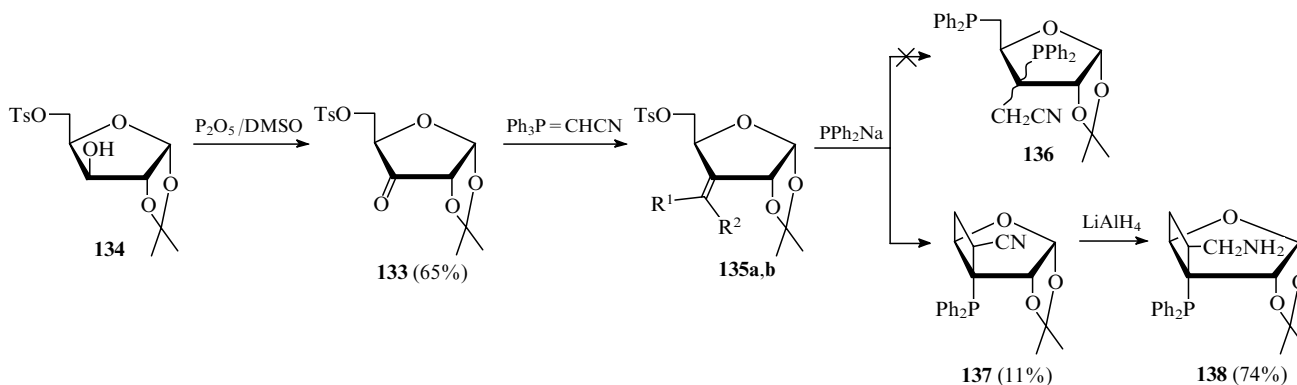
Chiral polyoxabisphosphines of the general formula **139** were synthesised from D-mannitol (**140**). Intermediate polyoxadioxolanes **141** were prepared according to two procedures, viz., by the reactions of chlorides with isopropylidenglycerol **142** under conditions of phase transfer catalysis or by the reactions of chloro ethers **143** with the corresponding alkoxides. Sodium alkoxide of *N,N*-diethylaminoethanol was used for the synthesis of dioxolane **144**, which was transformed into the target bisphosphine **145** (Scheme 7).⁵⁸

Acetonide **146** derived from D-mannitol (**140**) was used as the starting compound in the synthesis of diastereomeric epoxides **147a,b**, which were reduced to the key diols **148a,b** (Scheme 8). The latter served as the starting compounds in the synthesis of chiral organophosphorus ligands.

Examples of the use of diol **148a** in the synthesis of chiral bisphosphinites **149a,b**, bisphosphine **150** and phospholanes **151** and **152** were given in the study.⁵⁹ Diastereomers of these compounds were prepared from diol **148b** according to an analogous scheme (Scheme 9).

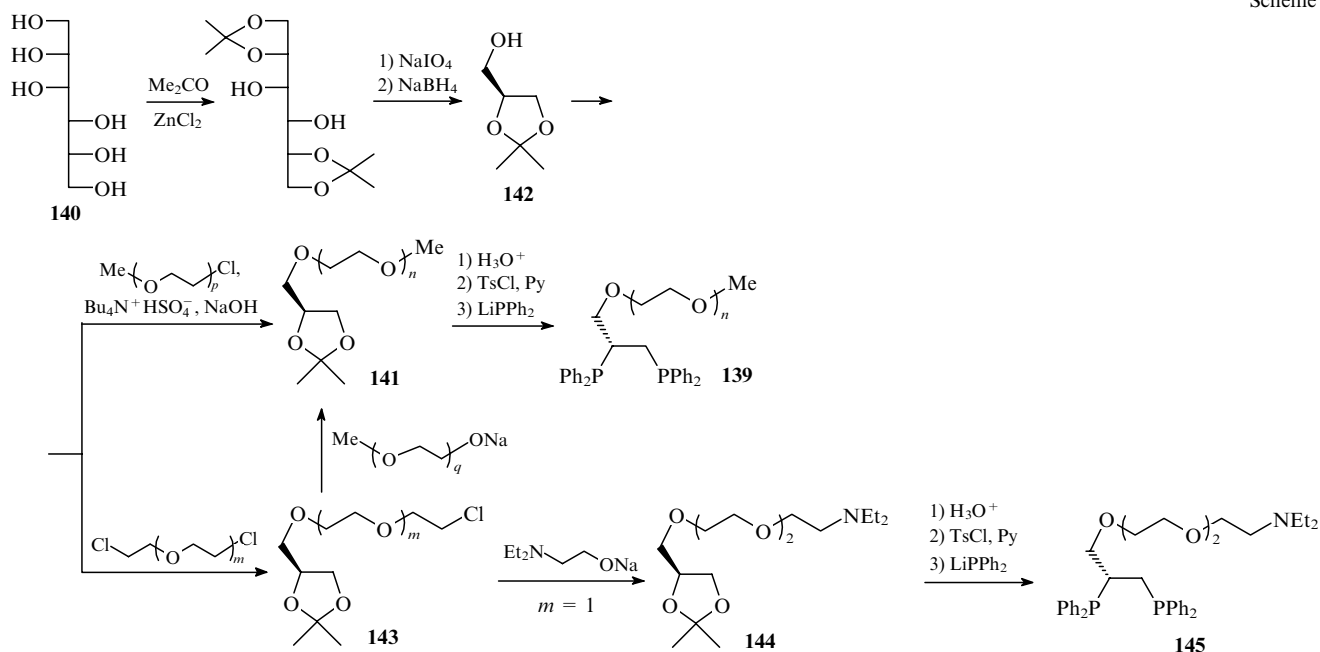
Examples of the use of oligosaccharides as the starting chiral compounds for the synthesis of organophosphorus ligands are much fewer in number as compared to monosaccharides. For

Scheme 6



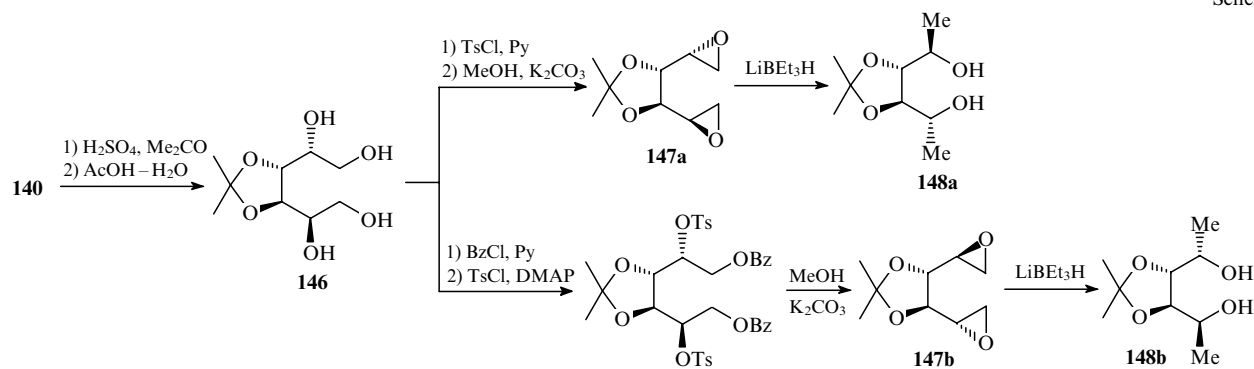
R¹ = CN, R² = H (**a**, 67%); R¹ = H, R² = CN (**b**, 24%)

Scheme 7

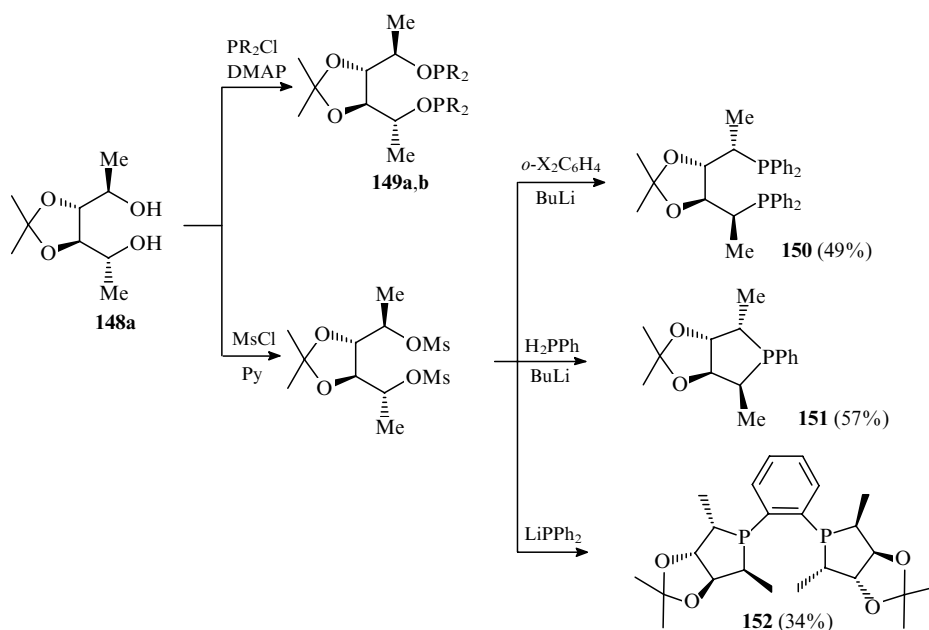


$p = 1-3, n = 1-5, m = 1, 2, q = 0-2$.

Scheme 8

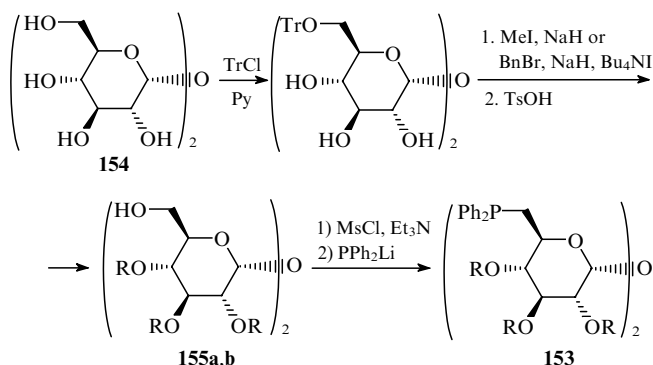


Scheme 9



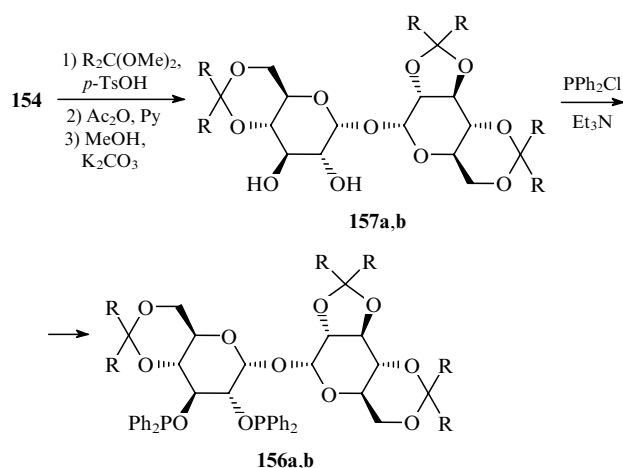
$\text{R} = \text{Ph}$ (**a**, 66%), 3,5- $\text{Me}_2\text{C}_6\text{H}_3$ (**b**, 42%); $\text{X} = \text{PPh}_2$; DMAP is 4-dimethylaminopyridine.

instance, phosphines **153a,b** were prepared from disaccharide α,α -trehalose (**154**) according to the standard sequence of reactions employed in carbohydrate chemistry. This procedure made it possible to synthesise the key intermediates **155a** (or **155b**), which were then transformed into the target ligands **153**.⁶⁰



R = Me (**a**), Bn (**b**).

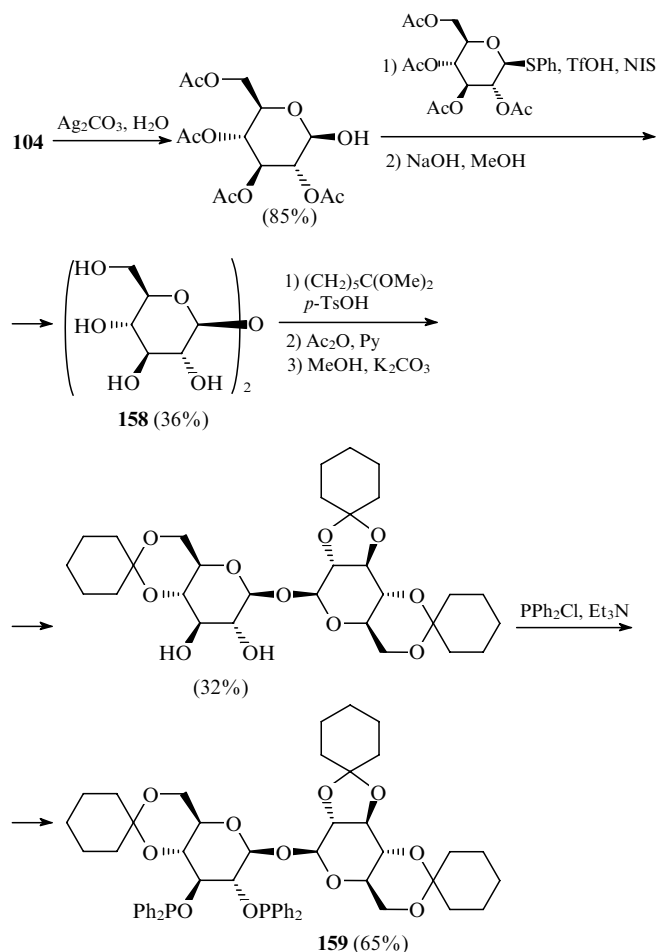
Bisphosphinites **156a,b** were prepared from α,α -trehalose (**154**) through the formation of alkylidene derivatives **157a,b** whose isolation involved successive acetylation–deacetylation steps.⁶¹



R = Me (**157a**, 14%; **156a**, 63%),

R – R = (CH₂)₅ (**157b**, 63%; **156b**, 65%).

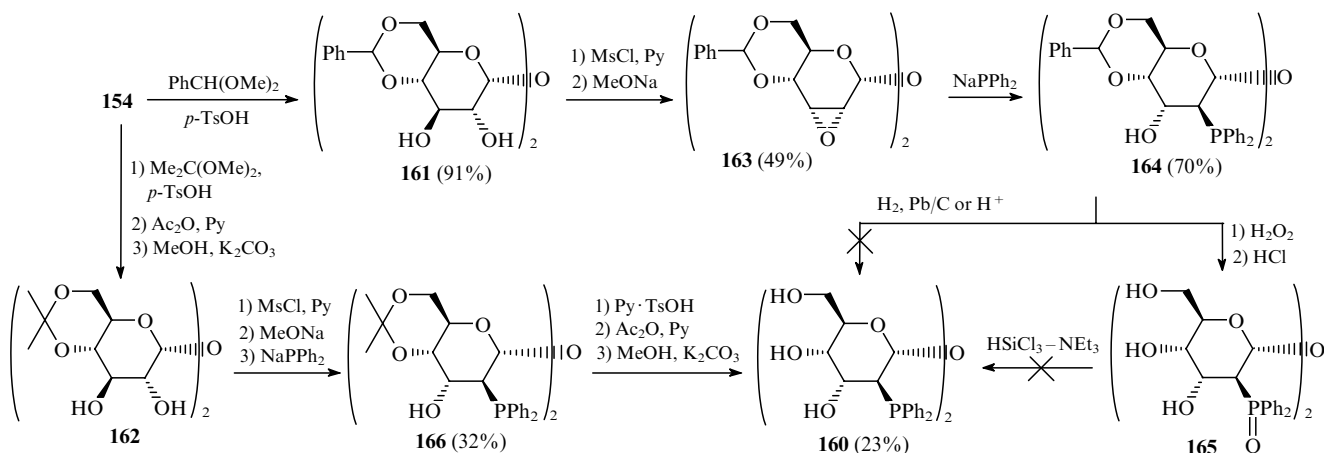
Unnatural carbohydrate β,β -tetrahalose (**158**) was produced from 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide (**104**) and used in subsequent transformations into bisphosphinite **159**.⁶¹



NIS is *N*-iodosuccinimide.

Several procedures were developed for the synthesis of 2,2'-bisphosphine **160**. These procedures are associated with the choice of protective groups, which can selectively protect hydroxy groups in the starting carbohydrate, viz., α,α -trehalose (**154**) (Scheme 10). Two derivatives of this disaccharide, viz., benzylidene (**161**) and diisopropylidene (**162**) derivatives, were prepared. Compound **161** was transformed into bis(epoxide) **163** in two steps. Treatment of the latter with sodium diphenylphosphide afforded phosphine **164**. Attempts to prepare 2,2'-bisphosphine **160** by direct hydrogenolysis of compound **164** on the Pd/C catalyst failed. An attempt to reduce intermediate phosphine oxide **165** with trichlorosilane was also inefficient. The procedure for the preparation of polyhydroxybisphosphine **160** through acetone **162**

Scheme 10



proved to be more successful. Hydrolysis of phosphinylated compound **166** with pyridinium *p*-toluenesulfonate produced the target ligand **160** (see Scheme 10).⁶²

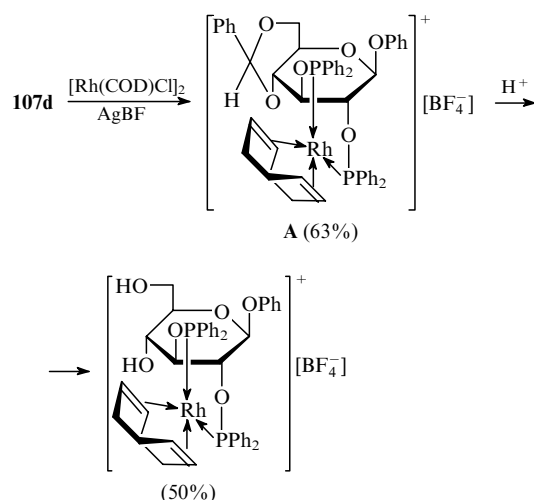
The above-considered examples demonstrate that a broad spectrum of chiral organophosphorus compounds can be synthesised based on carbohydrates. The compounds thus prepared were used for the synthesis of metal complex catalysts.

2. Use in asymmetric synthesis

Hydrogenation of a series of unsaturated acids and their esters in the presence of Rh(I) complexes with bisphosphines **100a,b** and bisphosphinites **101a,b** afforded the corresponding saturated products with an enantiomeric excess of 67%. Hydrogenation catalysed by the Rh(I) complexes with ligands **100a** and **101a** produced compounds having the (*R*) configuration, whereas hydrogenation in the presence of the Rh(I) complexes with their diastereomers **100b** and **101** yielded products with the (*S*) configuration.⁵³

Study of the behaviour of the Rh(I) complexes with chiral organophosphorus ligands **106a–i** in hydrogenation reactions demonstrated that the presence of equatorial substituents in the glucopyranoside ring of the ligand leads to a decrease in the enantioselectivity of the catalyst. For example, hydrogenation of methyl (*Z*)-2-acetamidocinnamate catalysed by the Rh(I) complexes with β -anomeric ligands **106c–i** afforded products in enantiomeric yields of 91%–92%, whereas the enantioselectivity of analogous transformations on the Rh(I) complexes with α -anomers **106a,b** was no higher than 71%. Asymmetric hydrogenation of *N*-acetylaminoacrylic acids in the presence of the Rh(I) complex with ligand **106d** proceeded with *ee* = 96%–99%. Hydrogenation of esters of these acids catalysed by the same complex proceeded with somewhat lower enantioselectivity (*ee* = 91%).

With the aim of studying the effect of intramolecular hydrogen bonds on the structure of a complex catalyst and its behaviour in enantioselective hydrogenation, the protective benzylidene group of ligand **107d** in rhodium complex **A** was subjected to hydrolysis.^{63–65}



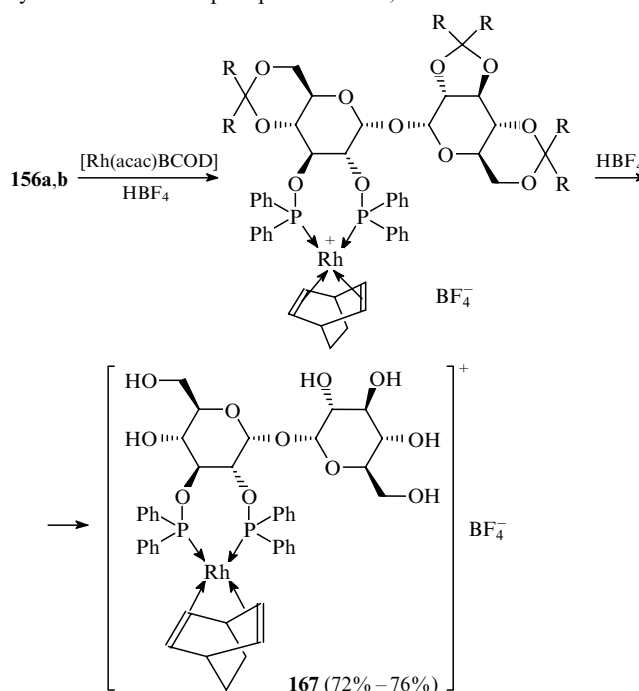
The use of Rh catalysts with ligands **106a–j** made it possible to carry out the successful synthesis of (*S*)-amino acids. By contrast, hydrogenation in the presence of complexes with 3,4-bisphosphinites **108**, **110**, **111**, **113**, **118** and **122**, in which the configurations of the carbon atoms [C(3) and C(4)] in the chelate ring of the catalysts are opposite to the configurations of the chiral centres [C(2) and C(3)] of the chelate ring of the catalysts with ligands **106a–j**, gave rise to (*R*)-amino acids. As in the case of ligands **106a–i**, the presence of equatorial substituents in the pyranose ring leads to a substantial decrease in the enantioselectivity of the catalyst.

The best results (*ee* = 93%–98%) were achieved in the presence of the complex with ligand **111** containing only axial substituents.^{56–56}

The Rh(I) complex with monophosphine ligand **129** exhibits moderate enantioselectivity (*ee* = 54%) in the hydrogenation of α -acetylaminoacrylic acids.¹⁵ Asymmetric hydrogenation of α -acetamidocinnamic acid proceeded with good enantioselectivity (92%) on the Rh(I) complex with monophosphine **137**, whereas hydrogenation in the presence of the Rh(I) complex with reduced ligand **138** afforded the reaction products with an enantiomeric purity of 39%.⁵⁷ Hydrogenation of dehydroamino acids on the Rh(I) complexes with ligands **139** and **145** proceeded with enantioselectivity of no higher than 86%.⁵⁵

When performing hydroformylation of styrene on Rh(I) complexes with bisphosphite ligands (compounds **115**, **119**, **120**, **121**, **125a,b** and **128**), the best stereochemical result (*ee* = 64%) was achieved in the presence of the Rh(I) complex with ligand **121**.⁵⁸

The Rh(I) complexes with disaccharide bisphosphines **153a,b** were used as catalysts for the hydrogenation of α -(*N*-acetylamino)acrylates. The enantioselectivity of hydrogenation catalysed by the Rh(I) complex with ligand **153b** containing benzyl groups appeared to be much higher (*ee* = 82%) than that of hydrogenation on the Rh(I) complexes with methylated analogue **153a** (*ee* = 10%).⁶⁰ Water-soluble cationic Rh(I) complex **167** was synthesised from bisphosphinites **156a,b** based on trehalose.



R = Me (**a**), R–R = (CH₂)₅ (**b**); BCOD is bicyclooctadiene.

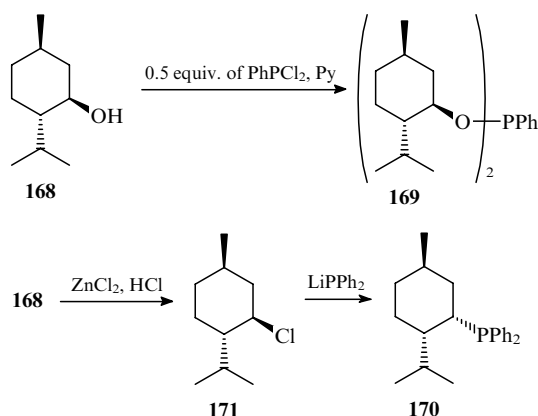
The Rh(I) complex with structurally similar ligand **159** was produced analogously. These catalysts prepared *in situ* showed high enantioselectivity (99%) in the hydrogenation of *N*-acetylaminoacinnamic acids and their esters both in water and a two-phase aqueous-organic system.⁶¹

Analogous water-soluble transition metal complexes suitable for catalytic asymmetric reactions in organic and aqueous media can be prepared based also on other chiral organophosphorus ligands containing free or protected hydroxy groups, *viz.*, bisphosphinites **149**, bisphosphine **150**, phospholanes **151** and **152**, their diastereomers and polyhydroxy-2,2'-bisphosphine **160**.^{59, 62} Investigations of the enantioselectivity of hydrogenation catalysed by metal complexes with organophosphorus ligands based on carbohydrates are being continued.

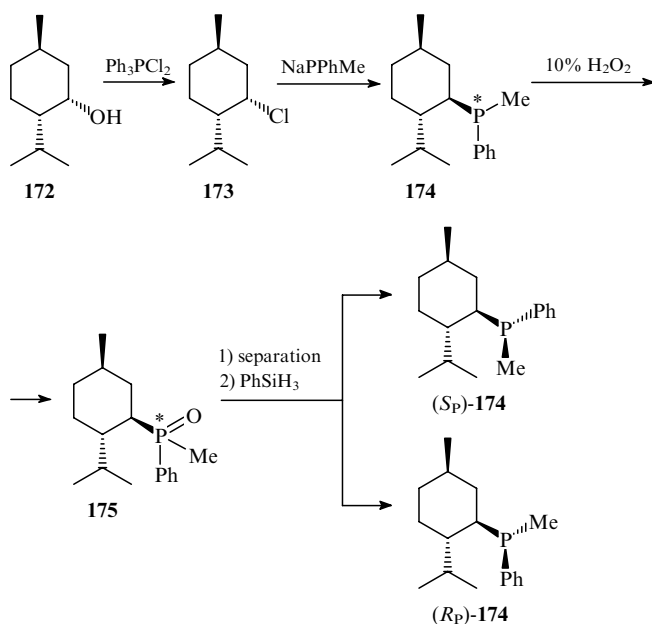
V. Organophosphorus ligands based on terpenoids and steroids

Syntheses of chiral ligands based on terpenoids are remarkable in that they use secondary metabolites of the plant origin (L-menthol, α -pinene, Δ^3 -carene, levopimaric and dehydroabietic acids) as the starting compounds. These compounds are comparable to the above-considered hydroxy acids, amino acids and carbohydrates (L-tartaric acid, D-glucose, D-xylose, L-arabinose, L-phenylalanine, *etc.*) in accessibility, optical purity and structural diversity.

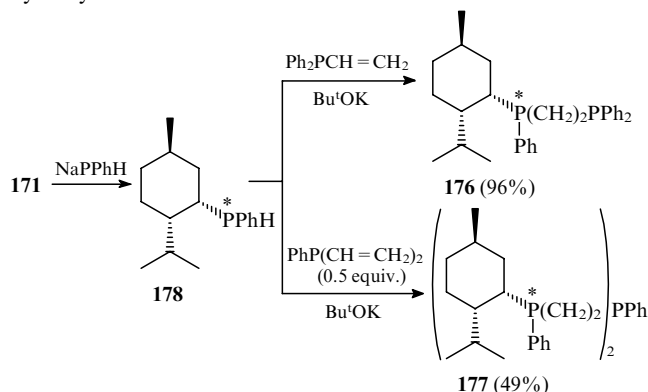
Chiral phosphonite **169**¹⁵ and phosphine **170**⁶⁶ were prepared from L-menthol (**168**) according to rather simple procedures. Phosphine **170** was also generated by phosphinylation of L-menthyl chloride (**171**).



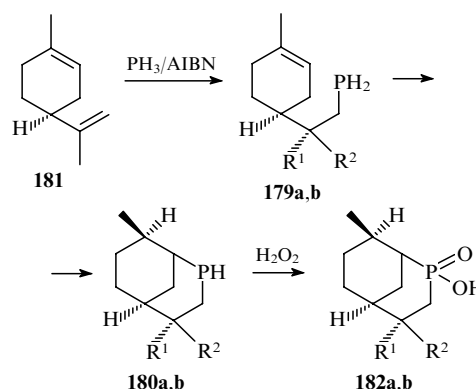
Neomenthol **172** was also used as the starting compound in the synthesis of chiral organophosphorus ligands. For example, treatment of L-neomenthyl chloride **173** with sodium phosphide containing different substituents afforded a mixture of diastereomers **174** possessing an additional asymmetric centre at the phosphorus atom. These diastereomers were purified and separated through chromatographically stable phosphine oxides **175**. After separation, all individual stereoisomers were reduced with phenylsilane to the corresponding menthylmethylphenylphosphines (*S_P*)-**174** and (*R_P*)-**174**. It was noted that, unlike the stable (*S_P*) isomer, the (*R_P*) isomer underwent partial epimerisation at the phosphorus atom (~13%–25%) under the reaction conditions.⁶⁷



Ligands **176** and **177** were synthesised from L-menthyl chloride (**171**) by nucleophilic hydrophosphinylation. The reaction of chloride **171** with sodium phenylphosphide afforded a mixture of diastereomeric secondary phosphines **178**, whose coupling with phenylvinylphosphines gave rise to the desired ligands **176** and **177**. Individual stereoisomers of these compounds were isolated by recrystallisation.⁶⁸

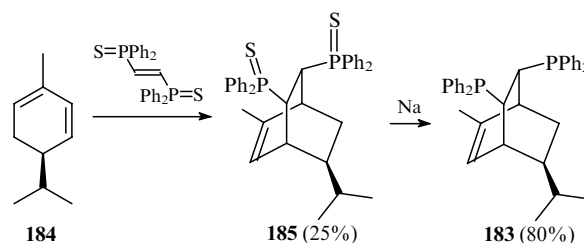


Mono- (**179a,b**) and bicyclic (**180a,b**) phosphines were prepared by radical hydrophosphinylation of limonene (**181**) with phosphine PH_3 . Bicyclic phosphines **180a,b** were oxidised to stereoisomeric phosphinic acids **182a,b**.⁶⁹

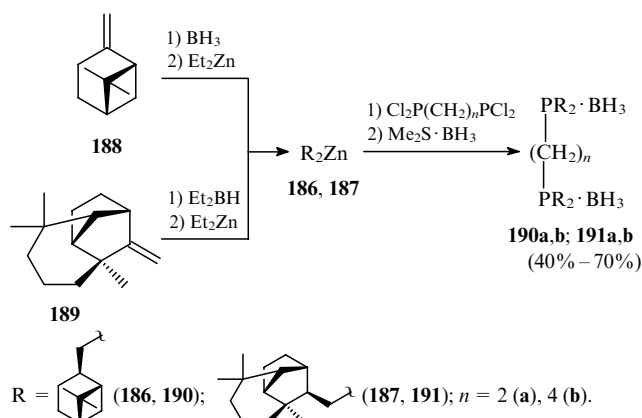


$\text{R}^1 = \text{H}$, $\text{R}^2 = \text{Me}$ (**a**); $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{H}$ (**b**);
AIBN is azobis(isobutyronitrile).

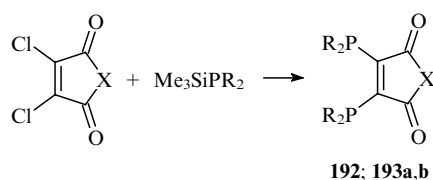
In the study,⁷⁰ the PHELLANOPHOS ligand (**183**) was derived from (–)- α -phellandrene (**184**) and used as a chiral diene in the Diels–Alder reaction with *trans*-vinylenebis(diphenylphosphine sulfide). Adduct **185**, which formed stereospecifically, was reduced to the target bisphosphine **183** by refluxing with sodium metal in toluene.



Chiral zinc organometallics **186** and **187**, which were prepared from β -pinene (**188**) and (+)-longifolene (**189**), respectively, by successive hydroboration and transmetalation, served as the starting compounds for the synthesis of the corresponding bidentate phosphines **190a,b** and **191a,b**. The latter were characterised as complexes with BH_3 . These phosphines were used for preparing ruthenium complexes. The latter catalyse hydrogenation of 2-methyl-3-phenylpropenol with moderate enantioselectivity (*ee* = 45%).^{71, 72}



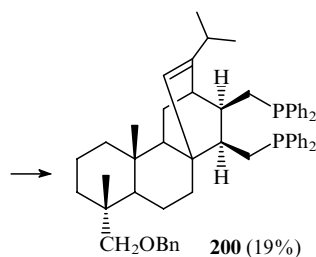
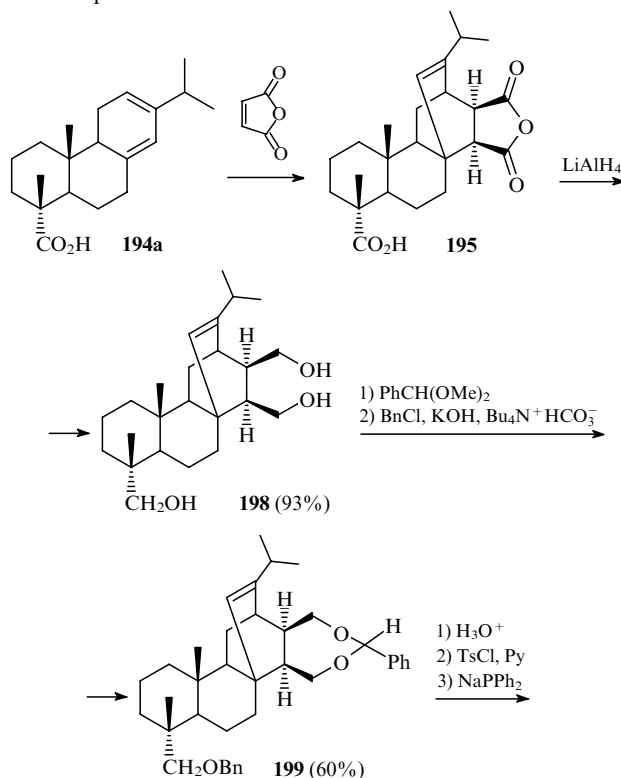
1,3-Bis(dimethylphosphino)maleic anhydride **192** and substituted maleimides **193a,b** were synthesised by the reactions of dimethyl(trimethylsilyl)phosphine with 2,3-dichloromaleic anhydride or 2,3-dichloromaleimides, respectively.⁷³



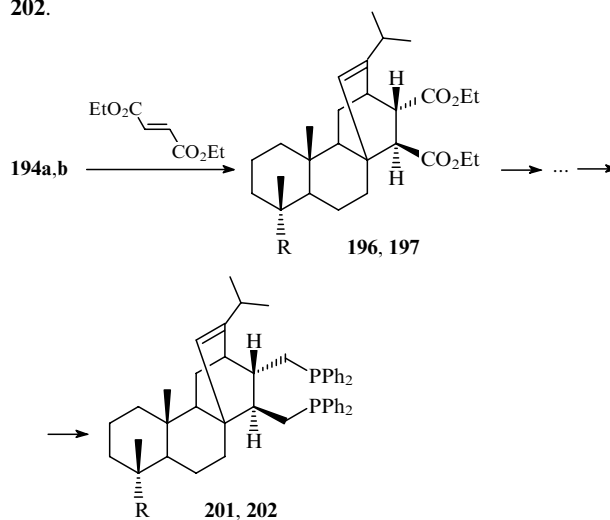
R is L-menthyl; **X** = O (**192**), NMe (**193a**), NPh (**193b**).

First syntheses of chiral organophosphorus ligands from diterpenoids were described in the studies.^{74,75} The authors of the cited studies used the known adducts of levopimaric acid (**194a**) with maleic anhydride (compound **195**) and diethyl fumarate (compound **196**) as well as the adduct of the benzyl ether of levopimarol (**194b**) with diethyl fumarate (compound **197**).

Reduction of adduct **195** produced triol **198**. Protection of all hydroxy groups in compound **198** gave rise to compound **199**, from which the target bisphosphine **200** was prepared according to standard procedures.



Adduct **196** was transformed into aminodiol through the formation of the morpholine derivative. Successive tosylation and phosphinylation of the aminodiol afforded bisphosphine **201**. Reduction of benzyl ether **197** with LiAlH_4 followed by standard transformations gave rise to analogous bisphosphine **202**.



R = CO_2H (**194a, 196**), CH_2OBn (**194b, 197, 202**), $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ (**201**).

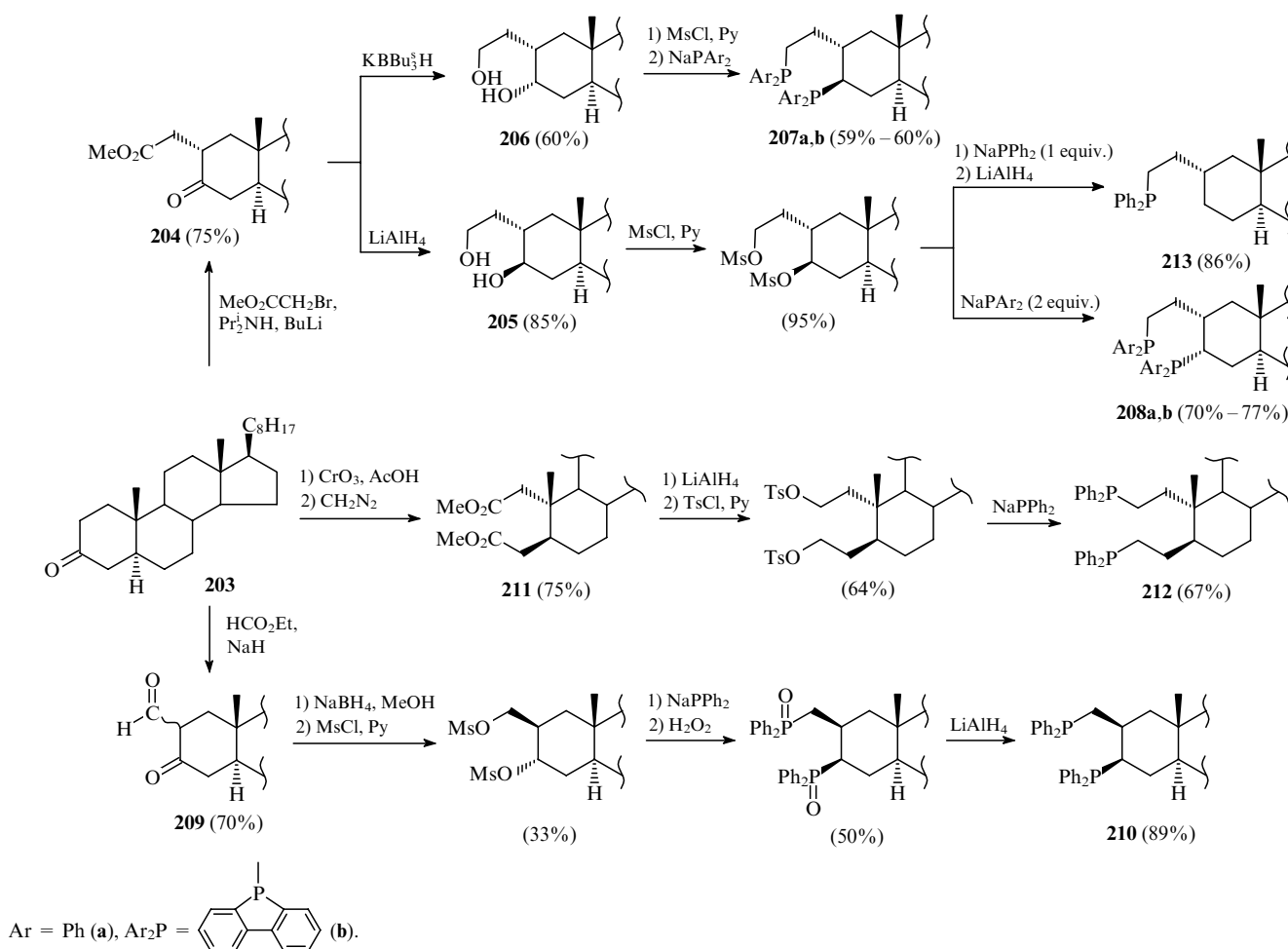
The reactions of bisphosphines **200**–**202** with di- μ -chloro-bis(1,5-cyclooctadiene)dirhodium and NaBF_4 produced complexes of the $[\text{Rh}(\text{COD})\text{L}]^+\text{BF}_4^-$ type. Rhodium complexes with phosphine **200** catalyse hydrogenation of (*Z*)-*N*-acetylaminocinnamic acid to give *N*-acetylphenylalanine in quantitative yield with *ee* = 37%. The optical purity of 3-(3,4-dihydroxyphenyl)-alanine prepared by hydrogenation of the corresponding precursor on this complex was 27%.

The Rh(I) complexes with phosphines **201** and **202** substantially accelerated hydrogenation of the above-mentioned unsaturated amino acids; however, these reactions gave rise to optically inactive products.

In the study,⁷⁶ chiral steroidal organophosphorus ligands were synthesised from cholestan-3-one (**203**). Alkylation of the latter compound with methyl bromoacetate afforded keto ester **204**, which was reduced to isomeric diols **205** and **206**. Then dimesylates were produced and used in the final step of the synthesis for the preparation of bisphosphines **207** and **208** using sodium diarylphosphides. 2-Formylcholestanone **209** was transformed into 1,4-bisphosphine **210** in several steps. 1,6-Bisphosphine **212** is rather readily generated from the oxidation product of cholestanone, *viz.*, seco acid ester **211**. The synthesis of monophosphine derivative **213** from diol **205** was also described in the study⁷⁶ (Scheme 11).

Phosphorus-containing derivatives of monoterpenes were used as chiral ligands in the hydrogenation of a series of prochiral substrates catalysed by Rh(I) complexes. Hydrogenation of (*E*)- β -methylcinnamic acid in the presence of the Rh(I) complex with ligand **170** produced (*S*)-(+)-3-phenylbutyric acid with an enantiomeric purity of 61%.⁶⁶ The rhodium catalysts with ligands (*S*_P)-

Scheme 11

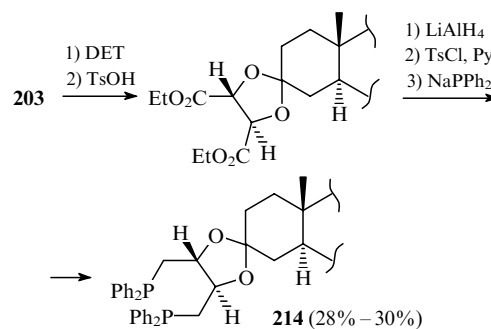


174a and (*R_P*)-**174b** showed higher enantioselectivity (*ee* was 71% and 67%, respectively) in reduction of the same substrate. It should be noted that the use of these diastereomeric ligands made it possible to prepare both enantiomers of 3-phenylbutyric acid.⁶⁷ The Rh(I) complexes with diastereomeric bisphosphine ligands **176** catalysed the asymmetric hydrogenation of α -acylaminocinnamic acids. The enantioselectivity of hydrogenation of the latter acids in the presence of these catalysts appeared to be higher (*ee* = 85%) than that of hydrogenation of their esters (*ee* = 31%).⁶⁸ The Rh(I) complex with the PHELLANOPHOS ligand (**183**) exhibits high efficiency in the hydrogenation of unsaturated precursors of α -amino acids. The optical purities of the products prepared with the use of this catalyst were 94%–95%.⁷⁰

The catalytic activities and enantioselectivities of Rh(I) complexes with steroidal ligands derived from cholestan-3-one in the hydrogenation of (*Z*)- α -acetamidocinnamic acid were estimated. The Rh(I) complexes with 1,4- and 1,3-bisphosphines **207a**, **208a** and **210** (*ee* = 75%–86%) appeared to be most efficient. Hydrogenation catalysed by the Rh(I) complexes with ligands **207a** and **210** afforded (*R*)-*N*-acetylphenylalanine, whereas hydrogenation on the complex with ligand **208a** gave rise to the product with the (*S*) configuration. The replacement of the diphenylphosphine groups in the ligands by the benzophosphindole groups leads to a substantial decrease both in the reaction rate and enantioselectivity of hydrogenation catalysed by the corresponding Rh complexes. The enantioselectivity achieved in the presence of Rh catalysts with such ligands (**207b** and **208b**) was 12%–22%.

Low enantiomeric yields of the products (*ee* = 44%) were observed in hydrogenation of (*Z*)- α -acetamidocinnamic acid on the Rh catalyst with 1,6-bisphosphine **212** as the ligand, whereas the Rh(I) complex with monophosphine **213** has no catalytic effect at all.⁷⁶

The Rh(I) complex with bisphosphine **214** of the mixed type, which was prepared from cholestanone and diethyl tartrate, exhibited high enantioselectivity (*ee* = 90%) in the hydrogenation of (*Z*)-*N*-acetylaminophenylpropenoic acid.⁷⁷

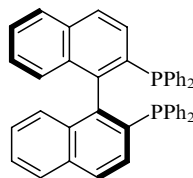


DET is diethyl tartrate.

Therefore, natural terpenes and steroids can be used as the starting compounds in the synthesis of chiral organophosphorus ligands for the preparation of metal complex catalysts for asymmetric homogeneous hydrogenation.

VI. Conclusion

The data surveyed in the present review raise the question of whether ligands prepared by transformations of natural molecules can compete with binaphthyl phosphorus-containing ligands of the BINAP type, which are by far the most efficient ligands for enantioselective catalysts.



In this competition, the advantage of the latter ligands is that they have been studied in much more detail as components of highly efficient catalytic systems. The best ligands serve as reference compounds and are used in fine organic synthesis. These ligands are widely advertised (which is also of importance) by manufacturing companies.

However, the most substantial drawback of binaphthyl ligands is their high price, which remains virtually unchanged over a long period of time. Hence, such ligands will find use in industrially promising processes only after the development of supercatalysts based on these compounds such that they can withstand tens and hundreds of thousands of catalytic cycles. As an example we refer to Rh(I) complexes with bidentate binaphthyl phosphines catalysing the enantiospecific shift of the double bond in the synthesis of L-menthol (Takasago process).

The main hopes, which stimulate investigations on the synthesis of chiral organophosphorus ligands based on available natural compounds, are pinned on the development of technological procedures for the preparation of inexpensive ligands, which can serve as components of catalysts for practically important reactions. These studies are in their infancy and, undoubtedly, will be continued.

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Fractal structures in disperse systems

V I Roldughin

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Abstract. The fractal structures that form in disperse systems are considered. Theoretical models of fractal aggregation and the kinetics of coagulation of fractal aggregates are described. The characteristics of deposited fractal films and of corroded surfaces are considered. The multifractal analysis of colloidal systems and related thermodynamics of fractal aggregates are outlined. The bibliography includes 380 references.

I. Introduction

The concepts of fractal structures or, simply, fractals have been widely used since the 1980s. Fractals are objects that are characterised by a fractional dimension. Pioneering studies on mathematical treatment of objects with fractional geometric dimensions date back to the early 20th century; however, they have rarely been the subject of physicochemical research. It was Mandelbrot who clearly demonstrated in his monographs^{1,2} that many systems in nature can be considered as fractals. This aroused the interest of physicists and chemists in fractal structures.

The most important property of fractal structures is self-similarity. The visual appearance of self-similar structures is identical at different length scales, which allows one to envision the structure of the whole object using a fragment of it. Since this property is also characteristic of many non-fractal structures, the second property of fractals becomes of crucial importance. Namely, the changes in various characteristics (mass, density, surface area, elastic modulus, *etc.*) of a fractal object, which are due to changes in the size of the object or in the corresponding length scale, obey a power law with a fractional exponent. In other words, some relationships established for conventional one-, two- or three-dimensional systems are valid for fractals if we assume that their geometric dimension is not an integer.

The concepts of fractals have provided a better insight into both the structural organisation and the laws governing various

nonequilibrium processes in various physicochemical systems. Simultaneously, many regularities of the changes in the physicochemical parameters with varying spatio-temporal characteristics have been revised.

The new concept of structural organisation of well-known objects gave an impetus to original experimental studies and to the development of novel theoretical models. Considerable efforts have been made in order to find, generate and examine fractal structures. It should be noted that the subjects of a large number of these studies were typical objects of colloid chemistry, namely, particle aggregates, porous media, composite materials and rough surfaces. Therefore, it is quite reasonable that the first reviews and monographs in the field concerned mainly fractal aggregates.

In spite of extensive literature on fractal objects,^{3–23} many issues dealing with the properties of colloidal fractal structures are still to be clarified. Besides, a considerable body of information on the fractal characteristics of various colloidal systems has been accumulated in the last decade. Because of this, it seems appropriate to generalise the results obtained.

In this review, the emphasis is placed on the studies reported in the 1990s and more recently and on a few publications from the 1980s which contain basic results. These are necessary to enhance the integrity of material presented below.

The contents of the review is self-explanatory, so we will not dwell on its structure. Mention can only be made that here we have restricted ourselves to the consideration of (mainly) theoretical models for growth and geometric characteristics of fractal aggregates. Many problems concerning the description of experimental studies on the physicochemical properties of fractal aggregates and their dispersions will be the subject of a separate review, which will be published in the near future.

It seems appropriate to begin with a definition of the fractal dimension, which will be implicitly used throughout the text. The point is that this notion can be introduced in several ways, some of which are mathematically inequivalent. Subtle details of the corresponding mathematical treatment can be found in, *e.g.*, monograph.¹³ From this point on we will consider that the fractal dimension of any physical object can be determined using the following relationship[†]

V I Roldughin Institute of Physical Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation.
Fax (7-095) 952 53 08. Tel. (7-095) 955 46 47.
E-mail: roldugin@phych.ac.ru

[†] Here and in some relationships listed below unity is implied to be a dimensional quantity whose dimension is inverse to that of the expression under the logarithm.

$$d_f = \lim_{\delta \rightarrow 0} \frac{\ln N(\delta)}{\ln(1/\delta)},$$

where N is the number of boxes (spheres) of size δ needed to completely cover a given object (the so-called box-counting technique). Therefore, calculations of d_f in a particular case require the number of boxes of a given size necessary to cover the object to be counted and the limit of the ratio of logarithms with $\delta \rightarrow 0$ to be evaluated. In the case of planar fractal objects one can use squares (disks) instead of boxes. This relationship, adapted to particular systems, is most often used in determining the fractal dimension of physicochemical objects. Some modification of this relation will be given below. It should be noted in advance that here we will not discuss the problems concerning possible differences between the fractal dimensions determined using different relationships because they are of little interest for physical chemists. Besides, the development of fractal theory is accompanied by the introduction of various fractal dimensions, which characterise particular physicochemical properties of objects under study. Some of them will be introduced in the next Sections of the review.

II. Fractal aggregates

Aggregates of colloidal particles were among the first objects described using fractal geometry concepts. The pioneering studies on fractal clusters have been well documented in a number of reviews.^{7,8,12} In this Section we will consider the main stages of development of the fractal concepts.

Interest in fractal aggregates was aroused after publication of two basic studies^{24,25} concerning aggregates of highly dispersed iron particles produced by flash evaporation of induction heated wires. Analysis showed²⁴ that the aggregates can be treated as fractal structures, while numerical experiments using a model of diffusion-limited aggregation of individual particles revealed²⁵ that the process involves formation of aggregates, which possess some properties of fractals. Next, it was found that fractal aggregates can be generated in numerical experiments with various growth models^{26,27} for diverse colloidal systems.^{28–37} These investigations were followed by dramatic increase in the studies on the formation and structure of aggregates of colloidal particles and other fractal objects. To date, fractal aggregates of gold,^{29,34} hematite,^{38,39} silica,⁴⁰ polystyrene⁴¹ and carbon⁴² particles have been obtained. The state-of-the-art in the field of research on fractal structures since 1985 is well illustrated by the book,⁴³ which gives a clear idea of both the expansion of avenues of investigation and diversity of the methods for studying fractals.

Computer simulation has played a significant role in the studies of fractal aggregates. Detailed analysis of the available literature in the field is presented in a monograph.¹⁸ Computer models allow different regimes of particle aggregation to be examined. They also serve as the basis for carrying out real experiments and processing large arrays of experimental data. Now it is appropriate to briefly outline the main models for description of particle aggregation, which are used in numerical simulation. We will often refer to them in the text below.

1. Classical models for fractal aggregation

Numerical experiments began with the simulation of random walk of particles on a lattice. This imposed some limitations. The next step was to simulate the motion in free space instead of the movement of particles over lattice sites. This caused no significant changes in the structure of clusters at longer length scales but led to a more realistic structural organisation of aggregates at short length scales. If numerical simulation concerns the random walk of clusters and particles on a lattice, the corresponding models are called lattice models. Otherwise (motion in continuous space), they are called off-lattice models.

The simplest model of aggregation was proposed by Eden. According to this model, a seed is initially introduced into the

system, which gives rise to a cluster. Growth occurs by attachment of a particle to a randomly chosen, unoccupied nearest-neighbour perimeter site. This repeats during each step of growth simulation. The model generates a dense cluster and is therefore usually considered as a model for growth of dense objects (e.g., crystals).

The ballistic model considers the motion of a pair of clusters (or a cluster and a particle) along randomly chosen linear trajectories. Collisions between clusters causes their aggregation. In the simplest version of the model the structure of the aggregate is determined by the mutual orientation of moving clusters at the instant at which they first contact each other. If the growth of a cluster occurs by attachment of single particles, the model is called the particle–cluster ballistic aggregation model. If the process of aggregation involves not only the primary particles (monomers) but also aggregates, the model is called the cluster–cluster ballistic aggregation model. The Witten–Sander model for diffusion-limited aggregation (DLA) assumes that aggregation occurs by attachment of a particle (or aggregate) to the seed (aggregate). Here, the particle (or aggregate) is introduced into the system at a rather long distance from the seed and experiences Brownian motion before collision with the seed. As particles or aggregates first contact each other, they combine irreversibly. Similarly to the ballistic model, two types of aggregation are considered, namely, particle–cluster and cluster–cluster aggregation in accord with the type of the object introduced into the system (single particle or a cluster).

Among the variety of models proposed to describe the processes of particle aggregation, the reaction-limited cluster–cluster aggregation (RLA) model is most widely used. According to this model, particles and clusters moving *via* Brownian motion must experience numerous collisions before aggregation. In numerical simulation, this is included by setting a low probability, p , of the collisional aggregation of particles. If this probability is rather high or even set to unity, the diffusion transport of particles can appear to be the limiting step and the DLA regime operates. In the limiting case ($p \rightarrow 0$), the reaction-limited particle–cluster aggregation model is transformed into the Eden model.

2. The fractal dimensions and the most important properties of fractal aggregates

Prior to considering some recently proposed, generalised aggregation models, let us give definitions of various fractal dimensions, which are used to describe the growth and properties of fractal aggregates.

The mass fractal dimension, d_f , is the dimensionless exponent in the relationship connecting the number, N , of particles in the aggregate to the linear dimension, R , of the aggregate

$$N = k_0 \left(\frac{R}{a} \right)^{d_f}. \quad (1)$$

The coefficient k_0 is called the prefactor, the structure factor or the first-order lacunarity and a is the size of the primary particles. Usually, the role of linear dimension is played by the radius of gyration, R_g , of the aggregate, which is given by

$$R_g^2 = \frac{1}{N} \sum_{i=1}^N (\mathbf{r}_i - \mathbf{r}_0)^2, \quad (2)$$

where $\mathbf{r}_i$ and $\mathbf{r}_0$ are the coordinates of the i th particle and the centre of mass of the aggregate, respectively.

The fractal dimension of aggregates grown in numerical simulation is determined using relation (1). This requires preliminary generation of clusters of different sizes followed by plotting of the logarithm of the number of particles *vs.* the logarithm of the radius of gyration, R_g ; the slope of this dependence equals the fractal dimension.

The mass fractal dimensions determined for the main models of particle aggregation (see above) are listed in Table 1. As can be

Table 1. The fractal dimensions of aggregates obtained by numerical simulation of cluster growth.^{12, 19}

d	Particle – cluster aggregation	Cluster – cluster aggregation
Diffusion-limited aggregation		
2	1.71	1.45
3	2.50	1.80
Ballistic aggregation		
2	2.0	1.55
3	3.0	1.95
Reaction-limited aggregation		
2	2.0	1.61
3	3.0	2.09

seen, the fractal dimension strongly depends on the dimension, d , of the space in which the aggregate was grown and on the aggregation regime. Hereafter we will use the values listed in Table 1 as references in comparing the results obtained using different models.

The mass fractal dimension is sufficient for characterisation of the properties of nearly spherical aggregates. In some systems, particle aggregates possess pronounced shape anisotropy. They are called self-affine aggregates rather than self-similar ones⁸ and can be described by two (longitudinal, d_l , and transverse, d_t) fractal dimensions given by

$$N = k_L \left(\frac{L}{a} \right)^{d_l}, \quad (3)$$

$$N = k_W \left(\frac{W}{a} \right)^{d_t},$$

where k_L and k_W are the corresponding prefactors and L and W are the longitudinal and transverse linear dimensions of the aggregate, respectively.

When considering anisotropic fractal aggregates, the averaged mass fractal dimension is also used

$$\langle N \rangle = k_M \left[\frac{(LW)^{1/2}}{a} \right]^{d_f}. \quad (4)$$

where the angle brackets denote the averaging over all aggregates characterised by the given length and transverse linear dimension and k_M is the effective prefactor.

Self-affinity of aggregates means that they are invariant with respect to expansion or contraction with different factors, A_L , A_W , for the longitudinal and transverse linear dimensions, respectively

$$L' = A_L L,$$

$$W' = A_W W.$$

By expressing the self-affinity coefficient in the form

$$A = \frac{\ln A_W}{\ln A_L},$$

it is possible to interrelate the three fractal dimensions mentioned above

$$d_l = \left(\frac{1+A}{2} \right) d_f, \quad (5)$$

$$d_t = \left(\frac{1+A}{2A} \right) d_f.$$

Introduction of the trajectory dimension, d_w , of the particles involved in the formation of aggregates (the random walk dimension) appeared to be useful for theoretical analysis. In the DLA regime, particles and clusters experience Brownian motion; the trajectory dimension for a Brownian particle is known¹² to be 2; therefore, $d_w = 2$. Ballistic aggregation is characterised by the motion of particles and aggregates along linear trajectories; hence, $d_w = 1$. For the reaction-limited regime of aggregation, the character of particles motion is of no significance, because particles experience multiple collisions before being added to aggregates and can therefore ‘forget’ their true trajectories (this holds for all particles). Here, the determining role is played by the point to which the particle or aggregate is attached; therefore, the trajectory dimension for the RLA regime is taken to be zero.

Many properties of fractal aggregates, which will be discussed below, are determined not only by the fractal dimension but also by the so-called chemical dimension, d_c , which is introduced as follows. Let R_c be the minimum distance, which should be travelled to pass from the particle i to the particle j without leaving the aggregate. Let a sphere B_c centred at the particle i be a set of particles j of the aggregate, for which $R_c \leq R_0$. Then, the number of particles belonging to B_c increases with increasing R_0 as follows

$$N_c \propto R_0^{d_c}. \quad (6)$$

which gives the chemical dimension of the fractal aggregate.

The growth laws of irregular fractals are to a great extent dependent on the conditions for penetration of particles into these structures. For instance, growth of a cluster in the DLA regime depends on the ability of a randomly walking particle to reach a particular site. If the sites on the surface of clusters are ascribed some ‘masses’ proportional to the probability of attachment of a randomly walking particle, it is possible to introduce a new fractal dimension (harmonic fractal dimension d_h) using the dependence of the total ‘mass’ on the size of the fractal aggregate. This parameter is of crucial importance for determination of various physicochemical characteristics of fractal objects. In particular, knowledge of the distribution of sites possessing activity towards the walking particle is of great importance in studies of adsorption, catalytic reactions, breakdown of dielectrics and dissolution processes.

In contrast to the fractal dimension and chemical dimension, which can be determined using relationships (1) and (6) immediately after aggregation, calculations of the harmonic dimension require either special computations or additional simulation. This parameter can be found by, *e.g.*, solving the Laplace equation for the potential distribution in the space outside of the aggregate at a given surface potential. In this case, the probability of aggregation at a given point is proportional to the surface potential gradient. This problem is too difficult to be solved analytically and therefore the parameter d_h is usually determined using numerical methods.

Meakin⁴⁴ reported a study on two-dimensional clusters grown using the Witten–Sander model for diffusion-limited cluster–cluster aggregation and some other models. The clusters were characterised by significantly different fractal dimensions; namely, the d_f values varied from 1.25 to 1.89. The activities of the growth sites were determined using the probe particles experiencing Brownian motion, *viz.*, the growth probability was assumed to be proportional to the number of contacts between Brownian particles and a given site. It was found that d_h has nearly the same value of 0.925 for all the systems studied. This is in agreement with the analytically predicted value $d_h = 1$ for all two-dimensional objects.⁴⁵ Grassberger⁴⁵ also introduced yet another fractal dimension, namely, the ballistic fractal dimension (d_b), which is determined analogously to the harmonic fractal dimension except that the probe particles are assumed to follow linear trajectories. Unlike the harmonic fractal dimension, d_b strongly depends on the nature of the fractal aggregate.

Generally, the surface of a fractal aggregate requires an infinite hierarchy of fractal dimensions for complete character-

isation,^{46,47} which corresponds to the so-called multifractal description of fractal objects (see Section IV). Moreover, an infinite hierarchy of fractal dimensions also arises⁴⁷ for those non-fractal surfaces which are characterised by a constant fractal dimension in a particular portion of the distribution curve.

Concluding this subsection, we will give some simple relationships, which characterise the properties of fractal aggregates.[‡]

The dependence (1) corresponds to the following radial density distribution in a fractal aggregate

$$\rho(r) \propto r^{d_f-d}, \quad (7)$$

where r is the distance from the centre of the aggregate.

The density distribution of the number of particles in aggregates is usually characterised by the density correlation function

$$C(r) = \frac{\langle \rho(r)\rho(0) \rangle}{\rho(0)^2} \propto r^{d_f-d}, \quad (8)$$

where the angle brackets denote the averaging over different orientation of the aggregate. It should be noted that this form of the correlation function is independent of the choice of the origin of coordinates. Namely, if the origin of coordinates is at any point in the cluster, including a point that is well off its centre, the density correlation function decreases obeying the relation (8). Any change in position of the origin of coordinates will affect only the coefficient on the right of expression (8) rather than the exponent. This property of the structure of fractal aggregates was tested by numerical simulation of clusters grown in the DLA regime.⁴⁸ As will be shown below, this property is responsible for many peculiarities of the physicochemical properties of fractal aggregates.

Running somewhat ahead, mention may be made that the correlation function (8) corresponds to the intensity of small-angle scattering of electromagnetic radiation by fractal aggregates given by

$$I(q) \propto q^{-d_f}, \quad (9)$$

where q is the magnitude of the scattering vector

$$q = \frac{4\pi}{\lambda} \sin \frac{\theta}{2},$$

and λ is the radiation wavelength and θ is the scattering angle. The scattering intensity obeys the relation (9) at

$$qR_g \gg 1 \text{ and } qa \ll 1.$$

Some generalisations will be considered below.

Using relationships (7) and (8) implies an infinite cluster. However, both real and numerical experiments deal with finite clusters. Because of this, the so-called cutoff function is introduced into relations of the types (7) and (8). For instance, the cutoff function $h(r)$ can be introduced into the density correlation function of an aggregate as follows

$$C(r) \propto r^{d_f-d} h\left(\frac{r}{R}\right). \quad (10)$$

The function $h(r)$ must satisfy the following conditions

$$\begin{aligned} h\left(\frac{r}{R}\right) &\approx 1, \quad r < R, \\ h\left(\frac{r}{R}\right) &\rightarrow 0, \quad r > R. \end{aligned} \quad (11)$$

‡ It would be more appropriate to introduce these relationships later but they are necessary for considering the results of some studies concerning the subject of this Section of the review.

In order for fractal dependence of the correlation function on the distance to be valid, the cutoff function should tend to the limiting values faster than power functions.

Knowledge of the cutoff function is required for correct reconstruction of the aggregate size distribution from light scattering data.⁴⁹ It should be noted that to a first approximation the introduction of the cutoff function has no effect on the dependence (9). Different cutoff functions were proposed, *e.g.*, an exponent,⁵⁰ a stretched exponent⁵¹ and a Gaussian function.⁵² A detailed study on the role of the cutoff function in determining the parameters of fractal aggregates has been reported.⁵³

3. Generalisations of classical models

Initially, numerical experiments were performed ignoring interparticle interactions. However, real experiments revealed production of clusters whose fractal dimensions differed from those predicted by simple DLA and RLA models. This was explained by specific features of interparticle forces. Therefore, a number of specific experiments and numerical simulation with inclusion of interparticle forces were carried out. The effect of the dipole–dipole interaction on the structure of fractal aggregates grown in the diffusion-limited cluster–cluster aggregation regime was studied.^{54,55} Taking the three-dimensional system as an example, it was shown that the d_f value gradually varies from 1.78 for weak to 1.35 for strong dipole–dipole interactions. The fractal dimensions obtained were in good agreement with the experimental values.^{56,57}

The effect of the interparticle interaction on the structures of aggregates growing in the reaction-limited cluster–cluster aggregation regime was studied.^{58–63} It was found that the structures and the fractal dimensions of the aggregates depend on the particular form of the interparticle interaction. The fractal dimensions obtained were both greater and smaller than the values determined using the classical models.

It should be noted that restructuring of fractal aggregates, which were preliminarily grown using the classical approaches, also allows the aggregates characterised by greater fractal dimensions (compared to the classical values) to be obtained.^{60,61}

Diffusion-limited aggregation of particles of different kinds was studied.^{64,65} Only particles of different types could bind to each other in a two-species DLA model,⁶⁵ which revealed a specific type of percolation transition. Namely, only finite clusters can grow in the system if the fraction of particles of one sort is small, whereas infinite clusters can grow only if the fractions of particles of each sort exceed some critical values.

The Eden model was generalised⁶⁶ by introducing an additional internal degree of freedom of the particles, the spin. The model assumes a cluster growing in an external magnetic field and the spin–spin interaction between the nearest neighbours. The new model allows two new fractal dimensions characterising particles with different spin orientations to be introduced. It appeared that the fractal dimension is a nonmonotonic function of the parameter characterising the energy of the interparticle interaction. At low and high interaction energies, the fractal dimension approaches the space dimension and passes through a minimum (the minimum d_f value is 1.79) at intermediate energies of the interparticle interaction. At these energies, the aggregation regime changes in such a way that the cluster structure becomes highly porous. The cluster grown at high energies of the interparticle interaction is characterised by a structure with uniform porosity.

The growth of fractal aggregates near surfaces of various nature was studied by numerical simulation.^{67–69} In all cases, aggregates grown in the presence of steric hindrances were characterised by reduced fractal dimensions.

Generalisations of the ballistic model were reported.^{70,71} The effects of biases of the trajectories of the particles following streamlines in the viscous fluid near the growing aggregate⁷⁰ and accretion of particles on seeds of different (finite) sizes were included.⁷¹

In most of the above-mentioned studies on the growth of fractal aggregates they were simulated using ensembles of mono-disperse particles. Studies on the influence of particle polydispersity on the structure and fractal dimension of aggregates^{34, 72–76} revealed that polydispersity has little effect on the fractal dimension even for an ensemble characterised by polymodal size distribution.⁷⁶ However, the local structure of aggregates can significantly change, thus affecting the calculated intensity of small-angle light scattering.^{75, 76} The cutoff function, which includes the finite size of aggregates, weakly depends on the degree of polydispersity.

4. Analytical models of aggregation

Most theoretical studies on the growth of fractal aggregates involve numerical simulation. There is only a few analytical models of the growth of fractal structures. The reason is the complexity of description of the fractal structure using analytical functions. The most interesting results obtained in this field are briefly outlined below.

Based on general considerations, without using any hypotheses of the structure of aggregates grown in the DLA regime of particle aggregation, it was established⁷⁷ that the largest separation between the centre and the most distant point of the aggregate cannot exceed $C_2 N^{2/3}$ for the two-dimensional space and $C_d N^{2/d}$ for the spaces characterised by greater dimensions ($d > 2$), where C_2 and C_d are constants. In fact, these relationships place limits on the growth rate of fractal aggregates. It was pointed out that some of the models proposed earlier predicted a faster increase in the aggregate size.

Formation of fractal aggregates in the DLA regime was also studied^{78, 79} using an approach which is similar to the Flory model for polymer molecules (see Ref. 80). The authors introduced the effective free energies of repulsion between and attraction of the aggregating particles. An equation for the fractal dimension of the growing aggregates was derived from the condition for the free energy minimum. If an aggregate was grown on the substrate with the dimension $d-m$ in the space with the dimension d , the d_f value for the aggregate is given by⁷⁸

$$d_f = \frac{d^2 + 1}{d + 1} - (d - m). \quad (12)$$

The fractal dimensions found using this relationship are in good agreement with the results of numerical simulation for the spaces and substrates of various dimensions.

The fractal dimensions of aggregates were also analytically determined^{81, 82} using the renormalisation group approach (see, e.g., Ref. 83). In this case, the fractal dimension is determined from some recurrent relations rather than from an explicit expression. The fractal dimensions of aggregates thus obtained were also consistent with the values found by numerical simulation.

Sander *et al.*⁸⁴ treated diffusion-limited aggregation as a deterministic process of propagation of the interface due to particle diffusion. In this case, calculations of the cluster's growth were reduced to the solution of the Laplace equation with the corresponding boundary conditions. It should be noted that processes of electrochemical deposition, viscous fluid flow in porous media and the breakdown of dielectrics^{85, 86} are described by similar equations. Numerical solution of the equations derived showed that the front propagation is accompanied by the development of perturbations on the initially smooth surface, thus resulting in the formation of a dendritic structure. The fractal dimensions of the dendrites growing in two-dimensional and three-dimensional systems were in agreement with the fractal dimensions determined by numerical simulation.

This method of simulation of the growth of dendritic structures has been intensively developed over a long period. Not only theoretical studies but also model experiments have been carried out. The initial model was generalised^{87–90} with inclusion of

various effects including the anisotropy of transport coefficients near the interface. Theoretical studies on the morphological stability of the growing dendritic structure were also reported.^{91–93} It was found⁹⁴ that the growing dendritic structures can be characterised by both periodic and random distributions of the secondary branches grown on the primary branch; doubling of the distance between the secondary branches is also possible. The change in the dendrite growth scenario was observed in model experiments. Studies on the growth of ammonium chloride crystals in agar gel revealed⁹⁵ that growth of fractal structures instead of crystals with smooth surfaces begins at particular supersaturations. This was explained by surface reconstruction of the growing face under the action of solvent. Transition from regular to chaotic branch growth in dendritic clusters was realised⁹⁶ in the experiments on quasi-two-dimensional growth of ammonium chloride crystals between two plates in solution at rather high supersaturations.

These investigations were to some extent reviewed in a study⁹⁷ concerned with possible morphologies of the growing structures and conditions for transitions between different scenarios of dendrite growth. Current interest in these models is due to the possibility of using them for growth of structures that do not possess isotropic symmetry (the so-called chiral structures).^{98, 99}

Qualitative analysis of aggregation laws^{100, 101} made it possible to derive an explicit expression relating d_f to the space and random walk dimensions with inclusion of incomplete accommodation of particles on the growing cluster

$$d_f = \frac{d^2 + \varepsilon(d_w - 1)}{d + \varepsilon(d_w - 1)}, \quad (13)$$

where ε is the particle accommodation coefficient. This equation was confirmed¹⁰² by Monte Carlo simulation of aggregation under conditions identical to those reported in the studies mentioned above.^{100, 101}

An analytical model was proposed, which allows one to follow the evolution of diffusion-limited fractal aggregation.¹⁰³ A closed equation was derived for the aggregate density and the concentration of primary particles, which predicted a power-law decrease in the density of the growing aggregate.

This model was extended¹⁰⁴ to the case of incomplete accommodation of particles on the surface of an aggregate, *i.e.*, diffusion-limited aggregation, reaction-limited aggregation and an intermediate regime of aggregation were considered in the framework of a unified model. The equations in the generalised model become somewhat cumbersome but not too complicated. Figure 1 presents the fractal dimension of a three-dimensional aggregate plotted *vs.* the particle accommodation coefficient. As can be seen, the model correctly reproduces the limiting cases. The region corresponding to the inflection in the $d_f(\varepsilon)$ curve has attracted considerable interest. The structures of the aggregates grown under these conditions exhibit two domains, a compact

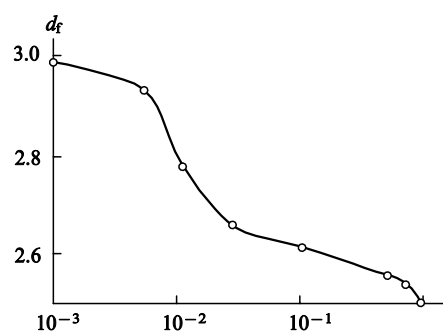


Figure 1. Fractal dimensions of aggregates growing in the DLA regime *vs.* particle accommodation coefficient.¹⁰⁴

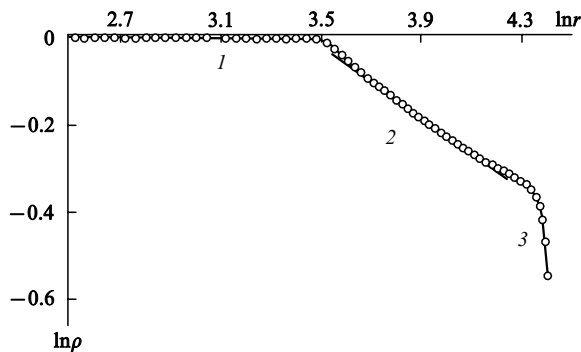


Figure 2. Density distribution for an aggregate grown at intermediate values of the particle accommodation coefficient. Core (1), fractal shell (2) and peripheral area (3).

core and a fractal peripheral area (Fig. 2). The presence of two domains indicates that the initial RLA regime is changed by the DLA regime with time. The change in the aggregation regime occurs almost without exception. Therefore, strictly speaking, fractal aggregates should exhibit a multifractal structure (see below).

A model describing the evolution of regularly branched polymers (dendrimers) also belongs to analytical models of fractal aggregation. Dendrimers are synthetic macromolecules with a definite architecture. They can be synthesised by performing repeated reactions.^{105–107} Successive ‘generations’ of branches are built of polyfunctional monomers, emerge from the same centre and form a dendritic structure.

The first theoretical description of the structure of dendrimers was reported by de Gennes and Hervet,¹⁰⁸ though primitive models of such structures were proposed somewhat earlier.² Different models of dendrimers were considered in a number of studies^{13,43,109} and generalised by McCoy.¹¹⁰ According to the generalised model, a total of Π branches grow at $t = 0$. In contrast to the earlier models, the branches can be characterised by different masses or lengths (some mass distribution of the emerging branches was preset). Then, a total of Π new, smaller branches successively grow at the end of each ‘old’ branch at regular time intervals. The model assumes that the ratio of the average mass of the new branches, m_i^{av} , to the average mass of the branches grown in the preceding step, m_{i-1}^{av} , is a constant

$$\frac{m_i^{av}}{m_{i-1}^{av}} = A. \quad (14)$$

In this case, the dendrimer grown is a fractal aggregate with the dimension

$$d_f = \frac{\ln \Pi}{|\ln(A)|}. \quad (15)$$

As mentioned above, this model is a generalisation of the models proposed earlier. In particular, at $\Pi = 2$ and $A = 1$, it describes the so-called Cayley tree.¹¹¹ The model was used to determine the temporal dependences of the number of branches, the masses and densities of dendrimers and the viscosities of their solutions.

The model of growth of dendritic structures is a particular case of regular models of fractal aggregation. Usually, regular models include some algorithms of generation of self-similar aggregates. One of them is presented in Fig. 3. It is an easy matter to extend this procedure to three-dimensional, self-affine and other aggregates. A comprehensive analysis of regular models of fractal aggregates was reported earlier,⁸ so we will not dwell on them here.

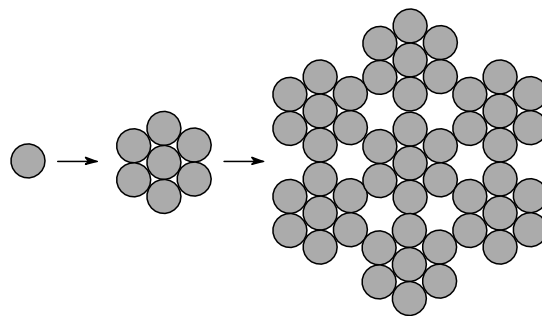


Figure 3. Growth scenario of a self-similar two-dimensional fractal aggregate with the dimension $d_f = \ln 7 / \ln 3 \approx 1.77$.

Concluding this subsection, mention may be made that thermodynamic characteristics are also suitable for the determination of fractal dimensions of different objects.^{112–114} In particular, the fractal characteristics of aggregates were determined using the principle of maximum information entropy production.¹¹³ The size distribution of aggregates was assumed to be lognormal. The fractal dimensions and the standard deviations found using the principle of maximum information entropy production were in agreement with the experimental data.¹¹⁵

In most of the models considered above the fractal dimension is governed by the aggregate growth algorithm. Recently, some models have been proposed,^{116–119} in which the cluster growth algorithm is prescribed by the fractal dimension and the prefactor in order to provide correspondence between the results of calculations and experimental data. In these models, aggregation occurs by attachment of single particles or fractal aggregates and the position of the attached fragment is preset by the fractal characteristics of the growing system. It can be found with ease using relationships (1) and (2) and the prescribed fractal dimension for both particle–cluster and cluster–cluster aggregations of overlapping and non-overlapping spheres.

5. The prefactor

Quantitative description of clusters using improved experimental methods requires the prefactor k_0 to be determined.^{120–123} This coefficient is of particular importance in determining the optical characteristics of clusters (in particular, their scattering power) and their radiating capacities.

Both the prefactor and the fractal dimension can be determined using relationship (1). In contrast to calculations of the fractal dimension, computations of the prefactor initially gave contradictory results. Based on the results of numerical simulation and model experiments, the prefactor was reported to be approximately unity.¹²¹ At the same time, the prefactors measured in studies of soot clusters formed under different regimes of combustion were 1.23 ± 0.07 (see Ref. 120) and 1.66 ± 0.4 .¹²⁴ Numerical simulation for diffusion-limited cluster–cluster aggregation gave¹²⁵ a k_0 value of 1.2 ± 0.15 . Analysis of stereoscopic images of soot agglomerates^{126,127} showed that $k_0 \approx 2.4$ and $d_f = 1.64$.

Probably, the reason for the observed differences between the experimental values of k_0 and d_f is an internal rearrangement and partial sintering of aggregates, which, as was mentioned in Refs 128 and 129, predetermine the change in their fractal dimension. An important fact was pointed out:¹³⁰ interparticle contacts in real systems should not be treated as point contacts. Hence, one deals with seemingly overlapping particles. Simulation of diffusion-limited cluster–cluster aggregation and processing of the data with inclusion of particle overlap showed that both the fractal dimension and the prefactor increase on increasing the degree of particle overlap (Fig. 4). This dependence can be described by the approximate relationship

$$k_0 = \tilde{k}_0 \Delta_d^{d_f}, \quad (16)$$

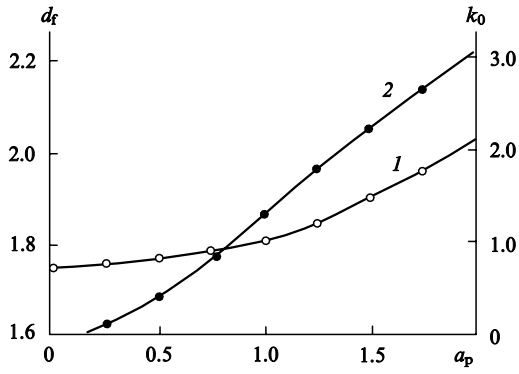


Figure 4. Fractal dimension (1) and prefactor (2) plotted vs. degree of particle overlap (a_p) in a fractal aggregate.¹²⁹

where

$$\Delta_a = \frac{2a}{2a + a_s}$$

(a_s is the distance between the surfaces of the particles) and $\tilde{k}_0$ is the point-contact prefactor.

It was also confirmed¹³⁰ that even at $d_f < 2$ the fractal dimension of the two-dimensional projection of a three-dimensional cluster is nearly 10% smaller than the fractal dimension of this cluster only for the point contact case. The inclusion of the monomer overlap increases the discrepancy between the fractal dimensions of the three-dimensional aggregate and its projection.

The assumption of the effect of the degree of particle overlap on the fractal dimension and prefactor was experimentally tested¹³¹ taking the coagulation of polystyrene latex particles with adsorption layers of different thicknesses in different regimes as an example. The fractal dimensions and sizes of aggregates were determined by static and dynamic light scattering, respectively. The results of processing of experimental data confirmed the validity of relationship (16).

III. Kinetics of coagulation of fractal aggregates

1. General relationships

Numerical simulation of the growth of fractal aggregates concerns the structure of aggregates and regularities of changes in their size distribution with time. It was shown¹³² that the size distribution, $N_s(t)$, of clusters containing a constant number (s) of primary particles changes with time obeying a self-preserving (or scaling) law

$$N_s(t) \propto s^{-2} f\left[\frac{s}{\langle s \rangle(t)}\right], \quad (17)$$

where $\langle s \rangle(t)$ is the average number of particles in the cluster at instant t , which is given by

$$\langle s \rangle(t) = \left[\sum_{s=1}^{\infty} s^2 N_s(t) \right] / \left[\sum_{s=1}^{\infty} s N_s(t) \right], \quad (18)$$

and f is some universal function.

Relation (17) for asymptotic cluster size distribution was proposed earlier based on the solution of the Smoluchowski coagulation equation, which in the general case has the form

$$\begin{aligned} \frac{\partial n_s}{\partial t} = & \frac{1}{2} \sum_{i=1}^{s-1} Z(i, s-i) n_i n_{s-i} - \sum_{i=1}^{\infty} Z(s, i) n_s n_i + \\ & + \sum_{j=1}^{\infty} Y(s, j) n_{s+j} - \frac{1}{2} \sum_{j=1}^{s-1} Y(j, s-j) n_s, \end{aligned} \quad (19)$$

where n_s is the concentration of clusters comprised of s primary particles, $Z(i, j)$ is the coagulation kernel and $Y(i, j)$ is the fragmentation kernel.

A more general relation obtained for a number of model aggregation kernels has the form

$$N_s(t) \propto s^{-\vartheta} f\left[\frac{s}{\langle s \rangle(t)}\right], \quad (20)$$

where $\vartheta = 2$ for systems characterised by conservation of the total mass.

The aggregation kinetics described by the Smoluchowski equation (19) is governed by the forms of the coagulation and fragmentation kernels (detailed analysis of the solutions to the Smoluchowski equation was reported earlier¹³³). A classification of uniform coagulation kernels was proposed,¹³⁴ which is based on comparison of the probabilities of coagulation of large clusters and of large and small clusters. Depending on which process prevails, it is possible to obtain different laws of aggregation and different cluster size distributions. If aggregation of large and small clusters predominates, no considerable changes in the masses of clusters occur and the size distribution curve becomes bell-shaped. If the interaction of large clusters dominates, small clusters are not involved in the 'battle' and the size distribution curve corresponds to a monotonically decreasing power function.

Two parameters, μ and ν , are responsible for different regimes of growth of the coagulation kernels with increasing cluster size. Namely, $Z(j, j) \propto j^\mu$ for large aggregates and $S(1, j) \propto j^\nu$ for the probability of coagulation of a large aggregate and a small cluster. For the classical Smoluchowski coagulation kernel, $\nu = 1/3$ and $\mu = 0$. For the same coagulation kernel and fractal aggregates, $\nu = 1/d_f$ and $\mu = 0$. It should be noted that the cases $\nu > 1$ and $\mu > 2$ are physically unrealistic. At $\mu > 1$, the Smoluchowski equation predicts that the formation of an infinite cluster takes a finite time (the so-called gel point). At $\mu \leq 1$, no gel transition occurs; the formation of an infinite cluster takes an infinitely long time.

At $\mu > \nu$ and $\mu < 1$ (no gel transition), the cluster size distribution curve is described by a decreasing power function

$$N_s \propto s^{-\tau}, \quad \tau = 1 + \mu,$$

(τ is sometimes called the polydispersity index). Under the same conditions, the mass-average molecular mass is described by an increasing power function

$$M_w \propto t^z,$$

$$z = \frac{1}{1 - \mu}.$$

The radius of gyration, R_g , of fractal aggregates changes with time as follows

$$R_g \propto t^{1/d_f}.$$

For diffusion-limited aggregation with the Smoluchowski coagulation kernel ($\mu = 0$) one has

$$R_g \propto t^{1/d_f}. \quad (21)$$

This dependence was confirmed experimentally. For instance, aggregation of silica particles of size 7 nm was studied by static light scattering.¹³⁵ The d_f value obtained using relation (21) coincided with the fractal dimension determined in the same study by small-angle light scattering.

If a gel transition is possible ($\nu < 1 < \mu \leq 2$), the size distribution of the growing clusters, which are smaller than some characteristic size, is also described by a power function

$$\begin{aligned} N_s & \propto s^{-\tau}, \\ \tau & = \frac{3 + \mu}{2} > 2, \end{aligned}$$

Near the gel point, the mass-average mass of the cluster increases as follows

$$M_w \propto |t - t_g|^{-\gamma},$$

where t_g is the gel transition time and

$$\gamma = \frac{1}{1 - \mu}.$$

At $\mu < \nu$, no gel transition occurs, because $\nu < 1$. In this case, the formation of a broad size distribution is impossible and the size distribution curve has a bell shape.

In a regime, which is intermediate between the regimes mentioned above, where both types of aggregation are equally significant (at $\mu = \nu \leq 1$), no gel transition occurs and the average mass of the cluster increases as follows

$$M_w \propto e^{ct}. \quad (22)$$

Attempts have also been undertaken to obtain an analytical solution to the Smoluchowski coagulation equation for fractal aggregates using some realistic approximations. Coagulation processes are also studied using aerosols. In this case, aggregation can occur in both free-molecular and continuum regimes. The expressions for the coagulation kernels in these two limiting cases are as follows

$$Z(i, j) = \frac{2kT}{3\eta} \left(i^{1/d_f} + j^{1/d_f} \right) \left(\frac{1}{i^{1/d_f}} + \frac{1}{j^{1/d_f}} \right), \quad (23)$$

for the DLA regime and

$$Z(i, j) = \left(\frac{6kT}{m_p} \right)^{1/2} \left(\frac{1}{i} + \frac{1}{j} \right)^{1/2} \left(i^{1/d_f} + j^{1/d_f} \right)^2, \quad (24)$$

for the free-molecular regime, where η is the viscosity of the disperse medium and m_p is the mass of the primary particle.

Correctness of relationship (24) for aerosol particles was the subject of a study¹³⁶ and good agreement with the results of numerical simulation was revealed.

Fractal aggregation in the continuum regime using the Smoluchowski equation with the coagulation kernels for DLA was studied.^{137, 138} Both analytical¹³⁷ (assuming a lognormal cluster size distribution) and numerical¹³⁸ solution of the coagulation equation were obtained. The former solution was reproduced by Park *et al.*¹³⁹ Figure 5 presents the temporal dependences of particle concentrations. As can be seen, the formation of fractal aggregates causes a faster decrease in the particle concentration;

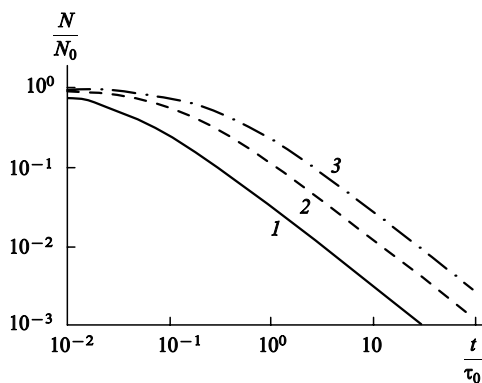


Figure 5. Reduced concentration, N , of aggregates with different fractal dimensions as a function of time.¹³⁹
 d_f : 1.5 (1), 2.0 (2) and 3 (3); N_0 is the concentration of primary particles and τ_0 is the half-coagulation time.

the reciprocal concentration increases linearly with time for different fractal dimensions.

The existence of a self-preserving solution of the Smoluchowski coagulation equation with the coagulation kernels (23) and (24) was confirmed both numerically and analytically.¹⁴⁰ Based on the numerical solution, simple approximate expressions were presented for the self-preserving solution of the Smoluchowski equation.

The possibility for the self-preserving solution of the Smoluchowski equation to exist was also reported^{138, 141–144} for the continuum (DLA) and free-molecular regimes of particle aggregation. The results of calculations^{141–144} were confirmed by experiments¹⁴³ with silicon and silicon nitride aerosol particles. At the same time, numerical calculations¹⁴⁴ showed that no self-preserving solution exists at $\mu > 1$ because of gel transition.

Sintering of particle aggregates^{145–147} and other processes related to the effects of surface phenomena¹⁴⁸ or dispersion composition¹⁴⁹ on the kinetics of particle aggregation¹⁴⁸ only slightly affect the possibility of obtaining the self-preserving cluster size distribution.

2. Coagulation in concentrated dispersions

Recently, considerable attention has been paid to the studies on aggregation in concentrated disperse systems. This is due to advances in computational procedures and to the development of new experimental methods. A feature of concentrated colloidal systems is a significant role of not only the average cluster size and the cluster size distribution but also the structure factor, which is given by (see also the next subsection)

$$S(q) = \frac{1}{N^2} \sum_{j=1}^N \sum_{i=1}^N \exp[iq(\mathbf{r}_i - \mathbf{r}_j)], \quad (25)$$

where $\mathbf{q}$ is the scattering vector, $\mathbf{r}_i$ and $\mathbf{r}_j$ are the coordinates of particles and N is the number of particles in the system. The structure factor characterises both long-range and short-range orders in the particle distribution and predetermines the optical properties of dispersions.

Aggregation in concentrated colloidal dispersions can be considered as a stage of phase[§] decomposition. Phase decomposition in molecular systems is accompanied by definite evolution of the structure factor. Numerous attempts to confirm or reject the validity of these evolutionary relations for colloidal systems have been undertaken.

Kolb and Herrmann¹⁵⁰ seem to have been the first to report significant differences between the aggregation in concentrated dispersions and aggregation in strongly dilute colloidal systems. The subject of their study was the numerical simulation of particle aggregation in two- and three-dimensional systems at high concentrations of clusters. The emphasis was placed on the effect of the diffusion coefficient on the structure of the growing aggregates. The diffusion coefficient was assumed to be a power function of the cluster mass. It was found that three types of aggregation can occur in the system at different values of the exponent and initial concentration of particles. These are (i) growth of fractal clusters whose dimensions vary over a wide range, (ii) growth of dense clusters with fractal surfaces and (iii) growth of dense clusters with smooth surfaces. Particular regimes of aggregation allow growth of infinite clusters (*i.e.*, percolation clusters or gel).

Monte Carlo simulation of diffusion-limited cluster–cluster aggregation of colloidal particles in concentrated dispersions was reported.¹⁵¹ The structure factor was calculated at different instants. The emphasis was placed on verification of the hypothesis of scaling invariance of the dynamical structure factor, according to which

§ The phase state of an ensemble of colloidal particles is kept in mind.

$$S(q, t) = R_g(t)^{d_f} F[qR_g(t)], \quad (26)$$

where F is a universal scaling function, which does not depend on time in an explicit form. Numerical calculations confirmed the scaling invariance of the dynamical structure factor. At the same time, it was pointed out that some details of the evolution of the colloidal dispersion are different from the model of spinodal decomposition, as was found in the model^{152, 153} and numerical¹⁵⁴ experiments. The main difference was attributed to different exponents in the power-law expression for the temporal dependence of the average size of the new-phase domains, namely, the exponent equals $1/3$ for spinodal decomposition while depends on the space dimension and on d_f of aggregates for fractal aggregation.

Scaling invariance of the structure factor was the subject of yet another study, numerical simulation of DLA and RLA in three-dimensional space.¹⁵⁵ Using a structure factor similar to that given by (26), the authors tested the validity of the relationship established¹⁵⁶ for spinodal decomposition

$$S(q, t) = q_m^{-3} F\left(\frac{q}{q_m}\right),$$

where $q_m(t)$ is the wave vector corresponding to the maximum value of the structure factor and d is the space dimension (for fractal aggregates, $d = d_f$). The structure factor was also compared with the pair correlation function and it was shown that the peak of the structure factor arises from the correlations between particles belonging to nearest-neighbour clusters. The exponents that relate the position and the height of the maximum of $S(q)$ to time differ from the spinodal decomposition exponents. Though the $S(q)$ for RLA exhibits no peak at short times, eventually its maximum becomes higher than that for the DLA regime. The final shape of $S(q)$ corresponds to a close packing of the clusters after gelation.

A numerical study on diffusion-limited aggregation in two-dimensional colloidal dispersions of various concentrations was also reported by van Garderen *et al.*¹⁵⁷ Conditions for gel transition in the system were established (see Section VI). In the gel state, the system contains a domain of size $r < \xi$ (ξ is the so-called correlation length, which characterises the spatial range of fractal properties of aggregates). At long length scales, the system is a homogeneous medium. The fractal dimension of the grown aggregates coincided with that found for diffusion-limited cluster–cluster aggregation. Variation of the concentration of primary particles affects only the parameter ξ .

The results obtained for three-dimensional systems were somewhat different.¹⁵⁸ The existence of two domains characterised by different length scales, $r < \xi$ and $r > \xi$, was also pointed out. At short length scales, the system has a fractal structure, while at long length scales, the system is a homogeneous medium. However, an increase in the fractal dimension of aggregates with increasing concentration of primary particles was reported, which contradicts the results of this study by van Garderen *et al.*¹⁵⁷ To eliminate the contradiction, a thorough study of aggregation of colloidal particles in dispersions of different concentrations was carried out.¹⁵⁹ Calculations for the three-dimensional space using the diffusion-limited and reaction-limited cluster–cluster aggregation models with inclusion of the dependence of the particle diffusion coefficient on the particle size showed that for both models the fractal dimension increases with increasing concentration of primary particles. This increase for the DLA and RLA regimes can be approximated by the corresponding relationships

$$d_f = 1.80 + 0.91\varphi^{0.51}, \quad (27)$$

$$d_f = 2.1 + 0.47\varphi^{0.66},$$

where φ is the volume fraction of particles. The cluster size increases as a power function of time for DLA and exponentially

for RLA. The exponent in the former case and the coefficient in the exponential expression in the latter case are also functions of the initial particle concentration. In both cases, self-preserving cluster size distributions were found, which correspond to the above-mentioned relations (20) with a bell-shaped function $f(x)$ for DLA. The corresponding function $f(x)$ for RLA has the form

$$f(x) \propto x^{-\tau} \tilde{f}(x), \quad \tau = 1.5.$$

Diffusion-limited aggregation in concentrated dispersions was analysed¹⁶⁰ by analytical methods using the known mean-field approximation model.¹⁶¹ The conditions for cluster formation and the cluster–cluster correlations were analysed with inclusion of the presence of domains with reduced concentrations of particles (monomers). The temporal evolution of the mean cluster radius coincided with that predicted by solution of the Smoluchowski equation. The angular dependences of the scattering light intensities by dispersions were calculated at different instants. Differences between the light scattering by dispersions characterised by the growth of dense and fractal clusters were pointed out. Model experiments showed that scaling invariance of the type (26) during the whole aggregation process is characteristic only of the scattering intensity calculated for the dispersions of dense clusters. The absence of scaling invariance for fractal clusters was explained by differences between the characteristic times of aggregation and of local changes in the concentration of monomers; namely, aggregation is governed by the fractal dimension while the formation of domains with reduced concentrations of particles (monomers) is governed by the space dimension. Scaling-invariant changes in the scattering intensity can occur only immediately prior to gelation.

3. Systems characterised by fragmentation and rearrangement of aggregates

In most cases, numerical experiments concerning fractal aggregation imply rather strong interparticle interactions. In fact, fragmentation of particles is possible, in particular, because of thermal motion. It was Kolb¹⁶² who pioneered numerical experiments on the growth of fractal aggregates by fragmentation. The inclusion of the possibility of cluster fragmentation can lead to an increase in the fractal dimension of aggregates. For instance, d_f increases from 1.78 in the absence of fragmentation to 2.03 if one assumes a low probability of interparticle bond breaking. An increase in the fractal dimension is readily explicable: most often, aggregates comprising fragments connected through a small number of bonds (*i.e.*, the loosest aggregates) undergo fragmentation. Of course, fragmentation of aggregates produces some mass distribution, but the average cluster mass has a finite value.

The effect of bond energy on the fractal dimension of aggregates grown in the diffusion-limited cluster–cluster aggregation regime was studied.¹⁶³ Using the two-dimensional model, it was shown that the fractal dimension strongly depends on the bond energy of the particles in the aggregate.

If the homogeneous coagulation and fragmentation kernels meet the conditions

$$Z(Ai, Aj) = A^{v_z} Z(i, j), \quad (28)$$

$$Y(Ai, Aj) = A^{v_y} Y(i, j),$$

where v_z and v_y are the homogeneity exponents, the average number of particles in the aggregate is given by¹⁶⁴

$$\langle s \rangle \propto \left(\frac{Z_0}{Y_0} \right)^{1/(2+v_y-v_z)}, \quad (29)$$

where Z_0 and Y_0 are the dimensional coagulation and fragmentation constants, respectively,

$$Z(i, j) = Z_0 \tilde{Z}(i, j),$$

$$Y(i, j) = Y_0 \tilde{Y}(i, j).$$

Here $\tilde{Z}(i,j), \tilde{Y}(i,j)$ are dimensionless functions [usually, $\tilde{Z}(1,1) = \tilde{Y}(1,1) = 1$].

Dimensional relationships (28) and (29) were used to establish the dependence of the average number of particles in aggregates, their average size ($\langle R \rangle$) and concentration (n) on the volume fraction, ϕ , of particles in the system.¹⁶⁵ A criterion for gel transition in the system was also proposed.

The growth of fractal clusters, which can undergo fragmentation induced by thermal motion, and gel transition in two- and three-dimensional systems was studied.^{166–170} The structure factor $S(q,t)$ of aggregates grown in the diffusion-limited cluster–cluster aggregation regime was determined at different instants by numerical simulation.¹⁶⁶ The height of the maximum of $S(q,t)$ is plotted vs. time in Fig. 6. Three main regions in the plot can be pointed out. At short times, the height of the maximum slowly increases [the lower the bond energy, the slower the growth of $S(q_m)$]. At intermediate times, the $S(q_m)$ increases as a power function of time. The duration of this stage is limited by the gel transition, which corresponds to the next, final, stage of the change in the structure factor $S(q_m)$. Here, the $S(q_m)$ slowly increases and reaches a plateau. The higher the bond energy, the slower the increase in the $S(q_m)$. At low bond energies, the plot exhibits no saturation. In this case, the system's behaviour corresponds to the classical pattern for ageing colloidal dispersions, which are characterised by a gradual increase in the size of compact 'droplets' (gel state will be considered in more detail in Section V).

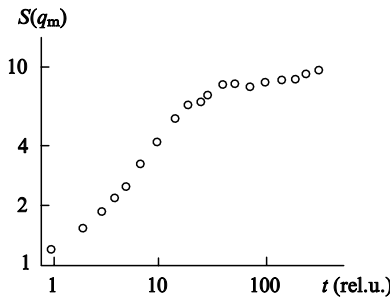


Figure 6. Maximum value of the structure factor, $S(q_m)$, as a function of time for a system of gel-forming aggregates.¹⁶⁶

Concluding this Section, mention may be made of a number of studies concerning the fragmentation of fractal aggregates by different mechanisms. Etching studies of fractal and non-fractal clusters revealed¹⁷¹ that the temporal dependence of the number of fragments passes through a maximum and that the number of fragments and the width of their distribution at maximum exhibit power-law dependences on the mass of the initial cluster and on the average coordination number of particles in the cluster. The corresponding exponents depend on the space dimension, starting geometry of the system and on the temperature (the bond breaking probability was assumed to be proportional to the Boltzmann factor). Simulation of etching of fractal objects (aggregates, surfaces and a porous medium) was carried out¹⁷² for both reaction-limited and diffusion-limited regimes. Each object under study was characterised by its own kinetics of etching, governed by the fractal dimension. For instance, the mass of a fractal cluster M decreases with time as follows

$$M \sim (1 - Kt)^{d_f},$$

while the area of the fractal surface obeys the t^{1-d_f} law. It should be noted that fragmentation of fractal aggregates is similar to fragmentation of percolation clusters, which are known to have a fractal structure. Studies on the fragmentation probability of a percolation cluster *via* random rupture of a finite number of bonds have been reported.^{173–177} It was shown that fragmentation of

such a cluster obeys some scaling relationships; however, they cannot be used in fragmentation studies of conventional fractal aggregates and are therefore not presented here.

IV. Multifractal analysis of fractal aggregates

Some fractal objects cannot be described by one fractal dimension,^{178, 179} so one should introduce a large number of parameters similar to the fractal dimension. In this case, the object under study is said to possess multifractal properties.

Often, the question arises as to the multifractal characteristics. For instance, a study on the motion of a fractal aggregate in viscous fluid showed¹⁸⁰ that the distribution of viscous forces applied to particles obeys multifractal relations. It was pointed out¹⁸¹ that the multifractal approach should be used when analysing the voltage drop distribution at the interparticle contacts in a composite material characterised by near-percolation concentration of the conducting phase. This methodology was also used to study the crack structure distribution in solids¹⁸¹ and the fluid flow distribution in a porous medium.¹⁸²

Let us consider the multifractal characteristics in more detail. We will examine a fractal object following a conventional formalism by tiling the space of the object into small boxes. Let any box have a unit mass. This allows the mass, M , and the density of the object of linear dimension L to be determined

$$\rho = \frac{M}{L^d}.$$

An increase in the linear dimension of the object by a factor of A causes the mass to increase by a factor of A^{d_f} and the density to decrease by a factor of A^{d_f-d} . Generally, we can write

$$M \sim L^{d_f}, \quad \rho \sim L^{d_f-d}.$$

Since all boxes have equal masses, the changes in the characteristics of the object, which are due to the change in its linear dimension, can be described using one parameter, namely, the fractal dimension d_f . Such an 'equality' of the masses (or other characteristics) of boxes not necessarily corresponds to the physical essence of the object under study. In the example considered above (see Section II), the characteristics of the perimeter of the growing cluster were determined with inclusion of the attachment probability of a new particle to a certain perimeter site. It was shown that different perimeter sites are characterised by different attachment probabilities p . Therefore, it is possible to introduce a probability distribution, $n(p)$, for different perimeter sites. In this way, other elements of the fractal object can also be described by some probability distributions. Like any other probability distribution, the distribution $n(p)$ can be characterised by moments of the order q [¶]

$$Z(q) = \sum_p n(p)p^q = \sum_i p_i^q. \quad (30)$$

Summation in the first sum is performed over the probabilities while summation in the second sum is performed over all the perimeter sites characterised by the corresponding probabilities.

Any parameter suitable for quantitative comparison of different regions of a fractal object can be used instead of the probability. Often, the parameters p_i are meant as generalised measures. Examples of the normalised quantities (measures) will be presented below.

Fractal objects belong to the so-called critical structures. According to the theory of critical phenomena, the probability

[¶] Literal designation of the moments as q is commonly accepted in the literature. Here, it should be recalled that the letter ' q ' has already been used in the review for notation of another quantity (see above).

distribution must be characterised by two critical indices only.¹⁸³ This means that it is impossible to obtain additional information on the system by examining the higher moments, because the $(q + 1)$ th moment is determined by the exponent, which is found from the q th moment, and some increment Δ . Let the moment be related to the linear dimension L by a power dependence with the exponent $\tau(q)$

$$Z(q) \sim L^{-\tau(q)}. \quad (31)$$

Then, $\tau(q)$ must be a linear function because only two numbers (critical indices) are required to find the dependence $\tau(q)$ (see above). Both numerical simulation and model experiments on many real fractal objects revealed that in the general case the relation between τ and q significantly differs from a linear dependence, which points to multifractality of these objects.

The generalised fractal dimension, D_q (more rigorously, the dimension spectrum), is given by the following relationship

$$(q-1)D_q = \tau(q). \quad (32)$$

As can be seen, $\tau(q)$ equals zero at $q = 1$.

Usually, yet another two characteristics are introduced. These are the so-called Hölder exponent

$$\alpha_m = \frac{d\tau}{dq}, \quad (33)$$

and the Legendre transformation of the function $\tau(q)$, or the multifractal spectrum

$$f(\alpha_m) = q\alpha_m - \tau(q). \quad (34)$$

For true fractal structures, this difference and the parameter D_q are constants.

The physical meaning of these characteristics can be understood taking the aggregation problem as an example. Assuming that the probability of particle attachment to some site changes with the change in the linear dimension of the aggregate (namely, decreases because of the lengthening of the perimeter) as follows

$$p \sim L^{\alpha_m}, \quad (35)$$

from relations (30), (32) and (34) the probability distribution density is given by

$$n(p) \sim C(\alpha_m)L^{f(\alpha_m)}, \quad (36)$$

where $C(\alpha_m)$ is a function independent of the length scale.

When analysing real objects using the multifractal approach, a number of characteristic parameters corresponding to $q = -\infty$, 0, 1 and $+\infty$ are usually considered. At $q \rightarrow \infty$, the parameter $\tau(q)$ equals the proportion of the multifractal set, which is characterised by the highest probability, and D_∞ equals the minimum α_m value for the system in hand. And *vice versa*, at $q \rightarrow -\infty$, $\tau(q)$ equals the proportion of the multifractal set, which is characterised by the lowest probability, and $D_{-\infty}$ equals the maximum α_m value. At $q = 0$, the parameter D_0 , which is equal to the maximum value of the function $f(\alpha_m)$, characterises the dimension of the measure carrier (*i.e.*, the multifractal object itself). For a monofractal object, D_0 equals the fractal dimension of the object. Finally, at $q = 1$, the parameter D_1 is equal to the dimension of information entropy (generally, it can be considered equal to the dimension of the generalised Renyi entropy).

Typical dependences $D_q(q)$ and $f(\alpha_m)$ are shown in Figs 7 and 8. Real systems can exhibit marked deviations from these dependences.

There is an analogy between the multifractal and thermodynamic formalisms. Let us re-write relationship (30) in the form

$$Z(q) = \sum_p e^{F(p)}, \quad (37)$$

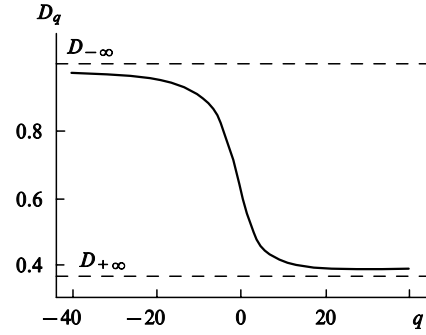


Figure 7. Typical fractal dimension spectrum.¹⁸⁰

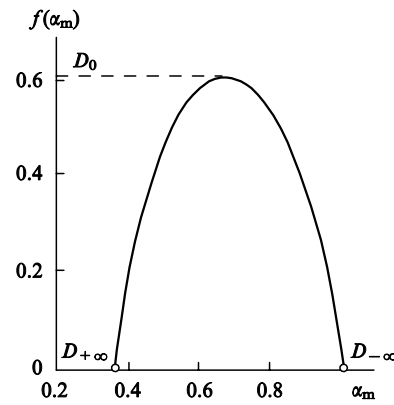


Figure 8. Typical multifractal spectrum and its characteristic points.¹⁸⁰

where $F(p) = \ln n(p) + q \ln p$. Suppose that the major contribution to the sum on the right of Eqn (37) comes from the terms with $p = p^*$, where p^* corresponds to the maximum value of the function under the summation sign. Then one gets

$$Z(q) \approx e^{F(p^*)} \propto L^{\tau(q)} = L^{f(\alpha_m) - \alpha_m q}. \quad (38)$$

As can be seen, the function $Z(q)$ formally plays the role of the statistical sum of the thermodynamic system while $\tau(q)$ is the free energy and q is the reciprocal of the temperature. The Legendre transformation $f(\alpha_m)$ is an analogue of the entropy, the parameter α_m is an analogue of the energy while the dependence $f(\alpha_m)$ is easily recognisable as similar to the relation between the entropy and energy of the thermodynamic system. The analogy between the fractal and thermodynamic formalisms has been the subject of a thorough study.¹⁸⁴

The multifractal thermodynamic characteristics of the fractal aggregates grown in the DLA regime have been reported.¹⁸⁵ The generalised Renyi entropies were calculated

$$I_q(L) = \frac{1}{q-1} \ln \sum_i p_i^q, \quad q \neq 1, \quad (39)$$

$$I_1(L) = \sum_i p_i \ln p_i,$$

and their changes during the aggregation simulated using the Brownian dynamics approach were followed.

The Renyi entropies depend on the fractal dimension of aggregates. An increase in the number, N , of particles in the aggregate causes the Renyi entropies to increase in proportion to $\ln N$. The coefficient of proportionality,

$$K_q = \frac{I_q}{\ln N}$$

for this dependence is determined by the fractal dimension of the aggregate and the q value. At $q \leq 1$, the parameter K_q decreases, while at $q > 1$ it increases on increasing the fractal dimension. This coefficient can be used to determine the degree of multifractality of aggregates, which is defined¹⁸⁶ as the entropy difference between the domains corresponding to the maximum ($q \rightarrow +\infty$) and minimum ($q \rightarrow -\infty$) measures, *i.e.*, $K_{-\infty}(N) - K_{+\infty}(N)$. According to calculations, this difference tends to zero as the number of particles in the aggregate increases. Thus, transition to a true monofractal is possible in the limit $N \rightarrow \infty$; the aggregate comprising a finite number of particles possesses multifractal properties.

An attempt has been undertaken¹⁸⁷ to go beyond the scope of a simple analogy between the multifractal and thermodynamic descriptions. The 'thermodynamic' behaviour of multifractal systems was compared with the thermodynamic behaviour of conventional physical objects. The 'thermodynamics' of multifractals was considered in the constant specific heat approximation. This choice is due to the fact that the specific heats of gases and solids remain constant over a rather wide temperature range. In this approximation, the function f should have the form

$$f(q) = a_m - c_m \ln q, \quad (40)$$

where a_m and c_m are constants and q is the constant specific heat. For the generalised dimension from Eqn (32) one has

$$D_q = (a_m - c_m) + c_m \frac{\ln q}{q - 1}. \quad (41)$$

The dependence $f(q)$ is plotted in Fig. 9. As can be seen, the constant specific heat approximation fits well the results of numerical experiments.

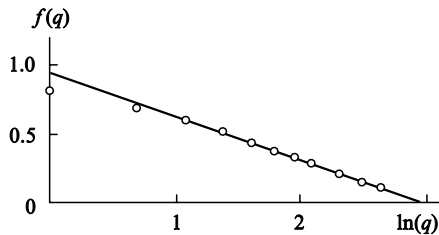


Figure 9. Multifractal spectrum calculated for the DLA regime (points)¹⁸⁸ and calculated in the constant specific heat approximation (straight line).

Analogous dependences for the generalised fractal dimension are presented in Fig. 10. The results of numerical simulation are in good agreement with the fractal dimension spectra obtained in the constant specific heat approximation. Interestingly, the slope ratio of the straight lines in Fig. 10, which is equal to the 'specific heat' ratio, is $\sim 3/2$, as in the case of the specific heats of three- and two-dimensional gases. It has been shown¹⁸⁸ that the constant specific heat approximation describes the multifractal spectra obtained by different authors for various systems (*e.g.*, stress distribution for percolation cluster, surface profile of corroding material, turbulent diffusion, *etc.*).

The multifractal analysis of the clusters growing in the DLA regime showed^{190–192} that the clusters are characterised by a more complex structure than could be expected based on the fractal dimension and anisotropy factor only.

Consideration of correlations between the measures of a multifractal object showed¹⁹¹ that the correlation function has the form

$$\langle p(r')^m p(r' + r)^n \rangle \simeq \left(\frac{R}{a}\right)^{d_{m+n}} \left(\frac{r}{a}\right)^{d_m + d_n - d_{m+n}}, \quad (42)$$

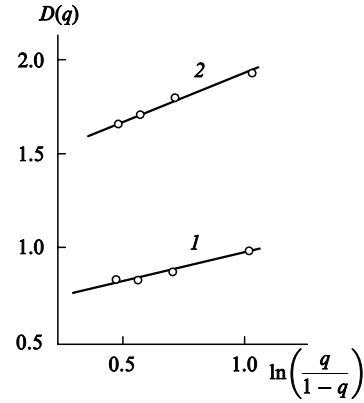


Figure 10. Fractal dimension spectra for two-dimensional (1) and three-dimensional (2) DLA¹⁸⁹ plotted in the constant specific heat approximation.

where a and R are respectively the lower and the upper bounds of the fractal behaviour of the measure carrier ($a < r < R$; a is the short cutoff and R is the overall radius of the object), $d_q \equiv (1 - q)D_q - d_f$ and d_f is the fractal dimension of the measure carrier. The existence of a single scaling form over the full range of radius indicates that the multifractal object is a set of blocks similar to those used in polymer physics rather than a superposition of fractal sets.

A similar approach to the description of fractals treats fractal aggregates as sets of 'branches' with certain masses m .¹⁹² For a typical cluster comprised of N particles, the branch mass distribution, $n(m, N)$, was introduced. Processing of a large body of data obtained by numerical simulation of aggregates showed that this distribution obeys the law

$$\frac{n(m, N)}{N} \sim m^{-\beta}. \quad (43)$$

More recently,¹⁹³ it was shown that this power law can be derived from the maximum entropy principle. In this case, the entropy is expressed through information necessary for growing a fractal object with prescribed structure and size. Taking a number of fractal objects, which can be grown iteratively, it was demonstrated that the maximum entropy principle allows, on the one hand, the power laws of changes in some characteristics of fractals to be established, and, on the other hand, the fractal dimension to be calculated without determining the spatial structure of fractal objects.

Theoretical conclusions were confirmed by the data of experiments¹⁹⁴ with polystyrene latex particles of size 600 nm, which floated on the surface of aqueous MgSO_4 solution. The image of the surface fluid with floating particles was tiled into boxes of a particular size δ . Each box was ascribed a measure p_i equal to the ratio of the number of particles in the box to the total number of particles in the system. The multifractal characteristics can be found with ease from the following expressions

$$\tau(q) = \lim_{\delta \rightarrow 0} \frac{\ln \sum_i p_i^q}{\ln \delta}, \quad (44)$$

$$\alpha_m(q) = \lim_{\delta \rightarrow 0} \frac{\sum_i \hat{p}_i \ln p_i}{\ln \delta},$$

$$f(q) = \lim_{\delta \rightarrow 0} \frac{\sum_i \hat{p}_i \ln \hat{p}_i}{\ln \delta},$$

where

$$\hat{p}_i = \frac{p_i^q}{\sum_i p_i^q}. \quad (45)$$

The multifractal spectra of aggregating two-dimensional dispersion at different instants are shown in Fig. 11. Some peculiar features should be pointed out. The maximum in the curve is related to the fractal dimension of the measure carrier, *i.e.*, to the fractal dimension of the substrate regions characterised by the nonzero measure. A large number of empty regions is also present in the system in question; because of this, the fractal dimension of the measure carrier is less than two. The information entropy and the fractal dimension of the measure carrier are plotted *vs.* time in Fig. 12. As can be seen, both dimensions decrease with time. This is typical of two-dimensional aggregation of colloidal particles. A decrease in the entropy dimension is explained by a decrease in the monolayer entropy upon aggregation.

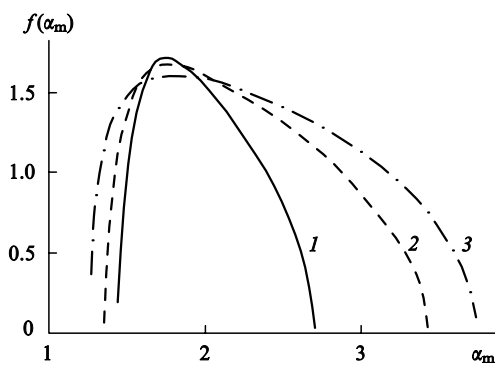


Figure 11. Multifractal spectra of aggregating two-dimensional dispersions at different instants of time.¹⁹⁴
t/s: 122 (1), 613 (2) and 2401 (3).

Using the relations mentioned above implies an all-scale self-similarity of the object analysed using the multifractal approach. Real objects are self-similar at certain length scales. This means that in the general case the multifractal spectrum depends on the length scale. Taking into account this scaling dependence, it is possible to draw some interesting conclusions concerning the length scales appropriate for multifractal analysis of objects.¹⁹⁵ Let us take an ensemble of particle aggregates as an example and analyse it using the multifractal approach.

Let us tile the entire space into boxes of linear dimension δ . Let the proportion of particles in the box i be the measure p_i . Clearly, the sum of the measures over all boxes equals unity. The average measure in the filled boxes equals the reciprocal of the number of the filled boxes

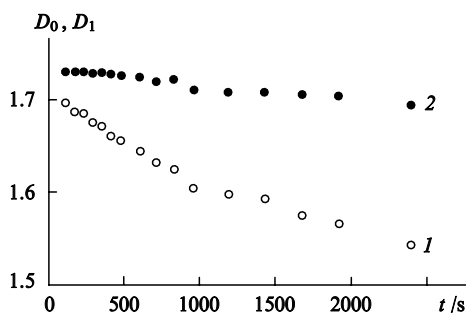


Figure 12. Information entropy (D_0) (1) and fractal dimension of the measure carrier (D_1) (2) plotted *vs.* time.

$$\langle p \rangle = Z(0, \delta)^{-1}. \quad (46)$$

The dispersion of the measure in the boxes is given by

$$\sigma_p^2 = \langle p^2 \rangle - \langle p \rangle^2 = \frac{Z(2, \delta)}{Z(0, \delta)} - \frac{1}{Z(0, \delta)^2}. \quad (47)$$

For monofractal objects one has

$$Z(0, \delta) \sim \delta^{-d_f},$$

$$Z(2, \delta) \sim \delta^{d_f}.$$

As a result, the measure dispersion remains constant upon changing the box size. For multifractal objects, the first term in Eqn (47) is proportional to $\delta^{D_2+D_0}$ and the second term is proportional to δ^{2D_0} ; *i.e.*, the measure dispersion varies with the change in the box size. Therefore, it is possible to find a box size (for a normal multifractal spectrum, where $D_2 < D_0$ on the long length scale, and for an anomalous multifractal spectrum, where $D_2 > D_0$ on the short length scale) such that the measure dispersion becomes equal to zero. Further change in the length scale will not affect the dispersion, because it cannot be negative. So one can say that, from the measure distribution standpoint, the system will be homogeneous beyond the limiting length scales. In the case of colloidal systems the minimum box size nearly equals the particle size or the correlation radius.

Yet another field of application of the multifractal approach is the determination of the fractal dimension of real finite systems. The point is that the use of the relationship given in p. 824 faces some difficulties, because this relation ‘works’ well only in the case of ideal (in the mathematical sense) fractal objects. Real systems are characterised by finite dimensions, which confines the range of fractal behaviour. Therefore, the fractal dimension is usually estimated rather than calculated. The procedures for reliably estimating the fractal dimension have been discussed in the literature.^{196–199} Usually, it is possible to determine several different fractal dimensions. A typical curve for the determination of the fractal dimension of an object, obtained using the box-counting technique, is shown in Fig. 13. The curve degenerates into a straight line only for true fractal object. Otherwise (including multifractal structures), a number of straight-line portions are observed. Usually, region 1 (large δ) characterises the fractal dimension of the space into which fractal objects can be embedded. The slope of the straight line in region 2 (small δ) determines the fractal dimension of the embedded object. Unambiguous interpretation of the intermediate region 3 is impossible, because its pattern is to a great extent determined by the character

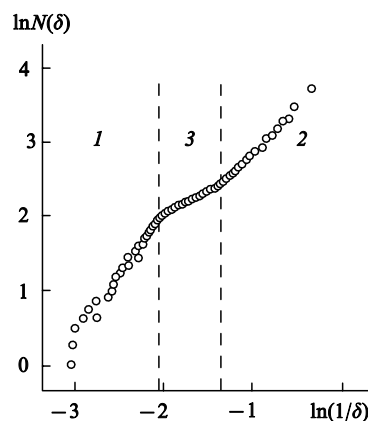


Figure 13. Typical curve for determination of the fractal dimension using the box-counting technique.
 (1–3) see text.

of the spatial distribution of fractal objects. It can be treated as the region of the fractal dimension distribution, corresponding to the multifractal properties of the system under study.

V. Fractal gels and emulsions

1. Fractal gels

The size of fractal aggregates increases much faster than their mass during the aggregation process. At a certain particle concentration, which is specific to each fractal dimension value, the aggregates grown can fill the entire space, thus forming a gel structure composed of a network of connected clusters. Colloidal diffusion-limited cluster–cluster aggregation in two-dimensional systems was studied using the Smoluchowski coagulation equation²⁰⁰ and by numerical simulation.²⁰¹ The evolution of the cluster size distribution was followed; the gel was treated as an infinite fractal cluster. It was shown²⁰² that, if the volume fraction of the primary particles exceeds some critical value, φ_c , diffusion-limited cluster–cluster aggregation results in a homogeneous network formed by fractal clusters of size ξ .

There is a large number of models, which describe the transition of colloidal dispersions to the gel state. They are based on the classical fluid theory equations adapted for colloidal systems.²⁰³ The approach employed includes the Brownian dynamics simulation^{204–207} with different potentials of interparticle interactions, *e.g.*, the Derjaguin–Landau–Verwey–Overbeek,^{204,205} Lennard-Jones²⁰⁶ or the depletion potential.²⁰⁷ The molecular dynamics approach²⁰⁸ is also employed in the studies of gelation at the molecular level.

The simplest models of gel formation upon particle aggregation usually assume²⁰⁹ that the fractal dimension of aggregates remains unchanged during their growth under, *e.g.*, the DLA or RLA conditions. The volume fraction of particles in the fractal aggregate can be found with ease from

$$\varphi_a = \left(\frac{R}{a}\right)^{d_f-3}. \quad (48)$$

Gel transition occurs if the volume fraction of particles in the fractal aggregate becomes equal to the volume fraction of clusters in the entire system (at $\varphi_a = \varphi$). All clusters are assumed to have the same mean size $R = \xi$. In this state, there is a region of size $r < \xi$ (see Section III) in the system where the aggregates possess fractal properties. At long length scales, the system is a homogeneous medium whose fractal dimension equals the space dimension. The correlation length, ξ , is determined by the volume fraction of particles and is given by

$$\xi \approx a\varphi^{-1/(3-d_f)}. \quad (49)$$

The simplest model for gel formation can be applied to explain the results of experimental studies on the dynamics of the structure factor of dispersions. Experiments showed^{152,153,210–214} that, if fractal aggregation in the system results in the formation of a gel, the dependence of the structure factor $S(q,t)$ on the wave vector at different instants passes through a maximum. Small-angle neutron, X-ray, and light scattering studies of a broad class of dispersions (aluminosilicate gels,²¹⁰ polystyrene latex particles,^{152,153} polymer gels²¹¹ and monodisperse oil droplets in water^{212,213}) also showed that the position of the maximum, q_m , is inversely proportional to the ξ value at a given instant. This maximum is interpreted as an indication of the transition from the fractal regime of scattering [at intermediate q values corresponding to $S(q) \propto q^{-d_f}$] to the scattering by a homogeneous medium (small q values). It was also established^{152,211,215} that

$$S(q_m, t) \propto \xi^{d_f}, \quad (50)$$

$$q_m \propto S(q_m, t)^{-1/d_f},$$

$$t_g \propto \varphi^{-d_f/(3-d_f)},$$

where t_g is the gel time.

These relationships were tested in the Monte Carlo studies of gel formation in the diffusion-limited cluster–cluster aggregation regime.^{158,216} It was found that in the short-time scale the cluster size changes as follows

$$\xi \propto \left(\frac{t}{t_g}\right)^{1/d_f}.$$

As time passes, the exponent decreases; it should be noted that the higher the concentration of primary particles in the system, the earlier the decrease begins. The power-law relationship between q_m and $S(q_m, t)$ was confirmed with high accuracy; however, the exponent remained constant on increasing the concentration of primary particles, whereas the fractal dimension of the growing aggregates increased substantially. On this basis, it was assumed that the gelating systems are also characterised by the apparent fractal dimension of aggregates, which governs the relation between q_m and $S(q_m, t)$. A detailed review on the kinetics of formation of fractal gels from colloidal particles was reported by Poon and Haw.¹⁷⁰ They considered the processes of gel formation from colloidal particles and from colloidal particles and polymers and analysed the peculiar features of small-angle light scattering by gels of colloidal particles, which are due to the existence of a mesoscopic fractal structure.

In fact, fractal gels have a more complex structure compared to that predicted by the simplest model and the process of gel formation involves several stages.²⁰⁸ At first, clusters are formed from monomers and then grow under DLA conditions. The initial gel network is comprised of the largest aggregates and then smaller aggregates and free particles are included. In this stage, intercluster interactions become increasingly significant. Thus, the formation of a gel network is accompanied by slow changes in the structural organisation of particles.²¹⁷ Breakage of certain bonds and the formation of new bonds induce restructuring of the gel, which is accompanied by an increase in the dimensions of fractal objects. The multistep process of gel formation in colloidal dispersions was confirmed in a series of experimental studies^{218–220} carried out using various methods of analysis of the gel structure, which allowed length scales from several nanometres to 5000 nm to be investigated.

Restructuring of aggregates after formation of a gel network is possible in the systems characterised by rather weak attractive interparticle interactions.^{167–170,221,222} Here, the lifetime of the gel network can be rather long. However, if the interparticle bonds can be broken, the network is restructured because this state of particles in colloidal systems is metastable compared to gas–liquid phase transitions. Usually, such gels are called transient gels,²²³ though in fact all gels of colloidal particles are treated as transient gels (though for some of them the time for transition to the equilibrium state is too long). Numerical simulation of the process of transient gel formation has been the subject of a large number of studies (see, *e.g.*, Refs 205, 206, 222, 224 and 225). Transient gels obey common relations for the pair correlation function, $g(r)$, and the particle density distribution, $n(r)$

$$g(r) = \left(\frac{r}{\xi}\right)^{d_f-3},$$

$$n(r) = n_0 \left(\frac{r}{a}\right)^{d_f}$$

(n_0 is the normalising factor) and for the correlation length; however, the parameters of these distributions (including d_f) change with time.

Modern experimental studies are mainly carried out in order to establish a relation between the parameters of gels and

conditions for gel formation. In particular, the effects of the properties of the disperse medium^{226,227} and of the regime of coagulation of the primary particles^{226,228} on the fractal dimensions and correlation lengths of gels have been studied. The range of substances used for the formation of hydrogels is extended^{229–233} (here, silica undoubtedly ranks first). New experimental procedures for the determination of the sol–gel transition point, kinetics of fractal aggregation and fractal characteristics of gels are elaborated (*e.g.*, rheological^{232,233} and electrical conductivity methods²³⁴).

Studies on the dynamics of the restructuring of gels are a particular avenue of experimental research. Here, the main difficulty is due to the low rate of the process. Nevertheless, interesting results have been reported recently.²³⁵ Experiments were carried out with gels of polystyrene latex particles of size 10 nm dispersed in a light/heavy water mixture, which provided neutral buoyancy of particles. The volume fraction of particles varied from 10^{-4} to 10^{-3} . The fractal dimension of the freshly formed gel was 1.82. It was established that the dynamical structure factors of the gels obtained obeys the law

$$S(q, t) \propto \exp \left[- \left(\frac{t}{\tau_f} \right)^{\beta_g} \right], \quad (51)$$

with $\beta_g = 1.5$ and $\tau_f \propto q^{-1}$. Ageing causes the time τ_f to increase substantially. The temporal dependences obtained for different q can be scaled on a single master curve, with τ_f growing linearly with age. It should be noted that the temporal dependence of type (51) was reported earlier²³⁶ for an identical gel of polystyrene latex particles of size 9.5 nm with a somewhat different β_g value (0.66). No changes in the relaxation time were observed, except for a rather strong dependence of this parameter on the concentration of primary particles.

To explain these observations, a model was proposed, which is based on the syneresis of a gel and on its local shrinkage [the case in point is (i) the compaction of fractal fragments and (ii) restructuring of the gel]. The model allows experimental dependences to be reproduced correctly at a qualitative level. Densification of the central part of aggregates was reported in a study²³⁷ on the evolution of gels formed in methylcellulose solutions.

Until recently, gel formation was observed only in liquid dispersions. The first experiment on the formation of gels initially in the gas phase was reported by Lushnikov *et al.*²³⁸ who prepared the so-called fractal wires. The metal surface was exposed to intense laser radiation; subsequent application of a strong external electric field induced the ‘growth’ of a thick wire formed by fractal clusters attaching to the metal surface. The mechanism of wire formation is rather simple, namely, metal vapours are condensed in the form of nanoparticles which form fractal clusters. The external electric field induces directed aggregation into macroscopic fractal structures. A feature of the process is that the fractal wires at first grow in the gas atmosphere and then are attached to the surface.

Fractal wires from steel, brass and carbon particles have been produced analogously.²³⁹ A thorough examination of the structures showed that the primary particles are 1 to 10 nm in diameter and up to several millimetres long and possessed pronounced anisotropy. The ‘lifetime’ of the wires reached several weeks at zero electric field between the electrodes. The mechanism of formation of these structures is still to be clarified. The point is that one should take into account not only accelerated coagulation of particles but also their deposition on the electrodes. Here, the main contribution comes from Brownian diffusion of the particles and from their motion in the electric field. The nonuniformity of the electric field should also play a significant role. This is unavoidable in the system under study both at the electrode surfaces covered with the deposits and in the space between the electrodes, filled with rather large and readily polarisable aggregates.

The formation of an aerogel from soot particles formed during acetylene combustion has been studied.²⁴⁰ The primary particles of size 10 to 30 nm, which are usually formed in flames, grow (most often, under DLA conditions) into fractal aggregates with the radii of gyration varied between 50 and 100 nm. The experiment involved determination of the structure factor and photography of the upper region of the flame at different flow rates of acetylene. Measurements and observations showed that at sufficiently low flow rates of acetylene the structure factor corresponded to the presence of flame fractal aggregates with a dimension of 1.8. At rather high flow rates of acetylene, the dependence of the structure factor on the wave vector exhibits a maximum and some contacting aggregates of size of at most 5 μm are observed in the system. This indicates formation of a flame aerogel. Estimation of the aggregation rate of soot particles showed that it much exceeds that expected from the Smoluchowski equation. The mechanism of accelerated aggregation is also still to be clarified; mention was only made that studies of the sol–gel transition in the liquid phase also revealed²⁴¹ accelerated aggregation.

2. Fractal emulsions and microemulsions

In studies of the mechanical properties of aqueous emulsions^{242,243} it was conjectured that their spatial structure is characterised by the presence of inhomogeneous regions possessing the properties of fractals. This was confirmed in a quenching study²⁴⁴ of the microstructure of silicate glass in a liquid with low glass affinity (fractal properties were observed at a certain fraction of the dispersed phase). The data were analysed based on the concept of the so-called connected cluster, which is similar to a percolation cluster. However, analysis was performed by inclusion of all particles in the entire system, so the total number of particles much exceeded the number of particles in the connected cluster. Therefore, the fractal structure reported in Ref. 244 cannot be explained by effect of this cluster.

The fractal structure of emulsions was also assumed to have a dynamical nature²⁴⁵ and numerical simulation of a two-dimensional ensemble of disks with short-range attractive interactions was carried out. The type of particle distribution in the system was determined from the relationship between the number of particles in the circle $g(r)$ and the circle size r . For a system of non-interacting particles or at a low energy of interparticle interaction

$$U < kT$$

the particle distribution was uniform. The system with strong interparticle interaction

$$U > 3kT$$

was characterised by the formation of associates followed by separation into two phases. At

$$kT < U < 3kT$$

clustering occurred. The composition of clusters varied with time. The function $g(r)$ for the region occupied by the cluster was found to be a power function with a fractional exponent equal to the fractal dimension of the growing clusters. It was established that the fractal dimension increases on increasing the concentration of disks in the system.

Microemulsions, or surfactant-stabilised, thermodynamically stable homogeneous mixtures of polar (water) and non-polar (oil) liquids, belong to yet another group of colloidal objects with fractal structures. The surfactant molecules are usually distributed over the oil/water interfaces, which confine nanodroplets of water or oil.

Microemulsions are characterised by diverse structural organisations. Here, only three of them will be pointed out. If oil is present in excess, the phase L_2 comprised of water-containing surfactant micelles distributed in oil is usually formed. Otherwise (water-rich compositions), a microemulsion is comprised of surfactant-coated oil droplets dispersed in water (phase L_1). The

presence of water and oil in nearly equal proportions leads to formation of a bicontinuous phase (structure with surfactant-separated interpenetrating domains of the oil and water phases). The phase state of the microemulsions is to a great extent determined by the temperature and salinity of the aqueous solution.

Interestingly, by increasing the water-to-oil ratio it is possible to pass from the phase L_2 to the phase L_1 through the bicontinuous phase. This transition is accompanied by changes in the physicochemical properties of the microemulsion. The most remarkable is a dramatic (by several orders of magnitude) increase in the conductivity of microemulsion, which is usually considered as a percolation transition.^{246–249}

Observation of this transition indicates that microdroplets must form a fractal structure corresponding to the percolation cluster.⁵ At the same time, treatment of microemulsions in the framework of the fractal approach is seldom the case, though the earlier Monte Carlo simulation²⁵⁰ revealed fractal aggregation in microemulsions. It is the concept of fractal aggregation that allowed agreement between the theoretical and experimental temperature dependences of the conductivity of microemulsions on the concentration of the conducting phase to be established.

It was shown²⁵¹ that dynamic light scattering in microemulsions can be described in terms of the fractal aggregation of microdroplets and that the fractal dimension of the percolation cluster (2.5) is quite appropriate to account for the experimental data. This approach was also used²⁵² to describe the temperature dependences of the viscosity and elastic modulus of a microemulsion and of the dependences of the ultrasound velocity, specific heat and viscosity on the concentration of droplets. The great potential of the fractal methodology for the theory of microemulsions was confirmed by the results of experiments on the kinetics of quenching of fluorescent probes²⁵³ and diffusion of water molecules,²⁵⁴ dynamical percolation transitions^{255,256} and fluctuation effects²⁵⁷ in microemulsions near the percolation threshold. The fractal nature of the structure of microemulsions is also indicated by numerical simulation data and analytical calculations of the dynamics of the processes in the oil/water/surfactant systems during the formation of microemulsions from a (initially) homogeneous ternary mixture.^{258–261} This also holds for the interfaces in microemulsions.²⁶² Thus, application of the fractal approach to such interesting systems as microemulsions offers considerable promise.

VI. Two-dimensional fractal structures

Numerical simulation of aggregation processes usually concerns the laws of aggregation in spaces of different dimensions. The case for two-dimensional space is most often studied. This is mainly due to considerable reduction of computational cost, while the results obtained differ from those typical of the three-dimensional systems only quantitatively. However, interest in two-dimensional systems is not only of theoretical but also practical value. Modern technologies require knowledge of the laws of the interfacial behaviour of colloidal particles. These can be, *e.g.*, the water/air or oil/water interfaces; aggregation of particles at the solid/liquid interface is also possible.

Because of the need for research on aggregation in the two-dimensional space, numerical simulation was followed by experimental studies nearly immediately. It should be noted that such experiments have some advantage over the experiments with three-dimensional systems, namely, the structures of two-dimensional aggregates can be observed immediately using various microscopy techniques without distorting the objects under study.

1. Air/liquid interfaces

The pioneering experimental studies on the laws of fractal aggregation at interfaces were reported by Hurd and Schaefer²⁶³ and Onoda.²⁶⁴ They used micrometre-sized, hydrophobised particles of silica²⁶³ and polystyrene²⁶⁴ distributed over the surface of

aqueous salt solution. The experiments were carried out under DLA conditions. The values of the fractal dimensions determined appeared to be close to those found from numerical simulation.

There are three main types of interaction between particles trapped at interfaces. These are the electrostatic repulsion, molecular attraction and capillary interaction, which can be both an attractive and repulsive interaction. The electrostatic and capillary forces can be controlled with ease by adding salts in solution and by changing the extent of modification of the particle surface. The possibility of controlling the interaction forces allows the regime of particle aggregation to be varied. In particular, no changes in the structure of aggregates were observed^{265–267} upon change in the regime of cluster–cluster aggregation of polystyrene latex particles on the surface of water from DLA to RLA.

Studies on the aggregation of glass beads at the water/octane²⁶⁸ and water/air^{269,270} interfaces were carried out in different regimes of particle aggregation including those allowing the aggregates to undergo restructuring. Experiments showed that the aggregates can have either a fractal or non-fractal structure depending on the regime of aggregation. The fractal dimension of the growing aggregates depends on the hydrophobicity of the particle surface and on the concentration of salt in solution. Under particular conditions, rather large aggregates are characterised by the internal structure, as indicated by a break in the plot of the logarithm of the cluster density *vs.* distance to the centre of the cluster. The break was ascribed to the action of capillary forces, which contract the soft peripheral area of aggregates (see below). The interior of the large clusters is characterised by the same fractal dimension as the small aggregates. Considerable attention was paid to the restructuring of the grown aggregates. No quantitative relationships were found, but simple estimation showed that restructuring of aggregates is to a great extent controlled by the repulsive electrostatic forces. This conclusion was confirmed in the experiments on aggregation of polystyrene latex particles on the surface of water. In this case, the possibility of restructuring of aggregates was provided by specific adjustment of the parameters of the colloidal system.²⁷¹ By varying the electrostatic repulsion between particles it was possible to grow both compact aggregates and two-dimensional ‘foam’ formed by chains of particles.

A comparison of the laws of aggregation of rod-like and spherical particles at the water/air interface was reported.²⁷² The experiments were carried out with polydisperse rod-like soot particles 35 μm thick and 140 μm long and monodisperse glass beads 75 μm in diameter with different extent of surface hydrophobicity. The fractal dimension of two-dimensional structures was determined using three methods (box-counting technique, density correlation function and the number of particles–box size correlation). Experiments showed that the shape of particles has no effect on the laws of aggregation because the fractal dimensions of the aggregates of soot particles and of glass beads differed only slightly; at the same time, the fractal dimension of glass beads was affected by the hydrophobicity of their surface. Based on the fact that in both systems the structures of aggregates exhibited the existence of two regions with different fractal dimensions, it was concluded that aggregation was accompanied by restructuring.

Zeiri *et al.*²⁷³ studied a specific process of two-dimensional aggregation, namely, deposition of silver particles, which were distributed over the water subphase/organic liquid interface, on a thin electrode just contacting the water phase. An ensemble of silver particles at the interface (the so-called metallic liquid-like films) was prepared following a special procedure.²⁷⁴ The organic phases were chloroform and dichloromethane and the water subphases were aqueous solutions of silver nitrate with various surfactant additives. The concentration of silver nitrate in solutions was varied over a wide range. The use of solutions with strongly different concentrations allowed silver deposition on the electrode to be carried out in three regimes, *viz.*, electroaggregation of particles, electrochemical deposition of silver in the absence of interfacial particles and a combined regime ‘electro-

aggregation particles/electrochemical deposition of silver'. In the last-mentioned case, aggregation proceeded by a new mechanism, which involved the formation of interparticle bridges due to electrochemical deposition of silver. The preparation of nearly poreless aggregates and wire-like structures revealed the possibility of basically changing the structure of the deposits and their fractal characteristics.

Studies on subtle details of structural organisation of fractal aggregates formed on the liquid surface have been reported^{275, 276} taking aggregation of polystyrene latex particles of size 1 μm , which floated in the surface of aqueous solutions, as an example. Analysis of changes in the structure factor $S(q, t)$ under reaction-limited cluster–cluster aggregation conditions²⁷⁵ revealed a power-law singularity in $S(q, t)$ at $t \rightarrow \infty$, $q \rightarrow 0$. This behaviour corresponds to the so-called self-organised criticality, where in the absence of external factors the system tends to reach a state characterised by the absence of characteristic time and length scales. The system comprises both small clusters and large clusters whose size is comparable with the size of the entire system. In this case, a crucial role is played by co-operative effects, which reflect the long-range order in the ensemble of two-dimensional aggregates.

Experiments with polystyrene latex particles on liquid substrates were accompanied by numerical simulations of two-dimensional aggregation process at rather high particle concentrations under diffusion-limited cluster–cluster aggregation conditions.²⁷⁶ Direct observations of the system's structure [numerical processing of the experimentally measured structure factor $S(q, t)$] and the results of numerical simulation showed that at intermediate times the system has a structure with a six-fold symmetry. The corresponding peaks of the structure factor become strongly diffuse with time. The six-fold symmetry is quite unexpected for the system under study and has no rigorous physical substantiation as yet. It was hypothesised that the instant at which the hexagonal structure is formed corresponds to the instant at which the average cluster size becomes comparable with the half-distance between clusters. At that instant, depletion zones are formed around clusters and weak long-range repulsion between the mobile clusters can provide conditions for the formation of a hexagonal structure. By the way, the authors²⁷⁶ pointed to weak points of this hypothesis.

Control of the interaction between particles located at the interface was a rather complicated task in most experiments considered above. This fact is responsible for the scatter of the fractal dimension values obtained in different experiments. Hansen and Bergström²⁷⁷ proposed a method of controlled variation of the potential of interparticle interaction by varying the extent of particle modification by alcohols and the length of the grafted alkyl chain. Estimates revealed that replacement of octyl by an octadecyl chain causes the bond energy of 2 μm silica particles at the air/toluene interface to decrease from 30 down to 15 kT . Video-enhanced microscopy and image analysis of the particle dynamics showed that the average cluster size and the cluster size distribution obey the scaling relationship (20). The structure of the octyl system is formed in the diffusion-limited cluster–cluster aggregation regime. This is indicated by the fractal dimension of aggregates determined from the dependence of the radius of gyration on the number of particles and using the grid method ($d_f = 1.45$). Aggregation of particles in the octadecyl system resulted in a more dense structure with $d_f = 1.55$. A feature of both systems is the characteristic time corresponding to a transition point between aggregation regimes, which was attributed to convective motion of the clusters at the interface. Convective motion considerably enhances the mobility of large clusters and is believed to be responsible for the transition from diffusion-limited to reaction-limited cluster–cluster aggregation.

Particles can form gel-like structures both at liquid interfaces and in the bulk of the liquid phase. Two- and three-dimensional gels exhibit no fundamental differences in their behaviour; because of this, we will not consider them. The characteristics of

such structures including their rheological properties have been thoroughly studied by Dickinson.²²²

A detailed investigation of two-dimensional aggregation of colloidal particles under the DLA and RLA conditions was reported.²⁷⁸ Numerical simulation was carried out for the rectangular lattice and off-lattice models. The emphasis was placed on the dependence of the fractal dimension on the initial particle concentration, which varied over a range of two and a half orders of magnitude. The relationship established for the fractal dimension was similar to that obtained for three-dimensional systems

$$d_f = d_0 + b_d \varphi^{c_d}.$$

The parameters b_d and c_d in this relationship depend on the aggregation regime and on the model employed. However, the exponent c_d was equal to nearly unity within the limits of the computational procedure. The temporal dependence of the cluster size was also calculated. At a rather long time scale, this is a power law with the exponent z , where z depends on concentration as follows:

$$z = z_0 + b_z \varphi^{c_z}.$$

Here, the values of the coefficients are also governed by the regime of aggregation and the model employed; however, the exponent significantly differs from unity and is close to 0.6.

The subject of the studies considered above was the DLA or RLA regime at the surface of liquid phase. Practical realisation of other mechanisms of aggregation in these systems is a complicated task. The authors of study²⁷⁹ succeeded in implementing a two-dimensional ballistic aggregation of particles. In the experiments, hydrophobic particles were successively placed at the top of a droplet on the substrate. Particles were gravity 'slipped' following 'linear' trajectories towards the peripheral area of the droplet where aggregation occurred (aggregates grew from the periphery towards the centre of the surface of the spherical segment). The surface was nearly completely covered by particles; the fractal dimension of the aggregates thus grown was 1.95. In the case of diffusion-limited cluster–cluster aggregation on a flat surface, the same particles formed fractal structures with a fractal dimension of 1.45.

Particle aggregation on liquid surfaces in specific regimes (neither DLA nor RLA) is accompanied by the formation of various structures including fractal ones.^{280–282}

2. Cluster deposition on substrates

Deposition of nanoparticles on solid substrates is also accompanied by the growth of clusters with fractal structure.²⁸³ Low-energy monodispersed clusters produced by condensation of vapours were vacuum deposited on the substrate, thus forming submonolayers of clusters comprised of several tens to several thousands of atoms. Such clusters do not break down upon collision with the substrate. Larger clusters are characterised by small surface diffusion coefficients; therefore, they virtually do not move across the surface and their aggregation is thus also strongly inhibited. As the number of clusters on the substrate increases, specific structures are formed, which correspond to successive deposition of strongly attaching particles. Most often, structures similar to two-dimensional fractal aggregates are formed. Experimental studies and the results of numerical simulation concerning a broad spectrum of problems related to cluster deposition have been reviewed.^{284, 285} However, a study on the growth of fractal germanium clusters by epitaxial deposition on lead-coated silica surface should be pointed out.²⁸⁶ A remarkable feature of this study is that the cluster structure corresponds to the RLA rather than DLA regime. This indicates the existence of an energy barrier, which precludes aggregation of clusters. The barrier is high enough to provide conditions for transition from the DLA (a common situation for clusters on solid substrates) to RLA regime at small surface diffusion coefficients.

Clusters with fractal structures were produced by pulsed laser deposition of gold vapours on substrate (highly oriented pyrolytic

graphite).²⁸⁷ The possibility of formation of fractal aggregates in similar experiments with a NaCl substrate was suggested earlier.²⁸⁸ The fractal dimension depended on the radiation intensity and on the length of the pulse train. An original model for the formation of fractal clusters was proposed. It is based on consideration of the motion of adatoms across the substrate surface. The model was transformed to the equations corresponding to the formation of Julia sets.¹¹¹ It correctly reproduced value of the fractal dimension of aggregates.

The subjects of studies^{289–294} were various theoretical models for growth of fractal aggregates from particles deposited on solid substrates. The models included the surface diffusion of adatoms²⁸⁹ and clusters²⁹⁰ as well as rotation of clusters²⁹¹ assuming deposition of both monodisperse particles and particles of different size^{292,293} and shape.²⁹⁴ Analysis of aggregation on solid substrates also revealed that the fractal dimension is related to the degree of surface coverage as follows

$$d_f = 1.455 + 1.322 \varphi.$$

Experimental studies in this field^{295–299} were concerned with the deposition of metal vapours on the surface of substances with well-developed crystal structure^{295,296} and on the surface of oil²⁹⁷ and glass.²⁹⁸ Deposition of mesoscopic particles on a solid substrate was reported.²⁹⁹

The fractal structures are formed on the surface not only on deposition of vapours or particles but also in surface chemical reactions. This was observed in the Dy–Co system (see Ref. 300) under the action of a beam in an electron microscope and on the surface of liquid gallium.³⁰¹ The formation of iron oxide clusters of size up to several millimetres on the surface of amorphous iron films several tens of nanometres thick was reported.³⁰² In all experiments, the cluster structures were identical to the structure of the particles grown in the DLA regime. The results of recent search for fractal structures on the surfaces of specially treated polymer films are available.^{303,304}

VII. Viscous fingering

Penetration of fluids into porous solids also produces fractal structures.¹³ Fluid flow in porous media is accompanied by the so-called viscous fingering, *i.e.*, formation of a specific kind of prominence at the interface. Viscous fingering is due to the instability of the propagating interface and usually occurs when the more viscous fluid is displaced from the porous media by the less viscous fluid. The fractal dimension of viscous fingers is determined using the following relationship

$$N_v = k_v R_g^{d_f}, \quad (52)$$

where N_v is the number of pores filled with the more viscous fluid, k_v is the corresponding prefactor and R_g is the radius of gyration of the liquid cluster. Studies on the mechanisms of viscous fingering and formation of related structures have been well documented.^{305,306}

Viscous fingering is most often analysed taking immiscible fluids¹³ and — much more rarely — partially miscible fluids³⁰⁷ as examples. This phenomenon can also occur when dispersions are displaced by neat solvents, because the former liquids are always more viscous than the latter.

The so-called Hele–Shaw flow, or displacement of a viscous fluid from the space confined between two transparent flat plates, is often considered as a model for flow in a porous medium. Transparency of the plates allows the propagation of the interface to be monitored.³⁰⁸ A complete analogy between the development of instabilities of the Hele–Shaw flow and the growth of dendritic structures was established.^{306,309} Stability studies of the Hele–Shaw flow are of great practical value, because the development of instabilities precludes a number of important technological processes related to, *e.g.*, oil displacement from pools. For this reason, attempts to suppress the development of instabilities are under-

taken. Studies on the flow of three immiscible fluids in the Hele–Shaw cell³¹⁰ and on the flow stability considerations in the presence of highly dispersed particles in the displacing fluid³¹¹ showed that under particular conditions it is possible to suppress the development of instabilities in different stages of flow.

There is an analogy between the flow in porous solids and fractal aggregation. In particular, the DLA model and the flow in porous solids are described by identical equations.^{13,312,313} However, this analogy does not necessarily hold. The laws of formation of the viscous interface in the case of porous solids characterised by a broad pore size distribution are significantly different from the laws of clustering under the DLA conditions.³¹⁴

The influence of inhomogeneities in the porous medium on the regularities of the growth of viscous fingers has been studied assuming a Gaussian distribution of the permeability of the porous medium centred at the mean value.³¹⁵ The fractal structure of viscous fingers was not determined. The authors calculated the width of the mixing interface between two fluids for different dispersions of the permeability (see also Section VIII). According to calculations, the width of the interface increases linearly with time.

Viscous fingering related to flow in fractal structures was studied.³¹⁶ This is the case of flow in, *e.g.*, porous media near the percolation threshold (at a small fraction of through pores). Clearly, in this case the fractal system of viscous fingers will also be governed by the structure of the percolation cluster of the porous solid. More sophisticated models for viscous fingering in porous media require the use of the multifractal approach to describe the media³¹⁷ or the self-affine geometry for the pore space.³¹⁸

Viscous fingering accompanied by polymerisation at the interface was simulated.³¹⁹ It was shown that three situations are possible depending on the capillary number

$$N_{Ca} = \frac{\eta v}{\gamma},$$

where η is the viscosity of the displacing fluid, v is the average interface propagation velocity and γ is the interfacial tension. Within some range, the reaction rate affects the interface propagation velocity; at lower reaction rates beyond the range mentioned above, the reaction has virtually no effect on the interface propagation. At higher rates (above the upper bound of the range), the interface propagation slows down. The smaller the capillary number, the wider the range of reaction rates affecting interface propagation.

The theoretical studies considered above were carried out using mainly two-dimensional models of porous media. Numerical solution to the three-dimensional hydrodynamics equations describing viscous fingering in the case of partially miscible fluids was also reported.³²⁰ It was shown that screening, spillover and coalescence of viscous fingers occur at all Peclet numbers in the range studied. At large Peclet numbers, splitting of viscous fingers occurs, similarly to two-dimensional systems. Broadening of the interface at long time scales occurs at a constant velocity, which is independent of the Peclet number. If flow occurs in the regime corresponding to rare splitting of viscous fingers, their number monotonically decreases with time. The authors pointed out that the solution obtained for the two-dimensional model by and large correctly includes peculiar features of the development of the process in three-dimensional systems.

A related study³²¹ dealt with the effect of kinetic fluctuations on the propagation of the interface between immiscible fluids. According to calculations, the width of the interface remains constant for three-dimensional systems. For the two-dimensional model of a porous medium, the interface width logarithmically increases with time.

A more complex process, namely, displacement of a viscous fluid from the porous body by the medium that can react with the body (dissolve it) was also studied.^{322,323} It was found that the

structure of the liquid–liquid interface is similar to the interface structure formed in the DLA regime. The results of simulation of the structure of a soluble porous solid were confirmed experimentally. This problem was also solved analytically³²⁴ in the asymptotic limit using the renormalisation group method. This system is characterised by the existence of two limiting regimes. Under these conditions, the interface structure corresponds to the structure of the DLA-grown clusters and it is possible to observe a successive transition from the interface with the structure of the DLA-grown clusters to a rather smooth interface and then again to the interface with the structure of the DLA-grown cluster.

Studies of the boundary effects on the structure of viscous fingers⁶⁸ revealed that the fractal dimension of viscous fingers in retarded flow is much smaller than in the three-dimensional system. As the bounding surfaces move away, the fractal dimension logarithmically approaches its bulk value.

Fractal structures are also formed when nonwetting fluids displace wetting fluids from porous solids. In particular, this is the case for the conventional mercury porosimetry technique.³²⁵ Simulation is usually carried out using a particular (prescribed) structure of pores and pore necks, which permits the fractal dimension of the growing structures to be varied over a rather wide range. Usually, the entire percolation cluster of the invaded fluid, its branches and the ‘backbone’, which is obtained by cutting the branches off, are considered.^{326–330} The structure of the porous solid has a strong effect not only on the fractal characteristics of different clusters but also on their structure.³²⁹ This holds for the systems both with and without trapping of the displaced fluid.

Viscous fingering was observed during the wetting/dewetting process of a solid surface.³³¹ In the experiments, a droplet of SnPb eutectic alloy at first spilled over an Au/Cu/Cr multilayered film. This droplet etched the Au/Cu films, which was followed by contraction of the droplet, because the chromium substrate was not wetted with the alloy. It was found that contraction of the droplet was accompanied by the formation of fractal structures similar to viscous fingers. At different stages of contraction, fractal structures with different structures were formed. At first, the fractal structure exhibited a DLA pattern, while the final structure was a dendrite-like one. The fractal dimensions of these structures were 1.83 and 1.79, respectively.

The problem of the flow of a fluid along the grain boundaries³³² is similar to the viscous fingering problem. The grain boundaries wetted with the fluid form a fractal cluster, which allows percolation transitions to be observed similarly to the case of fluid invasion into porous media.

VIII. Fractal films

1. Simulation

Recently, considerable attention has been given to the studies of vapour deposition of films.³³³ This is due to two reasons. On the one hand, vapour-deposited metal and semiconductor films are used in various microelectronic devices. On the other hand, development of scanning electron and atomic force microscopies has opened up new prospects for research on the properties of films and on the mechanisms of their growth.

Vapour phase deposition of films is usually accompanied by the formation of granular structures (protrusions of different height and width). Here, significant roles are played by the thermodynamics and kinetics of film growth. Thermodynamics predetermines the growth pattern (layer-by-layer or island-type) of the newly formed structure, while the kinetics prescribes the rates of nucleation and growth of islands (*via* parameters of the surface diffusion of atoms). The formation of a continuous surface layer is followed by the growth of films with rough surface, the roughness being more pronounced with time. This is due to the fact that protrusions ‘mask’ depressions, thus making them less accessible to filling. This mechanism of development of rough surfaces is realised in combination with the smoothing mecha-

nisms of film surfaces, among which the most important is surface diffusion.

Growth of vapour-deposited films is usually described using the ballistic model,³³⁴ according to which particles moving towards the surface follow random trajectories. The surfaces growing by this mechanism possess fractal properties. As mentioned above, fractals can be self-similar or self-affine. Rough surfaces are treated as self-affine objects.

The fractal dimensions of the growing films are usually determined from the dependence of the surface ‘thickness’ on the lateral size of the portion L rather than the fractal dimension of the profile. The surface thickness is calculated as the root-mean-square deviation of the profile over the length L

$$w(L) = \sqrt{\frac{1}{N_L} \sum_{j=1}^{N_L} [h_{ij} - \langle h_f(L) \rangle]^2}, \quad (53)$$

where N_L is the number of points of the profile of length L , h_{ij} is the height at the point j , and $\langle h_f(L) \rangle$ is the average height of profile of length L . Since the height h_f is a function of time, the surface thickness $w(L, t)$ also appears to be time dependent. For self-affine surfaces, $w(L, t)$ changes with increasing L as follows

$$w(L, t) \propto L^\alpha,$$

where α is the roughness exponent. For fractal surfaces, the roughness exponent is related to the fractal dimension

$$d_f = d' + 1 - \alpha,$$

where d' is the dimension of the interface (for non-fractal surfaces, $d' = 2$).

Using the ballistic model³³⁵ and Eden model³³⁶ for particle deposition on the substrate, it was established that the surface thickness is described by a universal (scaling) distribution

$$w(h_f) \sim L^\alpha f\left(\frac{h_f}{L^{\alpha/\beta}}\right), \quad (54)$$

where h is the average height of the layer deposited on the substrate, L is the width of the growing stripe (column in the case of three dimensions) and the function $f(x)$ meets the following conditions

$$f(x) = \begin{cases} x^\beta, & x \ll 1 \\ \text{const}, & x \gg 1 \end{cases}. \quad (55)$$

The parameters in relationship (54) are as follows: $\alpha = 1/2$ and $\beta = 1/3$ for two-dimensional systems and $\alpha = 1/3$ and $\beta = 1/4$ for three-dimensional systems. In the case of the ballistic mechanism, the deposit is a homogeneous medium while the layer deposited has a self-affine ‘surface’ with fractal structure.

Relationships (54) and (55) were verified for various models³³⁷ including those for ‘tree-like’ film growth (Fig. 14). Some additional scaling relationships for the tree height, h_f , tree width, w , and for the number, N_s , of trees of size s (s is the number of particles in the tree) were established. They are as follows

$$w \sim s^{v_1}, \quad (56)$$

$$h_f \sim s^{v_2},$$

$$N_s \sim s^{-\tau},$$

where the exponents are interrelated

$$(d-1)v_1 + v_2 = 1, \quad (57)$$

$$\tau = 2 - v_2,$$

and weakly depend on the deposition model employed.

When analysing the dynamics of film growth, relationship (54) can be re-written in the more general form

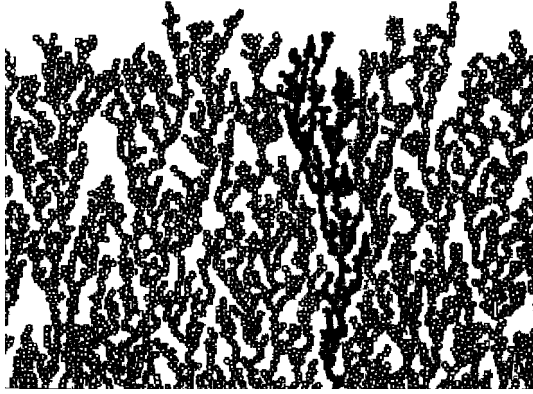


Figure 14. Structure of fractal aggregates formed upon deposition of particles on substrates. As can be seen, the number of 'trees' grown on the surface sequentially decreases (one 'tree' is shown in black).

$$w(t) \sim t^{\alpha} f\left(\frac{t}{L^{\alpha/\beta}}\right), \quad (58)$$

where t is time.

Various equations were proposed for analytical description of the film growth during vapour and particle deposition on the substrate. Consider the most important of them.

The simplest model was proposed by Edwards and Wilkinson.³³⁸ Here, the height of the surface is determined from the equation

$$\frac{dh_f}{dt} = v\nabla^2 h_f + \chi(x, t), \quad (59)$$

where $\chi(x, t)$ denotes the fluctuation (noise) contribution of the surface; $\chi(x, t)$ meets the following conditions

$$\langle \chi(x, t) \rangle = 0, \quad (60)$$

$$\langle \chi(x, t) \chi(x', t') \rangle = R \delta(x - x') \delta(t - t'),$$

where the angle brackets denote the averaging over the random variable χ , R is root-mean-square fluctuation of 'noise'.

This model describes smoothing of the surface by the capillary forces governed by the parameter v . The model can also be used to describe the propagation of an interface through a disordered medium and to study how the interface spreads out with time.³³⁹

The parameters of the model are as follows: $\alpha = (3-d)/2$ and $\beta = (3-d)/4$ for a one-dimensional substrate and $\alpha = 1/2$ and $\beta = 1/4$ for a two-dimensional substrate; the width of the surface logarithmically increases with time; for substrates of greater dimensions, the surface of the growing film is considered smooth.

This model was employed³⁴⁰ in calculations of interface growth on a fractal substrate characterised by the dimension d_s . The surface width exhibits the asymptotic behaviour given by expressions (54) and (55) with the parameter β

$$\beta = \begin{cases} \frac{1}{4}, & d' = 1 \\ \frac{1}{4} - \frac{d_s}{4}, & 1 < d_s < 2, \end{cases} \quad (61)$$

where d' is the substrate dimension.

A similar expression was obtained for the parameter α ³⁴¹

$$\alpha = \begin{cases} \frac{1}{2}, & d' = 1 \\ d_f \left(\frac{1}{d_s} - \frac{1}{2} \right), & 1 < d_s < 2. \end{cases} \quad (62)$$

The Edwards–Wilkinson model correctly reproduces the structure of surfaces grown by sedimentation of spherical particles.³⁴² Experiments were carried out with particles of size 440 nm in aqueous solutions. The profile of the sediment surface was determined using an atomic force microscope.

Trapping of polystyrene latex particles of size 0.8 μm at the meniscus of a thin film was studied in experiments on a deposition on a 'one-dimensional' substrate.³⁴³ It was found that $\beta = 0.267$, while the parameter α varied from 0.5 in the initial stage of the 'surface' growth to 0.71 a long time after the beginning of the process. The crossover of the regimes of the surface growth was explained by kinetic reasons. Initially, the 'deposit' moves with the meniscus and particles are deposited ballistically. Then, the deposit slows down and deposition due to Brownian-type particle diffusion is observed.

Kardar, Parisi and Zhang³⁴⁴ proposed a more sophisticated model for film growth, which is described by the following equation

$$\frac{dh_f}{dt} = v\nabla^2 h_f + \frac{\lambda}{2} (\nabla h_f)^2 + \chi(x, t), \quad (63)$$

here λ is the parameter of a model.

The additional term [cf. Eqn (59)] accounts for smoothing of the surface by lateral growth of protrusions. In the case of two dimensions, this model gives the parameters $\alpha = 1/2$ and $\beta = 1/3$, which exactly fulfils the relationship predicted³⁴⁵ for Eqn (63)

$$\alpha + \frac{\alpha}{\beta} = 2.$$

A comprehensive examination of Eqn (63) was reported.^{346,347} The parameters of Eqn (63) were related to the coefficients determining the asymptotic behaviour of the surface width at long time and long length scales

$$w(\infty, t) = C_t t^{1/3}, \quad (64)$$

$$w(L, \infty) = C_L L^{1/2},$$

The possibility of deriving a single-parameter (λ) universal relationship for the coefficients C_t , C_L was shown. Analogous analysis of the model for epitaxial film growth³⁴⁸ is described by the following equation

$$\frac{dh_f}{dt} = -v\nabla^4 h_f + \lambda \nabla^2 (|\nabla h_f|)^2 + \chi(x, t); \quad (65)$$

the model gives the parameters $\alpha = (5-d)/3$ and $\beta = (7+d)/3$ and is consistent with the results of numerical simulation of film deposition at the atomic level.

Various analytical models for film growth and interface propagation were proposed^{349–355} to generalise the models considered above. The model by Kardar–Parisi–Zhang was extended³⁵⁶ to the case for radial growth of spherical surfaces. The surface width is a complex function of time and exhibits a power dependence on a rather long time scale, the parameter β being equal to 1/3. Numerical simulation of the co-deposition of films was carried out³⁵⁷ with inclusion of the interactions between nearest neighbours and more distant particles and different probabilities of the deposition of the particles of a specified type at a given instant. It was shown that the parameters α and β depend on this probability, thus exhibiting a marked deviation from the dependence predicted by Eqn (63).

New models for particle deposition on substrates resulting in the formation of fractal surfaces have also been developed. In particular, an original model was proposed,³⁵⁸ which accounts for hierarchical deposition of debris during particle deposition from the atmosphere (particles reach the surface in order of size, largest first). Both regular and stochastic models for particle deposition on substrates were considered. Numerical simulation revealed that, in contrast to deposition of particles of the same size, in this

model the contour length (or surface area) increase logarithmically rather than obeying the power law as the length scale changes. For instance, the length of a line on the surface increases on decreasing the characteristic probe size δ as follows:

$$L(\delta) = \left(1 + A \ln \frac{1}{\delta}\right) L(1),$$

where A is a constant.

2. Experiments

Experimental studies on the interface growth were carried out using various systems.³⁵¹ The physical meaning of the equations considered above corresponds to the molecular beam epitaxy experiments. Deposition of gold,^{359–362} silver^{359,363} and iron^{359,364–366} films on various substrates was studied. A rather wide scatter of α values was obtained, which is apparently due to the use of different methods of determination of surface roughness. However, the scatter of β values is much smaller compared to that of α values. At the same time, in most cases the results of calculations and experimental data are in good agreement. This can be exemplified by the results of a study³⁶⁷ concerned with the analysis of the evolution of the surface of gold films deposited using the thermal evaporation technique. The characteristics of the surface were determined using scanning tunnelling microscopy; the experimental data were processed using Fourier analysis, which allowed the so-called power spectrum, $S_m(q, t)$, of the protrusion heights to be calculated. It was found that the surface width depends on time as $t^{0.25}$ and the power spectrum

$$S_m \sim q^{-4.1},$$

the parameter α being equal to nearly unity.

The dynamics of the interface growth was studied not only in the film deposition experiments but also in the experiments on paper imbibition,^{368–370} combustion³⁷¹ and tear.³⁷² The experimental results were described by the power dependences (54)–(58) but the values of the exponents differed from those predicted by theoretical models; the numerical values of the exponents obtained in different experiments were also different (for instance, paper imbibition experiments gave close values of the parameters α and β). Yet another feature of the experimental data is the crossover of the growth regimes of the interface width, which manifested itself as a change in the exponents α and β on increasing the time and length scales. No unambiguous explanation for this phenomenon has been reported as yet. It should be noted that some theoretical models include the possibility of changing the interface growth regime (see, e.g., Ref. 350). This change can be due to large-scale fluctuations of the growth direction in the active zone. However, the available models for growth of self-affine surfaces cannot correctly describe this crossover.³⁵⁰ Numerical experiments³⁷³ on epitaxial growth of the surface with inclusion of surface diffusion without desorption of adatoms revealed two growth regimes of the interface width. The regime found for short time scales was changed to that described by the Kardar–Parisi–Zhang equation over a long time scale. The new growth regime at short times is due to the inclusion of surface diffusion and is not observed if diffusion processes are ignored.

The establishment of different growth regimes is a complicated task because modification of models does not necessarily lead to crossover. In this connection, a representative example is provided by the study³⁷⁴ on a modified Eden model in which the growth process began after contact with ‘acceleration sites’, which were spatially distributed at random. The ‘acceleration site’ became an Eden cell immediately after contact with the surface of the growing film. The model revealed a percolation transition, i.e., the existence of some critical concentration of ‘acceleration sites’ corresponding to divergence of the growth rate of the surface area. However, no crossover of the growth regimes was found, even for this, basically modified, model. Moreover, the value of

the exponent α remained constant (0.5) over a wide range of ‘acceleration site’ concentrations.

The problem of etching of metallic surfaces is closely related to the problems considered above. It was reported³⁷⁵ that the perimeters of pits etched in thin aluminium films in NaCl solutions have a fractal structure and that the ‘roughness’ of the perimeter developed only at particular values of the potential applied. Detailed analysis of the corrosion pit profiles (corroded surface of stainless steel rods)³⁷⁶ revealed two different length scales (textural and structural) with different fractal dimensions (1.17 and 1.45, respectively). Further studies confirmed the existence of two characteristic length scales for the corrosion pit profiles in steel rods and aluminium sheets. Two fractal dimensions were also reported³⁷⁷ in a study of corrosion of vapour-deposited nanoscale Al films; the larger fractal dimension corresponded to the longer length scale. It was shown that the pit morphology can be varied over a rather wide range by varying the concentrations of iron and chloride ions in solution.³⁷⁷ Transition from a smooth to rough interface under particular regimes of corrosion is also possible.³⁷⁸ Corrosion of quasi-two-dimensional thin Al films was studied.³⁷⁹ Both model and numerical experiments were carried out. Model experiments were carried out using Al films 50 μm thick with etched end faces. Numerical simulation was performed with inclusion of higher electrolyte concentration in the pit during corrosion. The pit perimeter was characterised by one fractal dimension, which to some extent varied depending on the procedure employed for its determination. The results of the model and numerical experiments were found to be in good agreement.

Numerical (Monte Carlo) simulation of dissolution of a solid was carried out³⁸⁰ taking the case for the dissolution rate controlled by surface reactions as an example. It was shown that the predominance of stochastic lateral dissolution causes broadening of the interface; the parameters of Eqn (58) were found to be $\alpha = 1/3$ and $\beta = 1/4$. The inclusion of surface diffusion of atoms led to an increase in the α value to unity (β value remained unchanged) in the early stages and to transition to unstable interface in the later stages (β value increased from 0.25 to greater than 0.5). The inclusion of nonlocal effects caused an even greater increase in the parameter β .

* * *

In this review we considered the most important characteristics of fractal objects and the main types of fractal structures which can be found in disperse systems. The material presented gives an idea of the diversity of fractal objects and parameters that are necessary to completely characterise them. The large number of parameters reflects the variety of specific properties of fractal structures, which do or do not manifest themselves depending on external conditions. An attempt to present a comprehensive analysis of the properties of even those fractal structures considered in this review could lead to a considerable increase in the size of the text. Because of this, experimental methods for the determination of the fractal characteristics and physicochemical properties of fractal objects will be described separately.

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^c — *J. Exp. Theor. Phys. Lett. (Engl. Transl.)*

^d — *Techn. Phys. Lett. (Engl. Transl.)*

^e — *Crystallogr. Rep. (Engl. Transl.)*

^f — *Polym. Sci. (Engl. Transl.)*

^g — *J. Exp. Theor. Phys. (Engl. Transl.)*

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Microcomposites based on superconducting cuprates

P E Kazin, Yu D Tretyakov

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Abstract. Chemical aspects of the formation of microcomposites based on superconducting cuprates are considered. The materials are composed of a superconducting ceramic matrix and micro- or nanoinclusions of the non-superconducting phase, which are uniformly distributed in the matrix. Requirements on the operating characteristics of the superconducting ceramics are described and routes to high critical current densities are outlined. Phase equilibria in the generic systems are considered. Physical and chemical criteria for the choice of phases that can form non-superconducting inclusions are proposed. Methods of preparation and the microstructures and superconducting properties of the composites based on cuprates $\text{RBa}_2\text{Cu}_3\text{O}_{7-\delta}$ (R is the rare-earth element) and on $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ and $(\text{Bi,Pb})_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+\delta}$ are considered. The bibliography includes 247 references.

I. Introduction

Progress towards preparation and investigation of functional inorganic materials is closely related to complexity of the chemical composition and structure of systems in different levels of a material's organisation. On the atomic scale, advances are due to the preparation of multicomponent chemical compounds and to passage from simple to more complex crystal structures. For the nano- and micrometre-sized systems, the determining factor is an optimum organisation of domains, crystallites and ensembles of microscopic structural defects. The range of values of the operating parameters can be considerably extended by using multiphase composite materials. Some examples of the efficiency of such materials are provided by fabrication of magnets with high coercive force, intermetallide superconductors with high critical current densities, high-strength and heat-resistant ceramics

obtained by eutectic crystallisation, nanocomposites possessing specific optical properties, chemical sensors, *etc.*

Considerable advances in studies on superconductivity have been achieved in the last fifteen years. The discovery of high-temperature superconductivity in oxide ceramics by Bednorz and Müller¹ gave an impetus to expansion of the area of search for novel, chemically complex ceramic superconductors. A number of promising compounds were found, whose superconducting transition temperatures (T_c) much exceeded the boiling temperature of liquid nitrogen. However, the route to practical use of these compounds appeared to be rather long. Severe problems arose due to low efficiency of the magnetic flux pinning, weak intergranular contacts in the polycrystalline materials, brittleness and low mechanical strength of ceramics and the rather narrow range of external conditions for the formation of the superconducting phases.^{2–4} These difficulties can be to some extent resolved by carrying out international research collaboration. In particular, considerable progress has been achieved towards fabrication of silver-sheathed tapes and wires based on Bi-containing cuprates,^{5,6} $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$ tapes on bitextured metallic substrates,⁷ thin epitaxial films of various high-temperature superconductors (HTSC),^{8,9} bulk $\text{RBa}_2\text{Cu}_3\text{O}_{7-\delta}$ (R is the rare-earth element) ceramics¹⁰ and $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ rods.¹¹ Advances in development of graphotexturing techniques are also encouraging.¹²

In this review we analyse the currently available results of the studies on the synthesis of microcomposites based on superconducting cuprates containing highly dispersed inclusions of different phases. The significant role of such microcomposites in the development of materials science makes research in this field topical.

II. The problem of design of superconducting materials with high critical current densities

The most important operating characteristic of a superconducting material is the critical current density (J_c). Being considered as a function of the temperature and magnetic field, the J_c value characterises the maximum electric current which can flow through the conductor without energy loss.² The theoretical limit for the superconducting current density in HTSC is $\sim 10^8 \text{ A cm}^{-2}$; this value is due to kinetic energy induced unpairing of charge carriers (electron pairs).¹⁰ In real materials, the J_c values are much smaller. This is due to the fact that the critical current density depends on the force and energy of pinning of the

P E Kazin, Yu D Tretyakov Department of Chemistry and Department of Materials Sciences, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation.
Fax (7-095) 939 09 98. Tel. (7-095) 939 34 40.
E-mail: kazin@inorg.chem.msu.ru (P E Kazin). Tel. (7-095) 939 20 74.
E-mail: yudt@inorg.chem.msu.ru (Yu D Tretyakov)

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magnetic vortices present in the superconductor in a nonzero magnetic field and on the intergranular electric contacts in ceramics. Weak pinning in HTSC causes a rapid decrease in the critical current density with increasing magnetic field strength and on raising the temperature. Breakdown of intergranular electric contacts is responsible for the presence of weak Josephson junctions and for the low J_c , which dramatically decreases as the magnetic field increases. Therefore, the design of a material with high J_c requires efficient pinning of magnetic vortices and strong intergranular contacts. Besides, the material should possess a sufficiently high mechanical strength. To this end, the materials are prepared in the form of tapes and wires with a silver alloy core,^{5,6} films on single-crystalline oxide and metallic substrates^{7–9} and bulk composites.^{11,13} Intercrystalline contacts can be improved by forming pure grain boundaries containing no impurity phases and by texturing of ceramics (after, *e.g.*, deposition of epitaxial films or thermomechanical treatment).

The magnetic vortices are pinned to inhomogeneities, such as both point and extended lattice defects and inclusions of alien phases (Fig. 1). Enhancement of pinning can be achieved by forming a material containing micrometre- and nanometre-sized inhomogeneities.

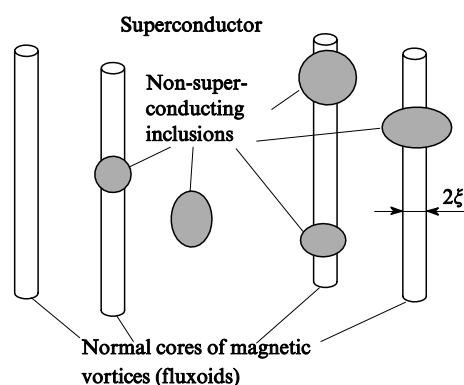


Figure 1. Illustration of pinning of magnetic vortices to non-superconducting inclusions.

The vortex energy decreases if its normal core (with destroyed superconductivity) passes through the non-superconducting inclusion. The vortex is pinned to such inclusions, so that its depinning and displacement require some force (pinning force) to be applied. Depinning and displacement of the vortex are accompanied by loss of energy in the superconductor;

ξ is the coherence length of the Cooper pairs.

According to calculations, the greatest pinning force can be attained if the dielectric inclusions or defects are of the order of the coherence length, ξ , of the Cooper pair^{2,14} (in most cases, several nanometres). In addition, the pinning force is expected to increase on increasing the concentration and, correspondingly, the volume fraction of inclusions up to 40 vol.% in the superconductor matrix.¹⁴ At higher concentration of inclusions, J_c decreases due to a marked decrease in the matrix cross-section area. For HTSC, the maximum J_c value due to a finite value of pinning energy is 10^7 A cm^{-2} .

One to several vortices can be pinned to large inclusions.¹⁵ According to calculations, in this case the pinning force is proportional to the total surface area of the inclusion–matrix interface; inclusions of size about $1 \mu\text{m}$ can provide the critical current densities lying between 10^4 and 10^5 A cm^{-2} .

The pinning centres in a superconducting material can be created using different approaches. The three main methods are as follows:

(1) exposure to accelerated particles and heavy ions, resulting in the appearance of amorphised domains and channels (of size of several nanometres) with destroyed superconductivity;^{16–19}

(2) heat treatment and mechanical treatment, which cause an increase in the density of the lattice defects or result in the formation of a fine-grained material with high concentration of grain boundaries (defects);^{20–25}

(3) introduction of micro- and nanoinclusions of the alien non-superconducting phases or creation of nanoscale inhomogeneities differing in the chemical composition and properties from the matrix phase.^{15,26}

The first method is highly efficient but is mainly applicable to small samples of thickness at most several tens of micrometres. It is often used in studies of the pinning mechanism.²⁷

Enhancement of pinning due to heat treatment and mechanical treatment can be exemplified by the formation of a fine-grained material based on Nb_3Sn (Ref. 20) and epitaxial HTSC films less than $1 \mu\text{m}$ thick. The maximum critical current densities for such films reach nearly 10^5 – 10^6 A cm^{-2} at 77 K, which can be explained by high concentration of dislocations at small-angle boundaries of submicrometre-sized domains.^{21–23} Similar results were also obtained in the experiments on creation of high concentrations of dislocations by mechanical treatment of HTSC.^{24,25}

The third method of pinning enhancement is of prime importance for bulk and long samples. It appeared to be rather promising for engineering of metallic superconductors based on Nb–Ti alloy.¹⁴ Using heat treatment and mechanical treatment (drawing), it is possible to prepare materials with controllable sizes of the second phase inclusions (Ti, Nb, Cu, V, Ni). The size of inclusions varies from several to tens of nanometres and the J_c value can be as high as $4.5 \times 10^5 \text{ A cm}^{-2}$ at a field of 5 T at $T = 4.2 \text{ K}$.¹⁴ Melt processing was used to obtain bulk samples of $\text{RBa}_2\text{Cu}_3\text{O}_{7-\delta}$ ceramics containing microinclusions of R_2BaCuO_5 phases (R is the rare-earth element). The critical current densities for such ceramics reach several tens of kiloamperes per square centimetre at 77 K.^{15,26} Considerable attention has been given to the formation of inclusions in bismuth-containing cuprates, for which the pinning of magnetic vortices is a challenge.^{28,29} Sometimes the critical current density can be increased by creating micro- and nanoinclusions of phases of the generic chemical system (*i.e.*, the system to which a particular superconducting complex oxide belongs) and the phases containing additional chemical elements (dopants). This effect is most pronounced at elevated temperatures ($> 20 \text{ K}$).

Thus, materials with high operating parameters should be composites. Taking into account the necessity of structuring the materials at micro- and nanolevels, we will call them microcomposites.

III. Main methods of preparation of microcomposites

Methodologically, the design of microcomposites is based on the principle of complication of the phase composition of the system,³⁰ according to which the material must be at least a two-phase system, in which the non-superconducting phase is uniformly distributed in the superconducting matrix in the form of micro- or nanoinclusions. These phases should be to the greatest extent chemically inert towards each other, while the entire system should be highly stable towards recrystallisation and segregation of the inclusion phase.

The chemical inertness of the phases in a composite is best achieved when using thermodynamically compatible components, which are in equilibrium at such values of the external parameters (temperature and the partial pressure of oxygen) that correspond to the conditions for the synthesis of the composite or to the operating conditions. Of course, this does not exclude the preparation of microcomposites containing incompatible phases; however, in these instances it is hard to prevent rather intense reactions between the constituents at high synthesis temperatures (850–1000 °C). This was confirmed by numerous observations of reactions between superconductors (and their melts) and the high-melting materials of crucibles and substrates.^{31–38} It should

be noted that inertness of different phases is of importance not only for microcomposites of the superconducting matrix–inclusion phase type but also for other types of materials, in which the superconducting phase immediately contacts some alien solid phases. This can be exemplified by substrate grown (deposited) films,^{7,9} composite wires of the ‘metal-sheathed superconductor’ type^{5,6} and reinforced superconducting composites.^{10,11} The problem of chemical inertness of phases in the composite is closely related to the problem of preparation of the so-called barrier materials, which prevent superconductors from being entered into chemical reactions with the environment during the synthesis and operation of microcomposites.^{31,38}

Sometimes, both the non-superconducting and superconducting phases of the microcomposite belong to the same chemical system, while the formation of the former phase is due to a shift of the system’s composition from the homogeneity region of the superconducting phase to the two-phase or multiphase region at particular values of external parameters. An alternative strategy involves the chemical complication of the system, *i.e.*, introduction of some extra components (chemical elements) to form the non-superconducting phase along with the components of the generic system. This technique has a greater potential for varying the system’s properties and, correspondingly, preparation of a material with the desired microstructure and operating characteristics.

Pinning centres (inclusions) can be created using different approaches (Fig. 2).

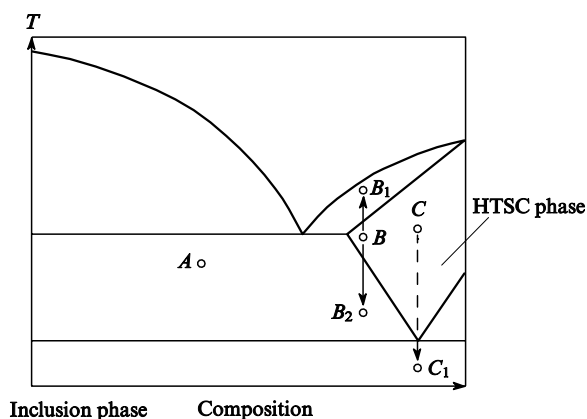


Figure 2. Scheme of the choice of system’s composition in the model phase diagram using the first (configurative point *A*) and second (configurative points *B*, *C*) methods of synthesis of microcomposites (see text).

The first method is to choose the chemical composition of the system in the two-phase or multi-phase region of the phase diagram at particular values of external parameters (temperature and partial pressure of oxygen) and to prepare the microcomposite material under these conditions (configurative point *A*).

The second approach involves the synthesis of the starting single-phase material followed by variation of the external parameters in such a way that the figurative point is in the instability region of the superconducting phase. The instability can mean either decomposition of the superconducting phase into non-superconducting phases ($C \rightarrow C_1$) or a change in the composition within the solid solution region without loss of superconductivity ($B \rightarrow B_1, B_2$).

Clearly, the first approach requires the decomposition to be stopped at some intermediate stage to retain the superconducting matrix. In the second case, the process can be carried out up to attainment of the phase equilibrium. A special type of decomposition is provided by separation of the starting superconducting phase into two solid solutions differing in chemical composition and, correspondingly, in the superconducting properties.³⁹ In this

case, structural similarity of the solid solutions allows a spinodal decomposition and formation of very small non-superconducting domains in the material.

Currently, the systems $R\text{--Ba--Cu--O}$ and $\text{Bi--(Pb)--Sr--Ca--Cu--O}$ are most practically valuable. They have been studied in most detail. Here, we will use them to illustrate some chemical problems concerning the design of superconducting microcomposites (see below).

IV. Phase relations in the existence regions of the superconductors $\text{RBa}_2\text{Cu}_3\text{O}_{7-\delta}$, $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ and $(\text{Bi,Pb})_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+\delta}$

To carry out successful syntheses of ceramic superconducting composites, one should obtain critically important information on the phase relations in the corresponding chemical systems, on the stability regions of the superconducting phases, and on the dependence of the superconducting properties (usually, T_c) on the chemical composition.

The $R\text{--Ba--Cu--O}$ systems containing rare-earth elements of small radii ($R = \text{Y, Dy, Ho, Er, Tm, Yb}$) form stoichiometric (with respect to cations) phases $\text{RBa}_2\text{Cu}_3\text{O}_{7-\delta}$ (R123).^{39–41} The highest superconducting transition temperatures (90–93 K) correspond to some non-stoichiometry with respect to oxygen ($\delta \approx 0\text{--}0.1$), which is usually achieved by annealing at moderate temperatures in oxygen. The Y123 phase has been studied in most detail. In the subsolidus region of the phase diagram ($\sim 900^\circ\text{C}$) in air the Y123 phase is in equilibrium with BaCuO_2 (011), CuO and Y_2BaCuO_5 (211) (Fig. 3). Raising the temperature causes the appearance of melt in the $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}\text{--BaCuO}_2\text{--CuO}$ field. At $1010\text{--}1020^\circ\text{C}$, the Y123 phase undergoes incongruent decomposition into Y211 and melt and at temperatures above $1100\text{--}1200^\circ\text{C}$ the system consists of Y_2O_3 and melt (Fig. 4).⁴² At lower temperatures (below 900°C and elevated pressure of oxygen), two new superconducting phases, $\text{YBa}_2\text{Cu}_4\text{O}_8$ and $\text{Y}_2\text{Ba}_4\text{Cu}_7\text{O}_{14}$, are formed, while the Y123 phase becomes unstable.⁴⁰ Studies of systems containing other rare-earth elements of the yttrium subgroup showed that in the subsolidus region the R123 phases exist in the same compositional triangles ($\text{BaCuO}_2\text{--CuO--R}_2\text{BaCuO}_5$) as the Y123 phase.^{39–41}

The rare-earth elements with large ionic radii ($\text{La, Nd, Sm, Eu, Gd}$) form solid solutions of the type $\text{R}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z$ (123ss).^{39–41,43} Figure 5 presents the isothermal section of the phase diagram of the Nd--Ba--Cu--O system. The solid solution $\text{Nd}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z$ ($x \approx 0$), which is characterised by the highest T_c , is in equilibrium with BaCuO_2 , CuO , $\text{Nd}_x\text{Ba}_{2-x}\text{CuO}_3$ and

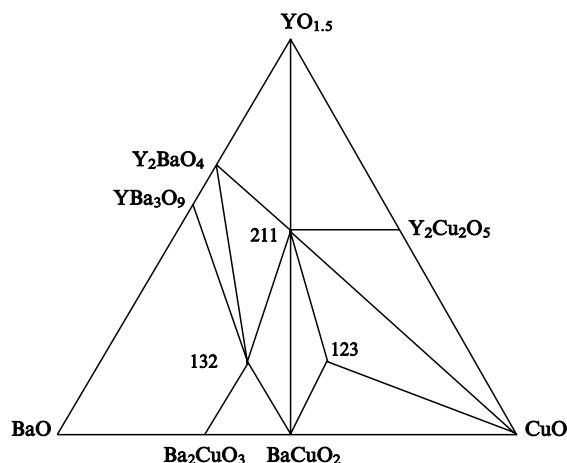


Figure 3. Phase relations in the subsolidus region of the $\text{YO}_{1.5}\text{--BaO--CuO}$ system in air.⁴¹

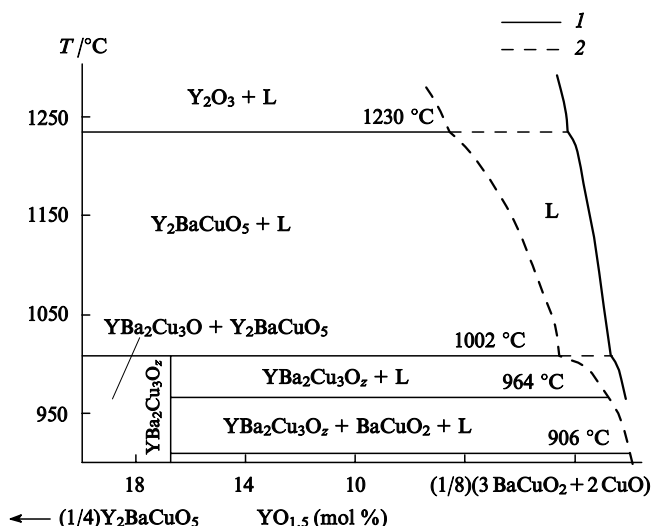


Figure 4. Polythermal section of the phase diagram of the $\text{YO}_{1.5}$ –BaO–CuO system in air.⁴²

Experiment (1) and calculations (2). Hereafter L stands for melt.

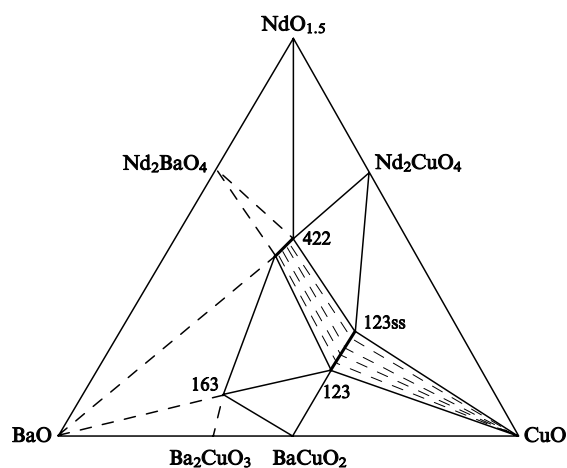


Figure 5. Phase relations in the subsolidus region of the $\text{NdO}_{1.5}$ –BaO–CuO system in air.⁴¹

$\text{Nd}_{4-2x}\text{Ba}_{2+2x}\text{Cu}_{2-x}\text{O}_{10-2x}$ (422). The last-mentioned phase is compositionally analogous to the Y_2BaCuO_5 phase but has another crystal structure.⁴⁴ The polythermal section of the phase diagram of $\text{NdO}_{1.5}$ –BaO–CuO is shown in Fig. 6. The homogeneity region of the $\text{Nd}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z$ phase ($-0.1 < x \leq 1$ at 1000 °C) narrows as the temperature decreases; the process can be accompanied by separation of the solid solution.^{45–47} In the system with $\text{R} = \text{Pr}$ the non-superconducting oxide $\text{Pr}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z$ ($x \approx 0$) coexists with BaCuO_2 , CuO and PrBaO_3 (Fig. 7). No $\text{RBa}_2\text{Cu}_3\text{O}_z$ compounds are formed in the systems with $\text{R} = \text{Ce}$ and Tb .⁴⁰

The quinary(sextenary) system $\text{Bi}(\text{Pb})$ –Sr–Ca–Cu–O exhibits much more complex phase relations. A considerable body of contradictory data on both the exact phase compositions and the phase fields in this system is available.^{40,48} Figure 8 presents the compositional tetrahedron and its section for the quasi-quaternary system Bi_2O_3 –SrO–CaO–CuO.⁴⁹ It is of importance that the phase diagram exhibits extended regions of solid solutions for both the superconducting phases and the phases coexisting with them and that the superconducting transition temperature is strongly dependent on the cationic composition of the phases and on the oxygen content. The

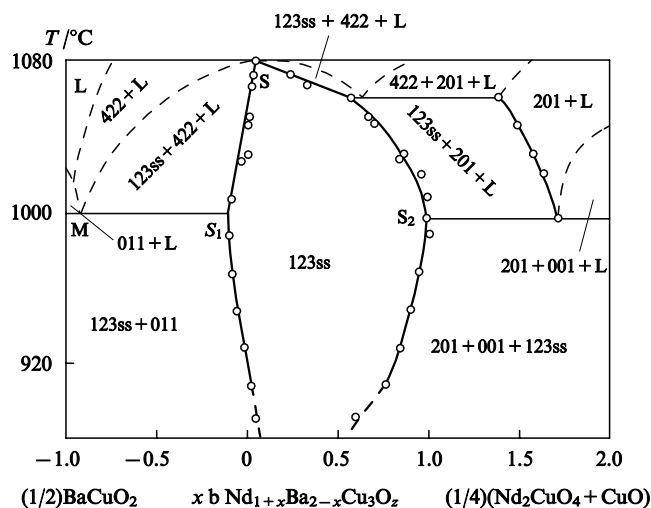


Figure 6. Polythermal section of the phase diagram of the $\text{NdO}_{1.5}$ –BaO–CuO system in air.⁴⁰

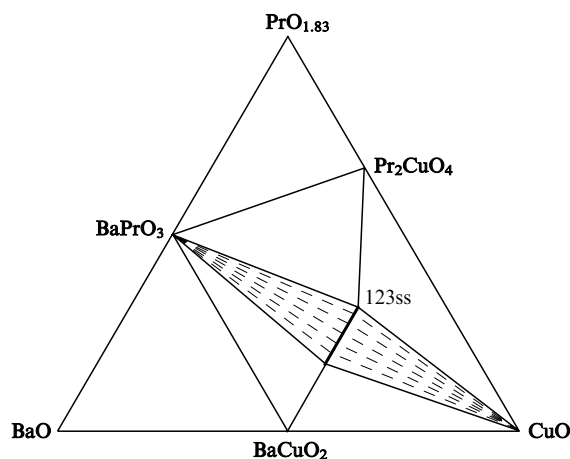


Figure 7. Phase relations in the subsolidus region of the $\text{PrO}_{1.83}$ –BaO–CuO system in air.⁴¹

system contains three superconducting phases, namely, $\text{Bi}_{2+x}\text{Sr}_{2-x}\text{CuO}_{6+\delta}$ ($\text{Bi}2201$ or $\underline{119x5}$, $T_c \approx 20$ K), $\text{Bi}_2\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ ($\text{Bi}2212$, $T_c \approx 90$ K) and $\text{Bi}_2\text{Sr}_2\text{Ca}_2\text{Cu}_3\text{O}_{10+\delta}$ ($\text{Bi}2223$, $T_c \approx 110$ K), which are the first three representatives of the homologous series $\text{Bi}_2\text{Sr}_2\text{Ca}_{n-1}\text{Cu}_n\text{O}_{6+2n+\delta}$. The second and third homologues are of practical value. In $\text{Bi}2223$, bismuth is, as a rule, partially replaced by lead.⁴⁹ The formation of the $\text{Bi}2223$ phase can also be significantly improved upon partial replacement of Bi by V, Nd, Ta (see Ref. 50) or Ga.⁵¹ It is more appropriate to write the formula for the second homologue ($n = 2$) as $\text{Bi}_{2+x}\text{Sr}_{2-x-y}\text{Ca}_{1+y-r}\text{Cu}_{2-r}\text{O}_{8+\delta}$.^{48,49,52–54} This compound is characterised by a relatively broad homogeneity region with respect to the strontium : calcium ratio (Fig. 9), which, according to different authors, can vary from 2.2 : 0.8 to 1.2 : 1.8.^{48,55,56} Strontium can be to some extent ($x \leq 0.2$) replaced by bismuth, while the content of copper can somewhat decrease due to the formation of stacking faults (sublayers of the first homologue). The third homologue has a narrower homogeneity region with respect to the strontium : calcium ratio (from 1.9 : 2.1 to 2 : 2); the content of bismuth (or bismuth and lead together) can exceed the stoichiometric value by $\sim 20\%$.⁴⁹

In air, the phase of the second homologue is stable from ~ 600 °C to the melting temperature (850 – 885 °C depending on the composition).^{48,57–63} The highest melting temperature refers to a composition similar to the stoichiometric composition

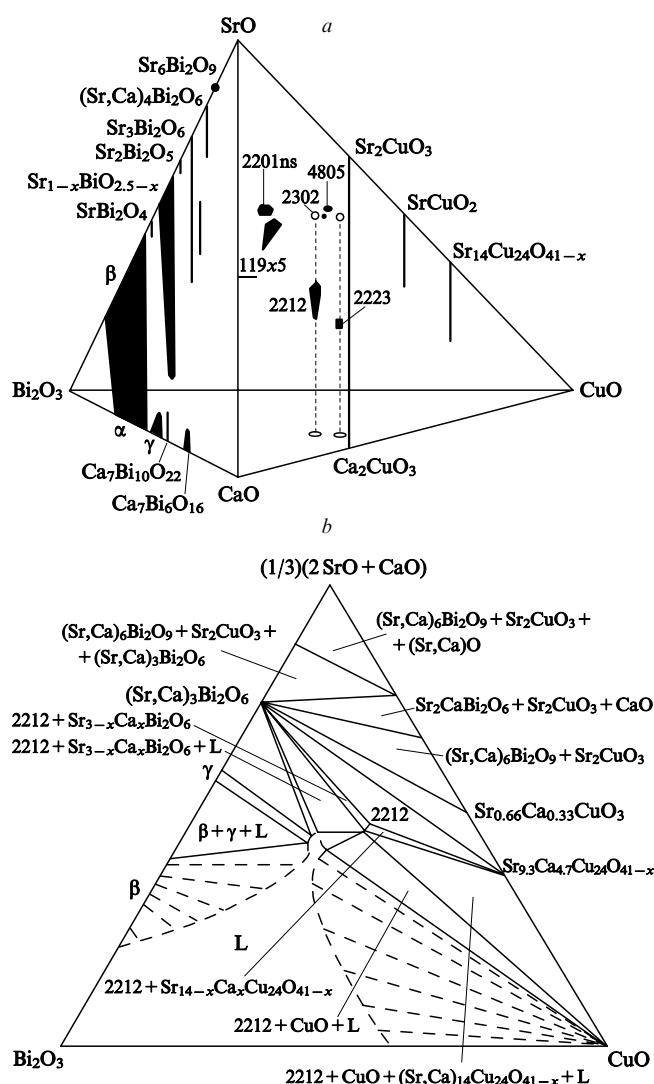


Figure 8. Phase relations in the Bi_2O_3 – SrO – CaO – CuO system in air at 850°C .⁴⁹

Compounds in the quaternary system (a) and the section of the compositional tetrahedron by the plane passing through the $(1/3)(2\text{SrO} + \text{CaO})$ – Bi_2O_3 – CuO points (b). The phases in the ternary and quaternary systems are denoted using their cationic compositions ($\text{Bi}:\text{Sr}:\text{Ca}:\text{Cu}$).

Bi2212. Melting and crystallisation processes play a significant role in the preparation of both bulk samples of HTSC (Ref. 64) and sheathed wires (tapes) possessing high critical current densities.⁶⁵ The melting diagram along the Bi2201 – Bi2223 compositional line is schematically shown in Fig. 10.

A great body of information on melting of the Bi2212 phase is available (see, e.g., Refs 48, 59, 63, 66–71). Often, the results obtained by different authors were essentially different. The most plausible order of processes is as follows. In air, Bi2212 undergoes peritectic decomposition into two oxides, $(\text{Sr,Ca})_{4-y}\text{Bi}_2\text{O}_z$ and $(\text{Sr,Ca})\text{CuO}_2$, and melt.^{66, 72, 73} This is accompanied by release of oxygen, which corresponds to reduction of the oxygen content.⁶³ Storage of the melt over a period of 1 h at a temperature which only slightly exceeds the melting temperature leads to crystallisation of yet another phase, Bi2201 .⁶⁷ Further increase in the temperature in the range 900 – 1000°C causes disappearance of the bismuth-containing phases and the following sequence of transformation of the cuprate phase^{66, 68, 72}

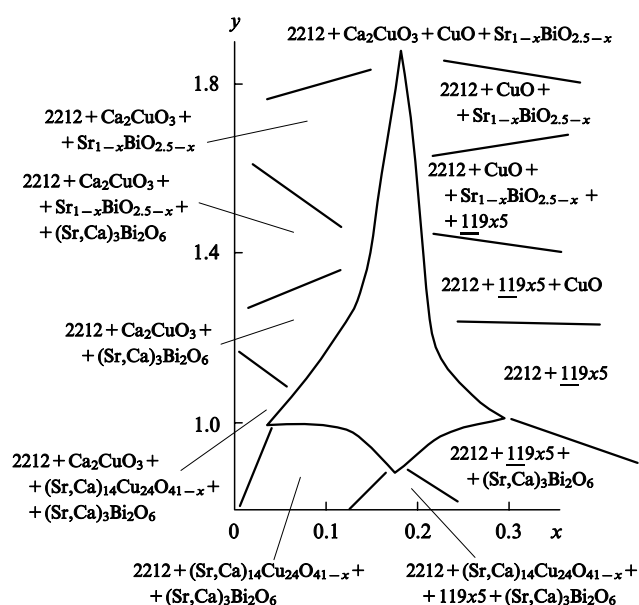


Figure 9. Homogeneity region of the Bi2212 phase for the $\text{Bi}_x\text{Sr}_{3-y}\text{Ca}_y\text{Cu}_2\text{O}_{8+\delta}$ composition in air at 800°C .⁴⁹

At temperatures above 1100°C the system consists of a melt only.^{66, 72}

The Bi2223 phase exists in the narrower temperature interval (840 – 890°C). Doping with lead shifts this temperature range towards lower temperatures.^{49, 52, 74} The extent of bismuth replacement by lead depends on the partial pressure of oxygen and can reach 30% for Bi2212 and 15%–18% for Bi2223 .^{48, 49, 52} In air, the $(\text{Bi,Pb})2223$ phase doped with lead oxide melts incongruently at temperatures above 870°C to give strontium–calcium cuprates of different compositions (the melting temperature reducing as the pressure of oxygen decreases).^{52, 75, 76}

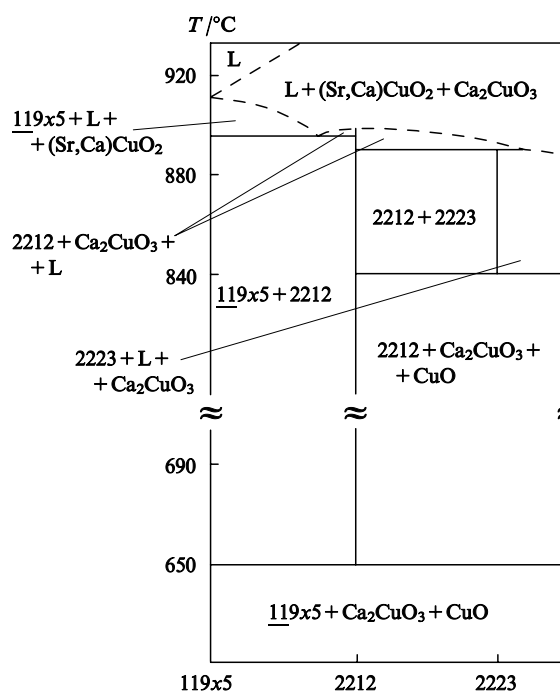


Figure 10. Polythermal section of the phase diagram of the Bi_2O_3 – SrO – CaO – CuO system along the Bi2201 – Bi2223 line.⁴⁹

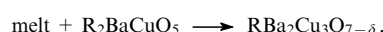
Cooling of the melt causes crystallisation of the second homologue as the major product. This significantly hampers the use of the melt technique in obtaining the third homologue, which is of the greatest interest.

In the temperature range 800–870 °C in air, the Bi2212 phase can be in equilibrium with CaO, CuO, (Sr,Ca)₁₄Cu₂₄O₄₁, Bi_{2.2}(Sr,Ca)_{1.8}CuO_{6+δ}, (Sr,Ca)_{1-δ}BiO_z, (Ca,Sr)₂CuO₃, (Sr,Ca)_{4-y}Bi₂O_z, Bi₄(Sr,Ca)₈Cu₅O_z, Bi₂Sr₂CuO₆, Bi2223 and melt.^{49,52,77–81} Other phases in this system were also found. These are (Sr,Ca)₃Bi₂O₆,⁴⁹ Sr₉Bi₁₁O_{25.5},⁷⁷ Ca_{0.86}Sr_{0.14}CuO₂,⁸⁰ (Sr,Ca)CuO₂ and (Sr,Ca)₆Bi₂O₁₁,⁸¹ which probably also coexist with the Bi2212 phase under particular conditions. Studies of the lead-doped system revealed^{82,83} that at 810–820 °C and $p_{O_2} = 0.075$ the (Bi,Pb)2223 phase is in equilibrium with CaO, CuO, (Bi,Pb)2212, (Sr,Ca)₁₄Cu₂₄O₄₁, (Ca,Sr)₂CuO₃, (Bi,Pb)_{2.2}(Sr,Ca)_{1.8}CuO_{6+δ}, (Bi,Pb)₂Sr₂CuO_{6-δ}, (Sr,Ca)_{4-y}.Bi₂O_z, (Sr,Ca)CuO₂, Ca_{0.86}Sr_{0.14}CuO₂, (Ca,Sr)₂PbO₄ and (Pb,Bi)₃Sr₂Ca₂CuO_z.

Thus, the generic (with respect to the superconducting phases) chemical systems contain a large number of thermodynamically compatible phases, which can be used as inclusions in the superconducting composites.

V. Microcomposites based on RBa₂Cu₃O_{7-δ}

The first method of preparation of composites can be well illustrated by taking the system RBa₂Cu₃O_{7-δ}–R₂BaCuO₅ as an example. Microcomposites are synthesised by crystallising the superconducting phase from a peritectic melt^{10,39} containing micrometre-sized particles of the R₂BaCuO₅ phase, which is partially consumed for the formation of the R123 phase in the reaction



while the remaining fraction of R₂BaCuO₅ forms inclusions in the superconducting matrix. Depending on the synthetic procedure and composition of the starting materials, the average size of the inclusion particles can vary from several fractions of a micrometre to tens of micrometres. The smallest inclusions are prepared by melting a mixture of RBa₂Cu₃O_{7-δ} with highly dispersed R₂BaCuO₅ and subsequent crystallisation of the melt.^{84,85} The R₂BaCuO₅ particles can be trapped with ease by the growing RBa₂Cu₃O_{7-δ} crystals, which leads to a uniform distribution of these particles in the material. However, sometimes (in the case of, e.g., doping with platinum) the distribution of Y₂BaCuO₅ particles over the volume of the Y123 crystal is nonuniform, which is described and explained using the pushing–trapping model.^{86–89}

Coarse-grained, textured composite samples obtained by the melt processing technique and containing 0.1–0.4 mole of R₂BaCuO₅ per mole of RBa₂Cu₃O_{7-δ} are characterised by the critical current densities of the order of 10⁴–10⁵ A cm⁻² at 77 K.^{10,15,90–93} Studies of the dependence of the pinning force (F_p) on the magnetic field (B)

$$F_p(B, T) = J_c(B, T) B$$

revealed a dominant role of the magnetic flux pinning by inclusions (or inclusion–matrix interface).^{94–96} However, the role of R₂BaCuO₅ is not restricted to the pinning effect, namely, the presence of the second phase favours a complete peritectic crystallisation of the superconducting phase.

Introduction of (micro)additives into the R–Ba–Cu–O system can lead to a further increase in J_c . In most cases, this approach results in R123–R₂BaCuO₅–alien phase composites. The efficiency of pinning can be due to the effects of both inclusion phases. Often, it is assumed that this parameter is mainly due to the dopant effect on the size of inclusions of the main non-superconducting phase R₂BaCuO₅. Doping with Pt(PtO₂), CeO₂ and SnO₂ (usually, of the order of a per cent) can cause a substantial increase in the degree of dispersion of the R₂BaCuO₅ phase.^{97–108} Introduction of platinum leads to a decrease in the

energy of the R₂BaCuO₅–liquid interface, thus facilitating nucleation and slowing down the growth of the R₂BaCuO₅ phase. The effect of the cerium and tin oxides is explained by heterogeneous nucleation of R₂BaCuO₅ on microinclusions of products of the reactions of these additives with the melt.⁹⁸

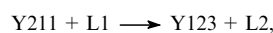
The platinum-doped system contains the following accompanying (and, possibly, thermodynamically compatible with Y123) phases: Ba₄CuPt₂O₉, Y₂Ba₃Cu₂PtO₁₀ and Y₂Ba₂CuPtO₈, which are more likely treated as undesired inclusions.^{100,109,110} Introduction of extra impurity (alumina) causes the formation of large (tens of micrometres in size) Ba₃YAl₂PtO_{9-δ} inclusions.¹¹¹ The addition of SnO₂ results in BaSnO₃,¹¹² YBa₂SnO_{5.5} (see Ref. 113) and YBa₃Sn_{2-x}Cu_xO_{9-δ}.^{101,114} The cubic double perovskite YBa₂SnO_{5.5} phase seems to be the most stable and introduction of platinum or cerium into the system causes the formation of solid solutions Y₂Ba₅(Sn_{3-y-x}Cu_yPt_x)₃O_z (see Ref. 115) and Ba₂(Y_{2/3-x}Cu_x)·(Ce,Sn)_{4/3}O_{6-δ}.¹⁰¹ Tin and platinum are insoluble in Y123, whereas cerium occupies some sites in the Y123 lattice.¹⁰¹

Particular emphasis should be placed on the doping of the Y123 system with oxides of ²³⁵U.^{116–118} In these cases, submicrometre-sized inclusions of the compositions Ba(U_{0.6}Y_{0.4})O₃ or Ba₂Y(U_{0.6}Pt_{0.4})O₈ (in the presence of platinum) are formed in the superconductor crystallites and the corresponding J_c values somewhat increase. Neutron irradiation causes fission of ²³⁵U nuclei and the appearance of numerous tracks in the superconductor matrix, which leads to a subsequent manifold increase in J_c due to the pinning of magnetic vortices to the new defects. This technique was used for preparation of a bulk material characterised by a record J_c value ($\approx 3 \times 10^5$ A cm⁻² at 77 K).¹¹⁷

Reactions of ceria, zirconia and hafnia with R123 result in stable phases (BaCeO₃, BaZrO₃ and BaHfO₃, respectively).^{101,112,119–121} In the case of melt growth of the superconducting phase, particles of these phases are pushed by the growing R123 crystal and segregated in the intercrystalline space, thus impeding the flow of the superconducting current between crystallites. These phases are inert and can therefore be used as barrier materials for crucibles, substrates and coatings in the synthesis of superconductors.^{122–124}

The estimates of thermodynamic parameters¹²³ indicated that the Y123 phase cannot be treated as being in equilibrium in the mixtures with TiO₂, ZrO₂, HfO₂ and CeO₂. This disequilibrium manifests itself in the chemical reaction, which proceeds on heat treatment of the mixture of the corresponding dioxide and Y123 and results in Y211, CuO and compounds of the starting dioxide with (mainly) barium oxide.

Among all metals, only silver is thermodynamically compatible with R123. In the presence of silver the melt crystallisation temperature of Y123 reduces down to 970 °C, while the overall process is described by a monotectic-peritectic reaction



where L1 is the BaO- and CuO-rich liquid and L2 is the Ag-rich liquid.¹²⁵ Crystallisation from oxide melt is accompanied by trapping of silver in the form of spherical or disk-like particles.^{125–128} The introduction of silver improves the mechanical strength of and precludes crack formation in the ceramics.

The second method of preparation of microcomposites is based on the decomposition of a solid solution in the R–Ba–Cu–O system. It can be exemplified by the synthesis of Nd_{1+x}Ba_{2-x}Cu₃O_z ceramics.^{39,129–133} Under particular heat treatment conditions (hypothetically, at a rather low temperature), a solid solution ($x \approx 0$) is separated into two solid phases. One phase is characterised by a high extent of replacement of neodymium by barium and low T_c while the other phase is characterised by a lower extent of replacement and higher T_c (> 90 K). The first phase forms nanometre-sized inclusions in the matrix of the second phase. A feature of such superconductors is the so-called peak effect (J_c first increases with an increase in the magnetic field and then decreases).¹³⁴ This effect is associated with

magnetic field induced destruction of superconductivity in nanodomains, which makes these domains efficient pinning centres at intermediate magnetic fields. The peak effect was also observed in $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$ ($\delta > 0$);^{134, 135} however, it was treated as a consequence of phase separation accompanied by the appearance of nanodomains enriched with and depleted of oxygen and, correspondingly, characterised by different superconducting transition temperatures.

The dependence of the pinning force in $\text{Nd}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z$ on the reduced magnetic field B/B_{ir} (B_{ir} is the irreversibility field induction) passes through a maximum at $B/B_{\text{ir}} = 0.4-0.5$, which indicates pinning of magnetic vortices to small regions with weakened superconductivity.^{95, 96, 136} For the composites $\text{R}\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}-\text{R}_2\text{BaCuO}_5$ ($\text{R} = \text{Y}, \text{Yb}$; see Ref. 94), the maximum value of the B/B_{ir} ratio is nearly halved and corresponds to dominant pinning at the interface between the superconducting matrix and inclusions of the second phase. As to the $\text{Nd}_{1+x}\text{Ba}_{2-x}\text{Cu}_3\text{O}_z-\text{Nd}_4\text{Ba}_2\text{Cu}_2\text{O}_{10}$ composite, both interface pinning and pinning to small regions with weakened superconductivity are possible.¹³⁷

Simultaneous introduction of several rare-earth elements into yttrium lattice sites is thought to have considerable promise. The $J_c(B)$ plots constructed for the superconductors $(\text{Nd}, \text{Eu}, \text{Gd})\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}$ and $(\text{Nd}, \text{Sm}, \text{Gd})\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}$ exhibit a pronounced peak effect, so that the maximum critical current density reaches a value of 10^5 A cm^{-2} at a magnetic field of about 2 T at 77 K.^{138, 139} It was established that the superconductor crystallites are characterised by fluctuations of the composition (variation of the rare-earth element : barium ratio) in the regions from several to tens of nanometres in diameter. The smaller the 'fluctuation' domain size, the more pronounced the peak effect in the materials. Besides, the character of the inclusion phase, R_2BaCuO_5 , also changes. Melting of $(\text{Nd}, \text{Sm}, \text{Gd})\text{Ba}_2\text{Cu}_3\text{O}_{7-\delta}$ is accompanied by redistribution of the rare-earth elements between the solid and liquid phases in such a way that the composition of the newly formed solid phase approaches $\text{Gd}_2\text{BaCuO}_5$. In the course of subsequent crystallisation the second phase of the composite $(\text{Nd}, \text{Sm}, \text{Gd})_2\text{BaCuO}_5$ first of all reacts with the melt. As a result, the end product contains a large number of small $\text{Gd}_2\text{BaCuO}_5$ inclusions, which are much smaller than the grain size of the second phase. Such a dispersion of the second phase causes an increase in the critical current density at zero magnetic field.

More than a twofold increase in J_c at 77 K was found in the large-domain composites $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}-\text{Y}_2\text{BaCuO}_5$ doped with microscopic amounts (hundredth fractions of a per cent) of zinc oxide.¹⁴⁰⁻¹⁴² It is assumed that the zinc ions replace copper in the crystal lattice and create nanoscale domains with destroyed superconductivity, which act as efficient pinning centres. This is indirectly confirmed by the shift of the maximum in the field dependence $F_p(B/B_{\text{ir}})$ from $B/B_{\text{ir}} = 0.31$ to 0.41 after relevant doping.

VI. Microcomposites based on phases of the Bi-(Pb)-Sr-Ca-Cu-O system

The system Bi-(Pb)-Sr-Ca-Cu-O is characterised by equilibrium between the superconducting phases and a large number of other phases and by extended regions of solid solutions for the superconducting phases. This allows a wider use of both methods of synthesis of composites (see Section III).

Cooling of a peritectic melt permits preparation of $\text{Bi}(\text{Pb})2212-\text{Ca}_2\text{CuO}_3$ (10 mol.%–15 mol.%) composites with the Ca_2CuO_3 inclusions (of size of several micrometres) uniformly distributed in the $\text{Bi}(\text{Pb})2212$ phase. These composites exhibit an increased (by several times) critical current density at $T \geq 20 \text{ K}$.^{143, 144} Magneto-optical studies revealed pinning of magnetic vortices to the Ca_2CuO_3 particles.¹⁴⁵ A considerable increase in J_c within grains of sintered $\text{Bi}2223-\text{Ca}_2\text{CuO}_3$ ceramics was also reported.¹⁴⁶ Single crystals of $\text{Bi}2212$ containing inclu-

sions of CuO (elongated particles 1 μm in diameter and 3–4 μm long) were obtained by melt-solution crystallisation from KCl .¹⁴⁷

Majewski *et al.*¹⁴⁸⁻¹⁵⁰ reported detailed phase diagram studies concerning the possibility of partial decomposition of the solid solution. If a solid solution of a particular composition is heat treated at a lower or, *vice versa*, a higher temperature, it loses homogeneity and submicrometre-sized inclusions of products are formed in the matrix of the starting compound. This approach was used for the synthesis of ceramic $\text{Bi}2212$ samples containing inclusions of the $\text{Bi}2201$, $\text{Sr}_3\text{Bi}_2\text{O}_6$, $\text{Sr}_{14}\text{Cu}_{24}\text{O}_{41}$ and Ca_2CuO_3 phases (see Refs 148 and 149) and of $\text{Bi}2223$ samples containing inclusions of the $\text{Bi}2212$, Ca_2CuO_3 and $(\text{Sr}, \text{Ca})\text{CuO}_2$ phases.¹⁵⁰ A scheme illustrating the trajectory of the figurative point in the phase diagram during heat treatment is shown in Fig. 11. The J_c value inside of the grains of the samples heat treated for a restricted time increases by three to six times at 30 K. Prolonged annealing causes coarsening of the inclusions and a decrease in the critical current density. It was shown¹⁵¹ that annealing of $\text{Bi}2212$ at 550 °C results in precipitation of smaller particles of size 0.02 to 0.1 μm and in greater nonuniformity of the distribution of the components in ceramics.

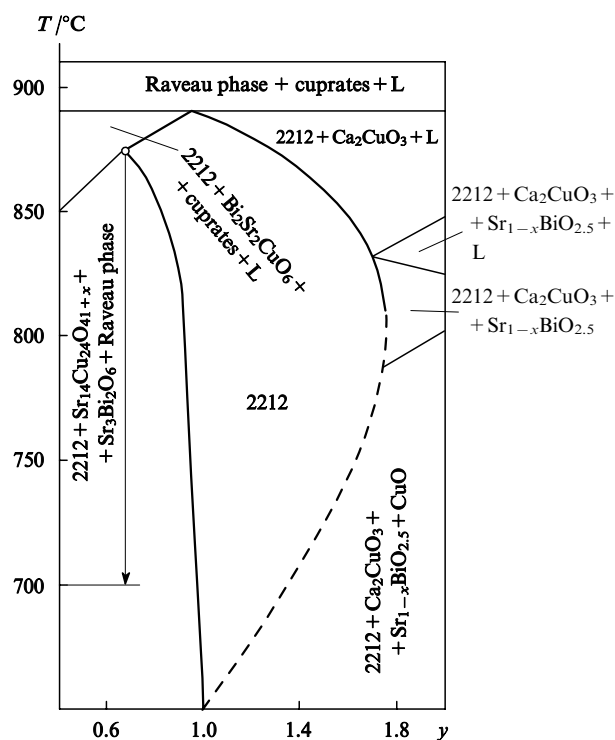


Figure 11. Section of the phase diagram of the Bi-Sr-Ca-Cu-O system along the $\text{Bi}_{2.18}\text{Sr}_{3-y}\text{Ca}_y\text{Cu}_2\text{O}_{8+\delta}$ composition.¹⁴⁹

Shown are the homogeneity regions of the $\text{Bi}2212$ (2212) phase and the trajectory of the figurative point of the system upon heat treatment (phase-forming annealing at 875 °C–low-temperature annealing at 700 °C).

Separation of the solid solution was found and studied in detail taking $\text{Bi}_{2-x}\text{Pb}_x\text{Sr}_2\text{CaCu}_2\text{O}_{8+\delta}$ ($x > 0.4$) samples as examples.^{152, 153} Melt processed single crystals and coarse-grained ceramics exhibited the formation of submicrometre-sized domains (in the form of stripes or closed regions), which were both depleted of and rich with lead. Such samples are characterised by increased irreversibility fields and J_c .

A study on the decomposition of $\text{Bi}2212$ solid solutions characterised by partial replacement of calcium or strontium by rare-earth elements *via* annealing at a reduced temperature has been reported.¹⁵⁴ Precipitation of the second phases was observed

only for the early rare-earth elements ($R = \text{La, Pr, Nd}$). The Bi2212 phase with $R = \text{Pr}$ decomposed much faster than other phases. This was associated with the fact that the starting phase contained praseodymium in the Pr^{3+} state, while annealing in air caused its oxidation to Pr^{4+} with a smaller ionic radius and subsequent destabilisation of the Bi2212 phase.

VII. Microcomposites based on phases of the Bi–(Pb)–Sr–Ca–Cu–A–O system

The best way of preparing superconducting materials with good intergranular contacts is to use melt techniques. However, under these conditions the generic second phases form rather large inclusions (of size greater than $1\ \mu\text{m}$). The reason is that in the melt all components of the system are present in comparable amounts. To improve the efficiency of pinning, one should make the inclusions smaller. This can be achieved by introducing some alien phases containing an extra component A into the system.

Multicomponent systems are extremely complex objects. Because of this, ‘engineering’ methods of doping of the generic system often fail. In most cases the introduction of some high-melting oxide additives is accompanied by partial decomposition of the superconducting phase and by the formation of the accompanying complex oxide phases.²⁸

The authors of this review believe that a consistent method for solving the problem of design of microcomposites based on superconducting cuprates must include:

- searching for new components, which do not destroy the superconductivity in the matrix material;
- establishment of phases which contain the new components and are chemically inert towards the superconductor; and
- elaboration of methods for synthesis of materials containing fine-grained, uniformly distributed inclusions of the above-mentioned phases.

The superconducting phase, which acts as the matrix, must be characterised by a rather high T_c value. The optimum compositions and the heat treatment regimes of such phases have been reported.^{48,49} In the search for various dopants it can appear that the simplest way is to retain the composition of the generic system because of the minimum solubility of the new component in the superconducting phase. As mentioned above, the chemical inertness of the system is best achieved if its components are thermodynamically compatible, *i.e.*, if the impurity and the matrix superconducting phase are in equilibrium at least at such values of the external parameters (temperature and the partial pressure of oxygen) that correspond to the conditions for the synthesis of the composite. Therefore, determination of the compositions of the equilibrium phases is of prime importance. The next stage involves preparation of the composite containing inclusions of the equilibrium phases. Here, one should take into account the effects related to the interface interactions, such as agglomeration and recrystallisation of the particles of the inclusion phase and their effect on the nucleation and growth of crystallites of the superconducting matrix. Besides, in the text below we will show that the presence of the equilibrium phase can change the phase relations in the system in the region above the solidus and, correspondingly, the crystallisation mechanism of the matrix phase.

The thermodynamic compatibility of silver with the superconducting phases in the Bi–(Pb)–Sr–Ca–Cu–O and Y–Ba–Cu–O systems has been established reliably.^{63,155–158} This is of crucial importance for fabrication of flexible sheathed HTSC wires and tapes.^{5,158} The solubility of silver in the solid phases Bi2212 and (Bi,Pb)2223 is at most 1% while its solubility in the corresponding oxide melts is nearly 5%, which leads to reduction of the melting temperature of the superconducting ceramics by $20–30\ ^\circ\text{C}$.^{82,157,159} It was found that the peritectic melt contains the same phases as the melt containing no silver (see Section IV). Because of doping, the melting temperature of metallic silver in the composite decreases by $\sim 10\ ^\circ\text{C}$. Gold also seems to be compatible with the above-mentioned phases.^{6,160–163}

Metallic platinum slowly reacts with the melts of the ceramic matrix and forms complex oxide phases containing alkaline-earth elements and copper along with platinum.^{163,164}

The compositions and properties of the microcomposites based on the superconducting Bi2212 matrix are listed in Table 1.

Apparently, MgO is the only individual oxide which possesses a sufficient chemical inertness towards the superconducting phases. Nevertheless, it was shown^{165,166} that the Bi2212 phase is in equilibrium with the solid solution $\text{Mg}_{1-x}\text{Cu}_x\text{O}$ ($x \approx 0.1$). Pure fine-grained magnesia causes decomposition of the superconductor phase due to partial removal of copper, while coarse-grained MgO does not readily react with either the solid Bi2212 phase or its melt. The solubility of MgO in Bi2212 is at most 1 at.%, so the T_c value of the superconducting matrix remains virtually unchanged.

The introduction of other chemical elements into the Bi–(Pb)–Sr–Ca–Cu–O system results in the formation of complex oxides. Alumina, gallium sesquioxide and oxides of rare-earth elements form two compatible phases with the oxides of the generic system each,^{164,168–172} while oxides of the other elements listed in Table 1 form one compatible phase each.^{28,72,167,172,173,176–182}

In spite of a wide variety of chemical compositions of the Bi2212-compatible complex oxides, some general trends were revealed. At the phase equilibrium, the components of the coexisting phases have the same chemical potentials. To a first approximation the oxide systems can be characterised by the chemical potential of the common component (O^{2-} anion), which reflects the acid–base properties of the system (reduced potential corresponds to an acid medium while increased potential corresponds to a basic medium).¹⁸³ The compatible phase must be stable in a range of chemical potentials of the O^{2-} anion which overlaps with the chemical potential range corresponding to the stability of the superconducting phase. Thus, the strongest acid oxides will form compounds with the stronger basic oxides of the generic system in order to increase the chemical potential of O^{2-} to a value corresponding to the lower boundary of the stability of the Bi2212 phase. Analogously, the basic oxides will form compounds with the stronger acid oxides. Clearly, the interaction between the strongest acid oxides and the strongest basic oxides is most energetically favourable. One should also take into account that the acidity of the oxide increases with increasing oxidation state and decreasing ionic radius of the element.

Analysis of general trends of changes in the compositions of complex oxides (see Table 1) suggests that the oxides characterised by high oxidation state of the corresponding element ($\geq +4$) and, hence, by relatively high acidity usually form compounds with strontium oxide, which is the strongest basic oxide in the generic system. Reduction of the acidity of the extra oxides formed by the triply charged cations leads to the formation of calcium, bismuth and copper oxide constituents of the non-superconducting complex oxide along with strontium oxide. In the case of rare-earth elements with the largest ionic radii, the composition of the complex oxide cannot include strontium oxide (see Table 1), which is consistent with the lowest acidities of the oxides of rare-earth elements. From the standpoint of the acidity criterion, MgO is compatible with the Bi2212 phase. Barium oxide (the strongest basic oxide) forms a compound with bismuth oxide (the strongest acid oxide in the generic system).

Sometimes, the Bi2212 phase contains a minor amount of dopant (less than 1 at.% with respect to all cations), which allows the rather high superconducting transition temperature of the composite to be retained (see Table 1). Small amounts of gallium sesquioxide and titania can be dissolved in the solid phase of the superconductor, which reduces T_c by several degrees. The values listed (~ 2 at.%) correspond to the lower bounds of the solubilities of these oxides in the Bi2212 phase, which is in equilibrium with the non-superconducting oxide phase. It is assumed that titanium occupies sites in the copper sublattice¹⁸⁴ while gallium can replace both copper and bismuth.^{164,171,185,186} It is also

Table 1. Compositions and properties of microcomposites with the Bi2212 superconducting matrix.

Dopant A	A-Containing phase compatible with Bi2212			Grain size of A-containing phase in composite / μm	Content of A in Bi2212 (at. %) (with respect to all cations)	T_c /K	R^a	Ref.
	composition	crystal system	structure type					
Mg	$\text{Mg}_{1-x}\text{Cu}_x\text{O}$, $x = 0.08 - 0.15$	cubic	NaCl	0.3 – 1.0	< 1	93	0.021	72, 165, 166
Ba	$(\text{Ba}, \text{Sr}, \text{Ca})\text{BiO}_3$	"	perovskite	submicrometre region	< 2	—	—	167
Al	$\text{Sr}_{3-x}\text{Ca}_x\text{Al}_2\text{O}_6$, $x = 1,^{162} 1.3$ (see Ref. 169)	"	$\text{Sr}_3\text{Al}_2\text{O}_6$	2 – 3	< 0.5	90	0.037	162, 164, 168, 169
Ga	$\text{BiSr}_{1.5}\text{Ca}_{0.5}\text{Al}_2\text{O}_6$	tetragonal	—	3	—	90	0.016	168 – 170
	$\text{Bi}_{0.2}\text{SrCa}_{0.8}\text{Ga}_2\text{O}_z$	orthorhombic	—	~ 10	2 ^b	84	0.004	171
	$\text{Bi}_{1.7}\text{Sr}_{2.3}\text{Ca}_{0.6}\text{Cu}_{1.6}\text{Ga}_{0.4}\text{O}_z$	tetragonal	$\text{Bi}_4\text{Sr}_8\text{Cu}_5\text{O}_z$	~ 10	—	—	—	171
In	$\text{Sr}_{1-x}\text{Ca}_x\text{In}_2\text{O}_4$, $x = 0.5 - 0.6$	orthorhombic	CaFe_2O_4	1×5^c	< 0.7	91	0.038	172
Sc	$\text{Sr}_{1.9}\text{Ca}_{0.1}\text{ScBiO}_6$	cubic	double perovskite	0.3	< 0.7	89	—	173
Lu	$\text{Sr}_2\text{LuBiO}_6$	monoclinic	the same	$1 - 5^d$	5 ^e	77	—	174, 175
	$(\text{Ca}, \text{Lu})_{1-x}\text{CuO}_2$, $x \approx 0.2$	orthorhombic	$\text{Ca}_{0.828}\text{CuO}_2$	1 – 5	5	77	—	174, 175
	$\text{Sr}_2\text{YbBiO}_6$	monoclinic	double perovskite	1 – 5	6.3 ^e	57	—	174, 175
Yb	$(\text{Ca}, \text{Yb})_{1-x}\text{CuO}_2$, $x \approx 0.2$	orthorhombic	$\text{Ca}_{0.828}\text{CuO}_2$	1 – 5	4.1 ^b	87	—	174, 175
	$\text{Sr}_2\text{TmBiO}_6$	monoclinic	double perovskite	1 – 5	8 ^e	52	—	174, 175
	$(\text{Ca}, \text{Tm})_{1-x}\text{CuO}_2$, $x \approx 0.2$	orthorhombic	$\text{Ca}_{0.828}\text{CuO}_2$	1 – 5	8 ^e	52	—	174, 175
Ti	SrTiO_3	cubic	perovskite	0.2	$\sim 2^b$	76	—	176
Zr	SrZrO_3	orthorhombic	"	0.2	< 0.7	93	0.092 ^f	177 – 179
Hf	SrHfO_3	cubic	"	0.2	< 0.7	93	—	28, 178
Sn	$\text{Sr}_{1-x}\text{Ca}_x\text{SnO}_3$, $x = 0.1 - 0.15$	"	"	0.3	< 0.5	92	0.074	180
Sb	$\text{Bi}_4\text{Sr}_4\text{Ca}_2\text{SbO}_x$	monoclinic	—	—	0	87	—	181
S	SrSO_4	orthorhombic	—	> 1	< 0.7	91	—	182

^a $R = \frac{J_c(60 \text{ K}, 10 \text{ mT})}{J_c(5 \text{ K}, 1 \text{ T})}$. This parameter characterises the average pinning energy of magnetic vortices.²⁸ For most composites, the R values increase (by up to hundreds per cent) compared to those of single-phase

superconductors ($R = 0.01$ for bulk samples of the pure Bi2212 phase; $R = 0.03$ for silver-sheathed tapes).²⁸ ^b Corresponds to the lower bound of the solubility in equilibrium with the A-containing phase. ^c Rod-like grains. ^d For Bi2212 – $\text{Sr}_2\text{LnBiO}_6$ composites. ^e Average values for the equilibrium with $\text{Sr}_2\text{LnBiO}_6$. ^f For silver-sheathed tape.

known that rare-earth elements can partially or completely replace calcium in Bi2212.^{187–189} Under particular conditions the equilibrium with the complex oxides containing the late rare-earth elements permits the content of the rare-earth elements in the Bi2212 phase to be limited, thus retaining the high T_c values (e.g., 87 K for the Bi2212–Sr₂YbBiO₆ composite).¹⁷⁴

Figure 12 presents the plots of the critical current density vs. the magnetic field induction for the single-phase Bi2212 sample and the Bi2212–SrZrO₃ composite in the form of silver-sheathed tapes.¹⁷⁹ At low temperature (5 K), the J_c values for both samples are comparable. It is assumed⁹¹ that under these conditions the critical current is governed by the pinning to a large number of small defects (e.g., atomic vacancies) with low pinning energies. Raising the temperature to 60 K causes a dramatic decrease in the efficiency of such pinning centres. At this temperature, the composite is characterised by higher J_c compared to the single-phase Bi2212 sample, the difference being increased with increasing magnetic field induction. Apparently, this indicates that inclusions of the second phase create new high-energy pinning centres, which can efficiently operate at a temperature of nearly 60 K.

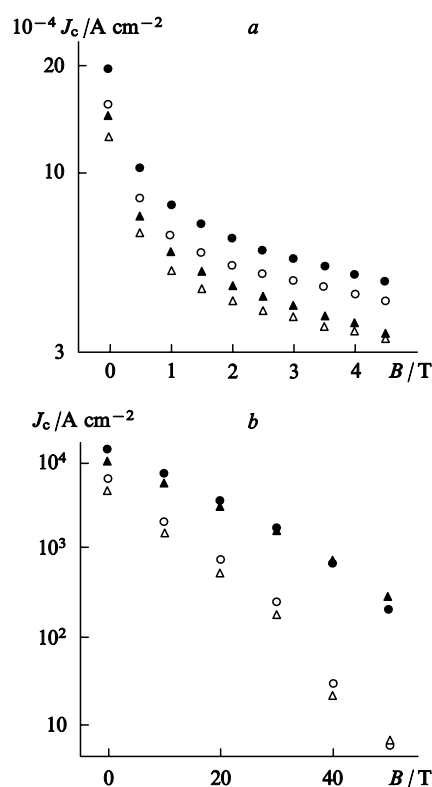


Figure 12. Critical current density vs. magnetic field induction for the superconducting silver-sheathed tapes based on pure Bi2212 phase (open circles and open triangles, two samples) and on the Bi2212 phase containing submicrometre-sized inclusions of SrZrO₃ (full circles and full triangles, two samples) at 5 (a) and 60 K (b).¹⁷⁹

Most studies on the superconducting composites were carried out using MgO as the inclusion phase. Magnesia was introduced into the Bi2212 samples in the form of micro- and nanoparticles^{165, 166, 190–193} and aligned whiskers several micrometres^{11, 194, 195} or nanometres¹⁹⁶ in diameter. Usually, MgO particles are uniformly distributed in both polycrystalline ceramics (Fig. 13) and Bi2212 single crystals.^{72, 164, 166, 193} The size of inclusions depends on the preparation procedure and on the dispersion of the starting powder; however, melt processing is accompanied by recrystallisation of the inclusion phase, so that the MgO inclusions in the composite were of submicrometre size

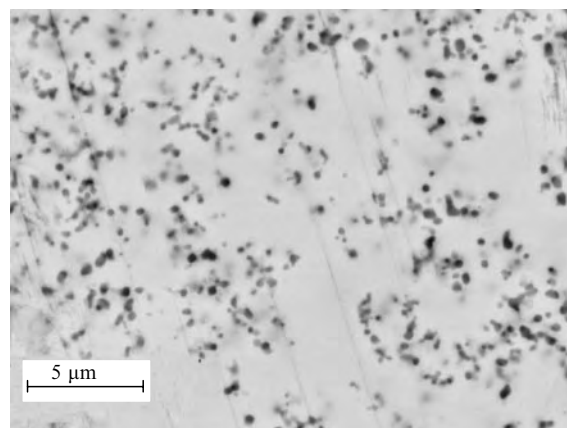


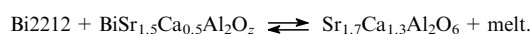
Figure 13. Electron microscopy (BSE) micrograph of Bi2212–MgO composite.

The grey background is the Bi2212 matrix and the dark objects are Mg_{1–x}Cu_xO inclusions.

even when nanocrystalline (~ 10 nm) powder was used. The samples exhibited an increase in J_c , which was most pronounced at elevated temperatures and at high magnetic fields and reached one or two orders of magnitude. For instance, a thick Bi2212 film with perpendicularly aligned MgO whiskers 20 nm in diameter was characterised by a critical current density of $\sim 10^4$ A cm^{–2} at a magnetic field of 0.5 T at 60 K.¹⁹⁶ Introduction of larger (micrometre-sized) MgO whiskers causes significant improvement of the strength of bulk composite samples and favours their texturing.^{11, 194, 195}

Doping with alumina is often used to modify the properties of the generic superconducting system. In this connection, the effect of Al₂O₃ on the superconducting transition temperatures of Bi2212 and (Bi,Pb)2223,^{197–199} on the ability of the phases in the generic system to undergo glass transitions,^{200, 201} on the microstructure of molten Bi2212,¹⁹⁷ on the mechanical properties of a (Bi,Pb)2223-based composite (see Ref. 198) and on the pinning force of the magnetic vortices in Bi2212 (see Refs 202 and 203) was studied. Considerable interest in alumina is due to the remarkable positive effect of this compound on the formation and growth of Bi2212 whiskers.^{170, 200, 204–207} A mechanism of formation of whiskers involving a phase of the Bi–Sr–Ca–Al–O system as a specific kind of microcrucible was proposed.^{204, 205, 207}

Bi2212-based composites with inclusions of compatible Al-containing oxides have been studied in detail.^{164, 168, 169, 208} It was found that the BiSr_{1.5}Ca_{0.5}Al₂O₆ phase is nearly completely segregated in the intercrystalline space of the Bi2212 phase, so that the intergranular electric contacts are broken. At the same time, Sr_{1.7}Ca_{1.3}Al₂O₆ mainly forms inclusions inside of the Bi2212 crystallites and, hence, the superconducting current can flow throughout the whole volume of the sample (Fig. 14). In the presence of BiSr_{1.5}Ca_{0.5}Al₂O₆ the melting temperature of Bi2212 reduces down to 860 °C and the process is described by the following peritectic reaction



A Bi2212–Sr_{1.7}Ca_{1.3}Al₂O₆ composite with substantially (by nearly an order of magnitude) reduced size of inclusions (down to 0.3 μm) was obtained from a glassy precursor (Fig. 14c).²⁰⁸ However, in this case the aluminate grains are partially aggregated in the space between lamellae of the superconducting phase.

If the composite is prepared by a melt technique, particles of the impurity phase (usually, this is the solid phase in the peritectic melt) are either trapped by the growing Bi2212 crystal or pushed by it depending on the energy ratio at the melt–superconducting phase–impurity phase interfaces. If pushing of particles of the impurity phase is energetically favourable, there is a critical growth rate of the crystal, v_c (if the crystal growth rate exceeds

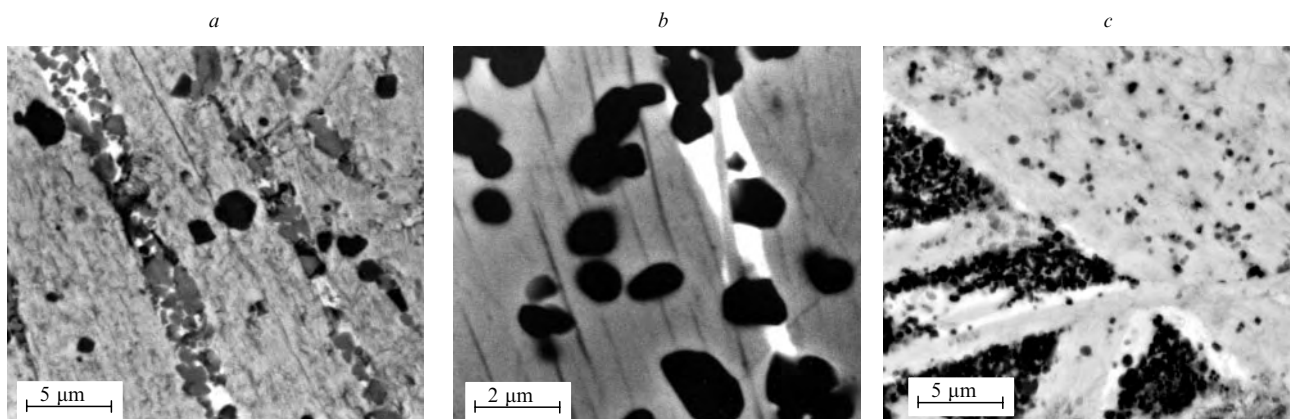


Figure 14. Electron microscopy (BSE) micrographs of Bi2212-based composites with inclusions of Al-containing oxides.

Compositions: Bi2212 + 0.5 BiSr_{1.5}Ca_{0.5}Al₂O₂ (a), Bi2212 + 0.2 Sr_{1.7}Ca_{1.3}Al₂O₆ (b) and Bi2212 + 0.2 Sr_{1.7}Ca_{1.3}Al₂O₆ (c) (prepared from oxide glass). The grey background is the Bi2212 matrix, the light-grey equiaxial objects are the BiSr_{1.5}Ca_{0.5}Al₂O₂ grains and the black equiaxial objects are the Sr_{1.7}Ca_{1.3}Al₂O₆ grains.

v_c , the particles are not displaced) and the extent of trapping by the matrix phase dramatically increases^{86, 88, 89}

$$v_c \sim \frac{\Delta\sigma}{\eta r},$$

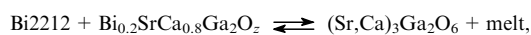
$$\Delta\sigma = \sigma_1 - \sigma_2 - \sigma_3,$$

where σ_1 , σ_2 , σ_3 are the energies of the particle–crystal, particle–melt and crystal–melt interfaces per unit of surface area, respectively; η is the melt viscosity and r is the particle radius.

The critical growth rate of the crystal increases with decreasing particle size. This provides an explanation for the fact that small Sr_{1.7}Ca_{1.3}Al₂O₆ particles are aggregated much more than large particles.

It was reported that the lattice parameter of Sr_{1.7}Ca_{1.3}Al₂O₆ is in good agreement with the interatomic distances in the CuO₂ layers of the matrix Bi2212 phase.¹⁶⁸ This means that Sr_{1.7}Ca_{1.3}Al₂O₆ can appear to be a promising substrate material for the preparation of epitaxial superconducting films. A study of the dielectric properties of this aluminate, aimed at using it in HTSC-containing composites, was carried out.²⁰⁹

Gallium sesquioxide additives were also used to obtain superconducting ceramics.^{171, 186} The composite prepared by solid-phase synthesis exhibited a higher J_c value compared to the single-phase sample.¹⁸⁶ The melt processed material contains large inclusions of gallate Bi_{0.2}SrCa_{0.8}Ga₂O₂ (crystallite size of the order of tens of micrometres) and is characterised by reduced T_c and J_c due to insertion of gallium ions into the crystal lattice of the superconductor.¹⁷¹ Melting of Bi2212 in the presence of the equilibrium gallate can be described by the reversible reaction



which is similar to the peritectic reaction involving the aluminate phase (see above). In both cases at temperatures above the melting temperature the systems contain no solid phases (cuprates and bismuthate of the rare-earth element) typical of the pure Bi2212 melt. Contacts with many other compatible oxides do not violate the nature of peritectic decomposition of the Bi2212 phase.²⁸

Bi2212-based composites containing inclusions of perovskite phases Sr(Ca)AO₃ (A = Ti, Zr, Hf, Sn) have been reported.^{176–179, 210} These composites are prepared using a melt technique and crystalline inclusions thus formed are much less prone to recrystallisation compared to MgO and Al-containing phases. Because of this, the size of inclusions is relatively small (~ 0.1 – 0.3 μm). As a rule, a considerable fraction of the second phase is inside of the Bi2212 lamellae in the form of submicrometre-sized inclusions while the space between large lamellae is

filled with relatively small aggregates of SrAO₃ grains, so that some intercrystalline contacts are retained (Fig. 15). Compared to the single-phase material, these composites (except for Ti-containing ones) are characterised by enhanced pinning of magnetic vortices and increased critical current density (by nearly an order

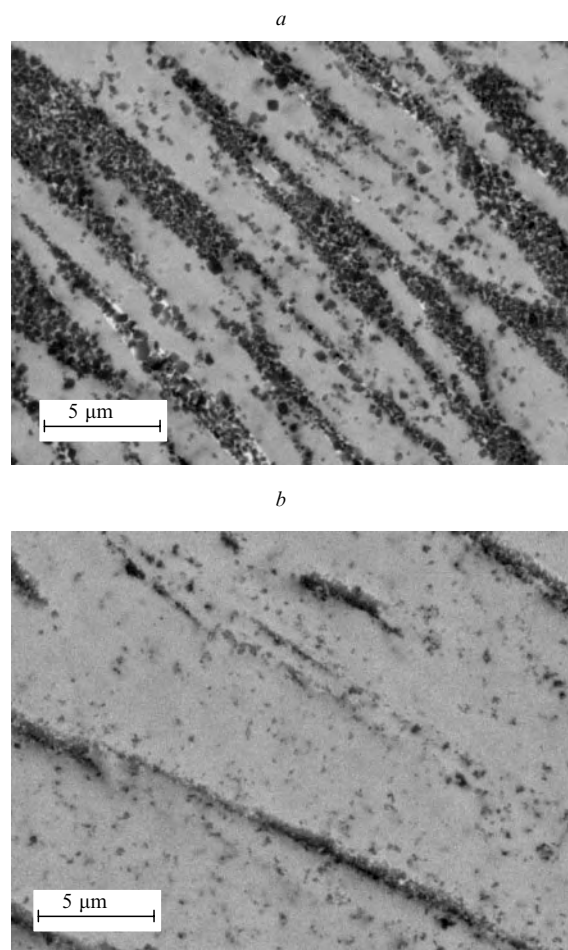


Figure 15. Electron microscopy (BSE) micrographs of composites Bi2212 + 1.6 SrSnO₃ (a) and Bi2212 + 0.5 SrZrO₃ (b).

The grey background is the Bi2212 matrix and the dark objects are submicrometre-sized grains of Sr_{1-x}Ca_xSnO₃ (a) and SrZrO₃ (b).

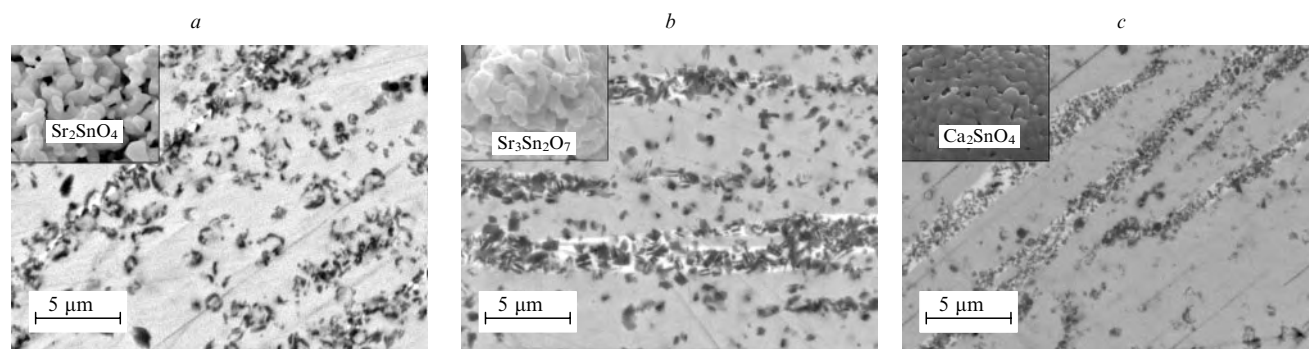


Figure 16. Electron microscopy (BSE) micrographs of Bi2212– $\text{Sr}_{1-x}\text{Ca}_x\text{SnO}_3$ composites prepared by reactions of molten Bi–Sr–Ca–Cu–O system with Sr_2SnO_4 (a), $\text{Sr}_3\text{Sn}_2\text{O}_7$ (b) and Ca_2SnO_4 (c).

The grey background is the Bi2212 matrix and the dark objects are $\text{Sr}_{1-x}\text{Ca}_x\text{SnO}_3$ inclusions of various shapes. The insets present micrographs of the starting powders of the corresponding tin-containing oxides.

of magnitude at 30–60 K). For instance, at 60 K silver-sheathed tapes of Bi2212– SrZrO_3 composite and pure Bi2212 phase are characterised by $J_c = 1.4 \times 10^4$ and $6 \times 10^3 \text{ A cm}^{-2}$, respectively (see Ref. 178).

It should be noted that the use of precursors of various chemical nature eventually leads to the formation of the same type of Bi2212–perovskite phase composites. In this connection a remarkable example is provided by the preparation of composites from a mixture of nonequilibrium substances *via* a chemical reaction between them.^{211–214} This approach allows modification of the shape and size of inclusions. An intense reaction proceeds between the solid phase containing the component A and the molten oxide precursor of the Bi–Sr–Ca–Cu–O system. For instance, micrometre-sized Sr_2SnO_4 grains are transformed into hollow perforated shells of equilibrium $(\text{Sr,Ca})\text{SnO}_3$; $\text{Sr}_3\text{Sn}_2\text{O}_7$ is transformed into corroded $(\text{Sr,Ca})\text{SnO}_3$ particles, while nearly $1 \mu\text{m}$ Ca_2SnO_4 grains are dispersed into much smaller $(\text{Sr,Ca})\text{SnO}_3$ particles (Fig. 16).^{211,212} When heated above 1000°C in the Bi2212 melt, strontium stannate SrSnO_3 is transformed into the $(\text{Sr,Ca})_3\text{Sn}_2\text{O}_7$ phase, which forms aggregates composed of mutually perpendicular plates located at positions of the grains of the starting stannate (Fig. 17). Cooling of the system is accompanied by the reverse process, *i.e.*, transformation into metastannate, which forms complex-shaped particles.²¹³ Similar particles are also formed as a result of transformations of Sr_2TiO_4 and $\text{Sr}_3\text{Ti}_2\text{O}_7$ into SrTiO_3 and of $\text{Sr}_3\text{Zr}_2\text{O}_7$ into SrZrO_3 .²¹⁴ It is assumed that complex-shaped particles formed during melt processing of a composite are less prone to agglomeration.²¹¹

The inclusion phases mentioned above have isotropic crystal lattices and, as a rule, form equiaxial grains. The crystal lattice of indium-containing oxide $\text{Sr}_{1-x}\text{Ca}_x\text{In}_2\text{O}_4$ has one-dimensional $\text{In}-\text{O}_2-\text{In}$ chains with strong bonds. This compound forms uniaxial particles in the composite matrix. Figure 18 presents the micrographs of Bi2212– $\text{Sr}_{1-x}\text{Ca}_x\text{In}_2\text{O}_4$ composites. Synthesis from nitrate solutions gives the composite containing elongated indate particles of size $1 \times 5 \mu\text{m}$, which are partially agglomerated in-between the Bi2212 lamellae.¹⁷² Synthesis from a glassy oxide causes the formation of more anisotropic indate particles, which are much less agglomerated.²¹⁵ One can expect that an anisotropic particle placed at a large angle with respect to the front of the growing crystal will be more readily trapped by the crystal compared to an equiaxial particle. A possible consequence is a much more uniform phase distribution in the composite.

The Bi2223 superconductor is less stable than Bi2212 (see Ref. 49) and is formed much more slowly. Namely, a complete solid-phase transformation of the precursor requires tens (hundreds) of hours; the Bi2223 phase cannot be crystallised immediately from melt. A vast majority of experiments were carried out using a lead-doped (Bi,Pb)2223 matrix instead of Bi2223, because

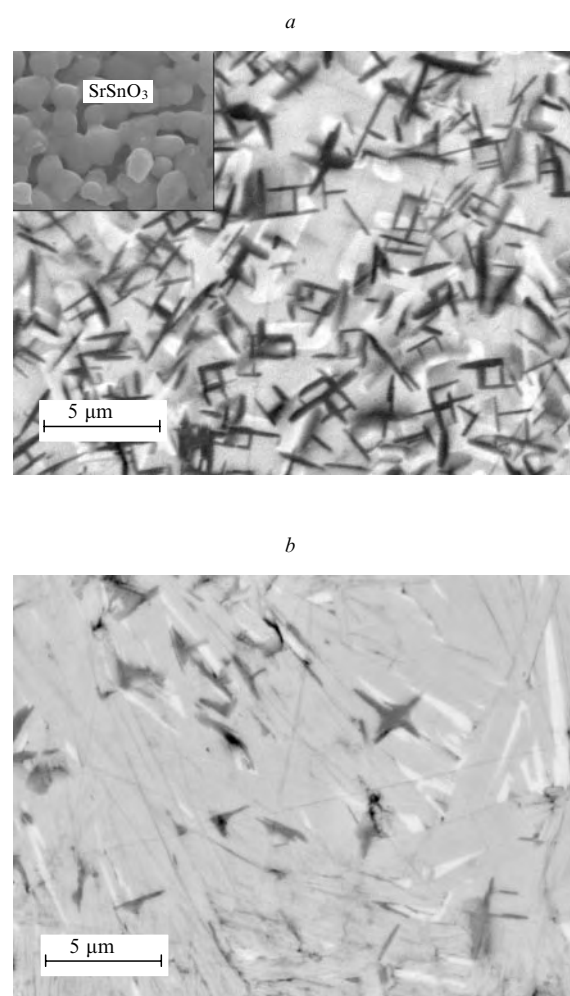


Figure 17. Electron microscopy (BSE) micrographs.

Sample prepared by melting of a mixture of Bi2212 and SrSnO_3 followed by annealing; the grey background is the Bi2212 matrix (solidified melt) and the black aggregates are scaly crystals of $(\text{Sr,Ca})_3\text{Sn}_2\text{O}_7$ (inset: starting SrSnO_3 powder) (a); Bi2212– $\text{Sr}_{1-x}\text{Ca}_x\text{SnO}_3$ composite prepared by heat treatment of the sample: the grey background is the Bi2212 matrix and the dark-grey and white objects are the $\text{Sr}_{1-x}\text{Ca}_x\text{SnO}_3$ and Bi2201 inclusions of irregular shapes (b).

phase formation in the former system proceeds much faster and to a greater extent as compared to the undoped system.

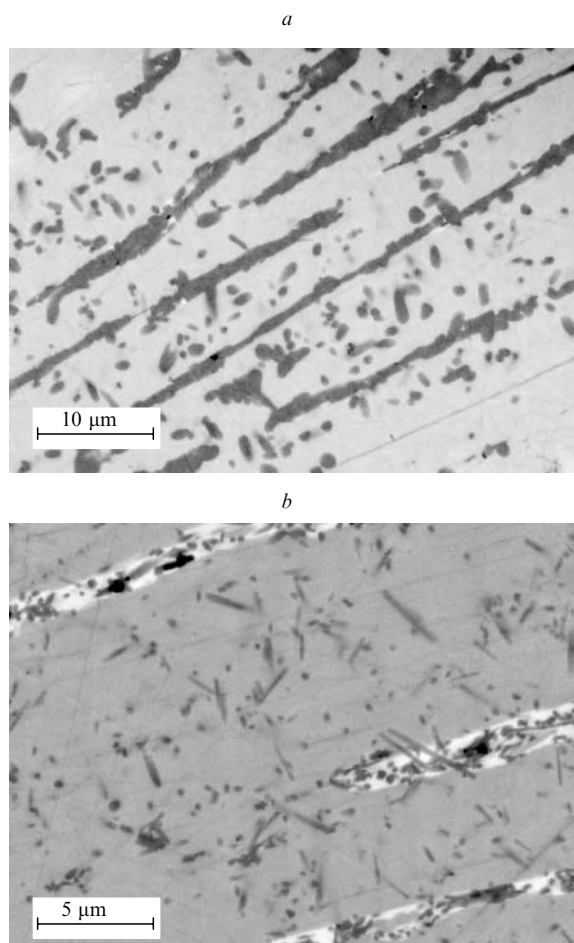


Figure 18. Electron microscopy (BSE) micrographs of Bi2212–Sr_{1–x}Ca_xIn₂O₄ composite prepared from nitrate precursor (a) and oxide glass (b).

Table 2 lists the data on the microcomposites containing different inclusion phases, which are thermodynamically compatible with (Bi,Pb)2223. The content of the impurity element in the matrix phase of the composite is at most 1 at.% and T_c varies in the narrow range from 106 to 110 K. A number of Bi2212-compatible phases (see Table 1) are also compatible with (Bi,Pb)2223. However, some phases including (Sr,Ca)₃Al₂O₆ and complex oxides of gallium react with the superconductor.^{164, 219}

At present, methods for preparation of (Bi,Pb)2223-based composite materials include only solid-phase synthesis. The impurity components strongly affect the rate of (Bi,Pb)2223 phase formation. The slowest reaction resulting in the (Bi,Pb)2223 phase proceeds between (Bi,Pb)2212, calcium cuprate and copper oxide.⁴⁹ Taking the reaction of the oxide precursor of (Bi,Pb)2223 with Sr_{1–x}Ca_xZrO₃ as an example, it was shown that during heat treatment the finely dispersed strontium zirconate absorbs the Pb-rich liquid, which is present in the system in small amounts and serves as an important factor of the phase transformation. The absorption slows down the formation of the (Bi,Pb)2223 phase.²²⁴ Acceleration of phase formation observed in the reactions with other additives is associated with the appearance of an additional amount of the liquid phase, which favours diffusion of the components.^{224, 225, 229, 230}

Introduction of submicrometre-sized SrZrO₃ particles into (Bi,Pb)2223 ceramics causes an increase in the current flowing within grains.¹⁷⁶ At the same time, the Ca₂B₂O₅ additive has little effect on J_c ,²¹⁸ while the addition of BiSr_{1.5}Ca_{0.5}Al₂O₇ and vanadium-containing oxide (see Table 2) leads to reduction of J_c , especially at nonzero magnetic fields.^{219, 225}

Table 2. Composition and properties of microcomposites with the (Bi,Pb)2223 superconducting matrix.

Dopant A	A-Containing phase compatible with (Bi,Pb)2223	Effect of dopant on phase formation of (Bi,Pb)2223	T_c /K	Ref.
Mg	Mg _{1–x} Cu _x O, $x \approx 0.1$	no effect	109	216
B	(Ca _{1–x} Sr _x) ₂ B ₂ O ₅ , $x = 0.3–0.4$	acceleration	110	217, 218
Al	BiSr _{1.5} Ca _{0.5} Al ₂ O ₇	"	108	219
In	Ca _{0.9} Sr _{0.7} Pb _{0.4} In ₂ O ₇	"	109	164
	Ca _{1–x} Pb _x In ₂ O ₄	—	—	220
Sn	Sr _{1–x} Ca _x SnO ₃	slowing down	110	28
	Ca ₂ SnO ₄	"	—	221
Ti	SrTiO ₃	"	106–107	57, 222, 223
Zr	Sr _{1–x} Ca _x ZrO ₃ , $x \approx 0.1$	"	110	224
V	Sr _{2.7–2.9} Ca _{0.3–0.2} Cu _{0.3–0.6} V ₂ O ₇ (see note a)	acceleration	104–106	225
	Sr ₃ V ₂ O ₆	"	—	57
Cr	Bi ₄ Sr ₈ Ca ₂ Cr ₃ O _y	—	109	57
Mn	SrCa ₅ Cu ₂ Mn ₂ O _y	—	104–107	57
	Sr ₄ Ca ₂ Cu _{1.5} Mn _{2.5} O _y	—	104–107	57
S	SrSO ₄	acceleration	110	28
U	(Sr,Ca) ₃ UO ₆	—	—	227, 228

^a Isostructural to Sr₅(VO₄)₃CuO.²²⁶

Considerable enhancement of magnetic flux pinning was observed upon introduction of MgO in the form of micro- and nanoparticles or nanowhiskers into the (Bi,Pb)2223 ceramics and silver-sheathed tapes.^{75, 231–234} Tapes containing additives of highly dispersed Ca₂PbO₄ were also prepared.²³⁵ Of special note is the doping of superconducting cuprates with uranium prior to neutron irradiation in order to create a high concentration of defects (tracks) as a result of nuclear fission of ²³⁵U.^{227, 228} The interaction of U₃O₈ with the (Bi,Pb)2223 phase is mainly reduced to the reactions with the calcium and strontium oxides. The superconductor phase is in equilibrium with the solid solution (Sr,Ca)₃UO₆ containing nearly equal amounts of strontium and calcium.

It is noteworthy that doping of both bulk (Bi,Pb)2223 ceramics^{236–240} and silver-sheathed wires with some microcomponents^{24, 230, 241, 242} causes significant changes in the grain microstructure and the material's texture and finally results in an increase in the critical current density. It was shown²³⁷ that introduction of nanodispersed TaC (0.1%) is followed by a twofold increase in J_c in the sintered ceramics; a further increase in the TaC content leads to reduction of the critical current density. Analogous changes in J_c were observed upon doping with microamounts of NbC (see Ref. 236) and HfN (see Ref. 238). It was assumed that the effect of these dopants is due to the changes in the content and composition of the intermediate liquid phase and to the formation of impurity phases. It was found²⁴¹ that (Bi,Pb)2223 tapes sheathed with the silver alloy doped with Ti, Zr or Hf exhibit higher J_c and that their microstructures are characterised by the larger size of the (Bi,Pb)2223 lamellae. This effect seems to be associated with the diffusion of micro amounts of dopants from the sheath to the superconducting core of the tape.

Investigations on the preparation of composites based on other high-temperature superconducting cuprates are on the initial stage yet. The introduction of nanoparticles of high-melting oxides into the TlBa₂Ca₂Cu₃O₇ matrix (see Ref. 243) leads to the

formation of inclusions of reaction products (particle size 30 to 100 nm). The product of the reaction with Al_2O_3 was identified as BaAl_2O_4 . Phase formation of the superconductor $(\text{Tl,Bi})\text{Ba}_2\text{Ca}_2\text{Cu}_3\text{O}_x$ in the system containing micrometre-sized LaAlO_3 particles was studied.²⁴⁴

Partial replacement of barium by strontium and of mercury by lead in the superconducting phase $\text{HgBa}_2\text{Ca}_2\text{Cu}_3\text{O}_{8+\delta}$ accompanied by a sharp increase in the irreversibility field at temperatures above 77 K was reported (see Refs 245 and 246). Initially, this effect was associated with a decrease in the anisotropy of the superconducting state due to lattice compression along the c axis.²⁴⁵ A more recent study²⁴⁷ of the material revealed wave-like fluctuations of the Hg and Pb content with a period of tens of nanometres and pinning of magnetic vortices in the regions with weakened superconductivity [similar to the Nd123 and $(\text{Bi,Pb})2212$ phases] was assumed.

* * *

Material presented in this review illustrates the importance of taking into account the chemical properties of components in the design of superconducting microcomposites based on cuprate superconductors. Considerable advances can be achieved only by carrying out basic research on the multicomponent oxide systems, formation of the matrix and inclusion phases and on peculiar features of physicochemical interactions between these phases during the composite formation, which is to a great extent governed by the interface energy.

Further progress in the field of design of superconducting microcomposites is related to thorough choice of additives and conditions for the preparation of microcomposites for each particular generic system in order to retain high superconductivity parameters of the matrix phase, reduction and stabilisation of inclusion size at nanolevel and control of the inclusion shape and distribution in the superconductor matrix. On this basis, the potentialities of the chemical complication of the systems under study are still far from being exhausted. It seems not improbable that multiphase materials containing several additives rather than a single extra component will exhibit optimum operating characteristics.

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Circumambulatory rearrangements of cyclopolyenes containing element-centred migrants

V I Minkin, I E Mikhailov, G A Dushenko, A Zschunke

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Abstract. Data on circumambulatory rearrangements caused by rapid migrations of substituents formed by Group 13–17 elements around three- to nine-membered cyclopolyenes are generalised and systematised. Depending on the ring size, the nature of the migrating group, substituents in the ring and the medium, the rate constants of circumambulatory rearrangements vary over a wide range from 10^6 to 10^{-8} s $^{-1}$ at room temperature. Particular attention is given to analysis of the mechanisms of these rearrangements ([1,*j*]-, [2,3]- and [3,3]-sigmatropic shifts, haptotropic rearrangements and ionisation–recombination) and to the correlation of these mechanisms with the structural characteristics of the compounds that undergo rearrangements. The bibliography includes 241 references.

I. Introduction

The molecular structure theory is closely related to the notions of space and time continuity. The three-dimensional space is insufficient for a detailed description of molecular structures; the fourth dimension is required to characterise the internal dynamics of a molecule, *i.e.*, the distribution of the times of occurrence of this molecule in different conformational, topomeric or isomeric states. The most detailed information on the internal dynamics can be gained from the data on energy barriers to various intramolecular processes.

Hindered rotations about single bonds and the related conformational transitions characterised by particular energy barriers were among the first dynamic processes which have been

studied extensively due to the development of IR spectroscopy and radiospectroscopy.^{1,2} Internal rotations leave sequences of bonds in molecules unchanged. These rotations are characterised by relatively low energy barriers. An insight into these processes can be gained within the framework of conventional models of molecular structures, including mechanical models. In the 1950s, reports were published on the fluxional behaviour of organometallic and organic compounds associated with rapid and reversible degenerate intramolecular rearrangements, which are accompanied by the cleavage and formation of covalent bonds (some of these rearrangements are characterised by rate constants of 10^6 – 10^9 s $^{-1}$ at room temperature; these processes have been surveyed in Refs 3–7). These data radically change the views of the degree of rigidity of molecular structures. The decisive breakthrough has been achieved due to the development of methods of dynamic NMR spectroscopy,^{3,8–10} which allowed the researchers to reveal the diversity of molecular fluxional structures and mechanisms of main intramolecular processes. It appeared that the stereochemical non-rigidity rather than rigidity of molecules is the most general characteristic of molecular structures. When speaking about NMR spectroscopy as the main method for studying the structural (or stereochemical) non-rigidity, it should be emphasised that the detection of structural non-rigidity is directly associated with the characteristic NMR time scale. It was suggested¹¹ that the term ‘structurally non-rigid molecules’ be used for molecules which undergo reversible rearrangements characterised by energy barriers (ΔG) no higher than the values determined by conventional methods of dynamic NMR spectroscopy ($\Delta G_{25}^\ddagger \leq 25$ kcal mol $^{-1}$).

The structural non-rigidity of the molecules of organometallic compounds was first discovered by Wilkinson and Piper,^{12,13} who described very rapid migrations of the Fe(η^5 -Cp)(CO) $_2$ (Cp is cyclopentadienyl) and Hg(η^1 -Cp) groups around the five-membered ring in the π -cyclopentadienylirondicarbonyl- σ -cyclopentadiene and dicyclopentadienylmercury molecules, respectively. At that time, the techniques at hand did not enable Wilkinson and Piper to observe directly the migration, but they recorded the only averaged signal for the protons of the η^1 -Cp ring and correctly attributed this fact to rapid (on the NMR time scale) migrations of the metal-centred groups around the five-membered ring.

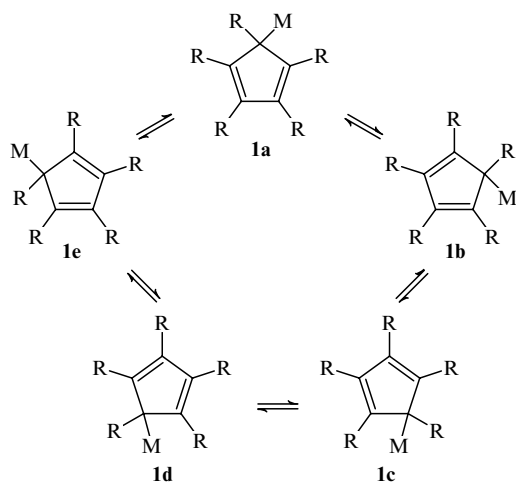
V I Minkin, I E Mikhailov, G A Dushenko Research Institute of Physical and Organic Chemistry, Rostov State University, prosp. Stachki 194/2, 344090 Rostov-on-Don, Russian Federation. Fax (7-863) 243 46 67. Tel. (7-863) 243 47 00. E-mail: minkin@ipoc.rsu.ru (V I Minkin), mikhail@ipoc.rsu.ru (I E Mikhailov)

A Zschunke Institute of Chemistry, Humboldt University, Brook Taylor str. 2, 12489 Berlin, Germany. Fax (49-30) 2093 75 61. Tel. (49-30) 2093 73 41. E-mail: Zschunke35@aol.com

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Only ten years later, this assumption was confirmed¹⁴ by the data from complete analysis of line shapes of the temperature-dependent ¹H NMR spectra of the MC₅R₅ compounds (**1**), where M is the migrating group (this discovery has been described in detail in the study¹⁵).

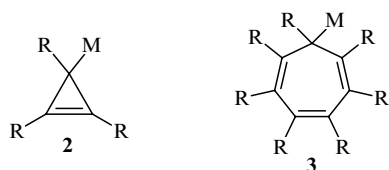


M = Fe(η^5 -Cp)(CO)₂.

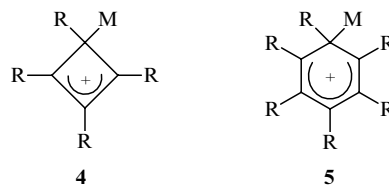
Rapid circumambulatory migrations of metal-centred groups M (formed by both transition and main-group metals) around the ring have been found in numerous cyclopentadiene derivatives containing such groups as substituents in the ring.^{4, 15–17} The term ‘circumambulatory rearrangements’ has gained acceptance as the most general term for describing rearrangements in the course of which an atom or a group of atoms migrates around the ring in such a way that they can finally be bound to any carbon atom of the ring.¹⁸ There are also alternative terms for these rearrangements, such as ‘merry-go-round’, ‘walk’, ‘ring-whizzing’, and ‘ring runners’.^{4, 15–18}

The tendency of σ -bound (η^1) cyclopentadienyl derivatives of transition metals **1a–e** to fluxionality correlates well with the polarity of the C_{Cp}–metal bonds, the ease of their ionisation and the ability of transition metal ions to form multicentre bonds. It was demonstrated that rapid circumambulatory rearrangements are typical also of cyclopentadiene derivatives containing covalently bound substituents formed by Group 13–15 elements in the ring (see comprehensive reviews published earlier^{17–22}). Investigations which we carried out in the last decade in cooperation with researchers from Rostov-on-Don, Berlin and Novosibirsk extended the range of fluxional η^1 -cyclopentadienes by including not only derivatives of Group 13–15 elements but also compounds in which migrating substituents are formed by Group 16 and 17 elements.

Circumambulatory rearrangements of cyclopentadiene derivatives belong to one of the most extensively studied areas of the dynamic stereochemistry of structurally non-rigid compounds. By contrast, analogous rearrangements of derivatives of the preceding and following members of the family of conjugated carbocyclic structures, *viz.*, cyclopropene (**2**) and cycloheptatriene (**3**), respectively, were poorly studied. In recent years, our research group has obtained new data on the fluxional behaviour of cyclopropenyl and cycloheptatrienyl derivatives of Group 15 and 16 elements.



Circumambulatory rearrangements are typical also of cyclic carbocationic systems **4** and **5** containing an even number of carbon atoms.



In the present review, particular attention is given to mechanisms of circumambulatory rearrangements, structures and estimates of the relative energies of transition states and intermediates for different reaction pathways. An important role of theoretical simulation in the identification of the major reaction pathway is demonstrated. Compounds in which groups M exhibit high ability to migrate in conjugated rings can serve as convenient carriers of functional groups in intermolecular reactions with substrates possessing higher affinity for migrating groups than the molecules of the starting compound. The possibilities of using compounds **1–5** as efficient soft carrier reagents are illustrated in Section X. The non-degenerate rearrangements of cyclopentadiene derivatives **1** discovered recently extend the range of functionalised Cp ligands involved in metal complexes, which can serve as catalysts for various stereospecific reactions (see Section X).

In the present review, we restrict ourselves to thermal rearrangements of derivatives of compounds **1–5** and some higher cyclopolyenes containing Group 13–17 elements. Data on the rearrangements of analogous derivatives of transition metals are considered only for comparison. Circumambulatory rearrangements of migrating substituents formed by Group 13 and 14 elements (B, Si, Ge, Sn) and phosphorus were studied in detail. Excellent comprehensive reviews^{17–19} devoted to this problem surveyed the data published up to 1985 inclusive. In the discussion of the rearrangements, we focus our attention on nitrogen-, oxygen-, chalcogen- and halogen-centred groups, whose migrations around the periphery of conjugated cyclopolyenes were discovered and studied primarily in the last 10–15 years. For cyclopentadiene derivatives, which belong to the most extensively studied fluxional cyclopolyene systems, the elements serving as centres of migrating groups are given below (according to their positions in the Periodic table); the central atoms of the groups, whose migrations were unknown before the mid-1980s (when we began our investigations) are shaded.

B	C	N	O	F
Al	Si	P	S	Cl
Ga	Ge	As	Se	Br
In	Sn	Sb	Te	I

The review is arranged as follows. It is known that the tendency of a molecule to undergo structural rearrangements depends on the presence of several stationary points on the potential energy surface (PES), which are comparable in energy, belong to two or more isomeric forms and are related by trajectories containing low-energy saddle points of transition states. Hence, we begin with the consideration of the structural types of isomers of conjugated cyclopolyenes. The tendency of these structures to undergo ionisation or η^1 – η^n transformations dictates the pathway of circumambulatory rearrangements. Alternative possible pathways of circumambulatory rearrangements of compounds **1–5** depending on the ring size, nature of the migrating group M and substituents in the ring are considered in Section III. In subsequent sections, the experimental and theoret-

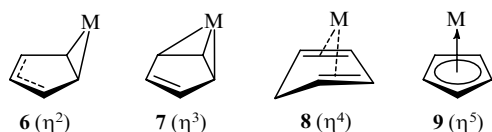
ical results are discussed in the order of increasing structural complexity, starting from the smallest cyclopropene derivatives.

II. Structural types of monosubstituted cyclopolyenes

Two main factors responsible for the mutual orientation of the fragments in cyclopolyenyl–M systems **1–5** and the type of the resulting structure are Coulombic and covalent interactions between these fragments. Cyclopentadienyl derivatives of alkali and alkaline-earth metals occur as ionic compounds containing aromatic cyclopentadienyl anions. In the solid state, these salts generally form polymeric structures. By contrast, the C–M bond in cyclopropene derivatives **2** and cycloheptatriene derivatives **3**, which are stable in the cationic form due to requirements for aromaticity, undergoes ionisation only if the group M possesses high electron affinity.

The multicentre mode of binding giving rise to sandwich (metallocene) structures is most common to transition metal complexes with cyclopolyenyl ligands. Although only the s and p orbitals of Group 13–17 elements can be involved in binding with the cyclopolyene fragment, their compounds of general formulae **1–3** are also characterised by considerable structural diversity. The usual covalent two-centre two-electron (2c–2e) binding is the dominant interaction in the cyclopolyenyl–M system. However, numerous stable π complexes with the cyclopentadienyl ligands in which the migrating groups M are formed by main-group elements are known (see the reviews^{23–27}).

Hoffmann and co-workers²⁸ analysed the role of covalent binding for cyclopentadiene derivatives in terms of projections of the centre M bound to the five-membered ring onto the plane of this ring. Taking into account the isolobal analogy,²⁹ this approach allows one to extend analysis to all CpM compounds, where M is a transition metal or a main-group element.²⁶ The position of the projection point is considered as a structural parameter based on which the compound is assigned to one of the η^n structural types (n is the number of p_π centres of the ligand involved in the multicentre bond with the substituent). σ -Bound (η^1) compounds **1** (as well as compounds **2–5**) generally belong to the most stable structural type of cyclopolyenyl derivatives of Group 13–17 elements, and η^2 – η^n structures (for cyclopentadiene derivatives, $n_{\max} = 5$) **6–9** are possible isomeric forms. Different simple models for electronic calculations, which enable one to predict the structures of the energetically most favourable η^n isomers, were developed.^{30, 31}



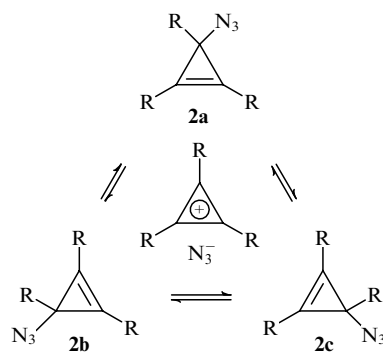
For some cyclopolyenyl, particularly, cyclopentadienyl, derivatives of Group 13–17 elements, the energy differences between various η^n -isomeric structures are very small. Tris(1,2,3,4-tetramethylcyclopentadienyl)aluminium is a prominent example.³² In the solid state, all three tetramethylcyclopentadienyl ligands in this compound are η^1 -coordinated, but signals in the ¹H and ¹³C NMR spectra of its solutions are completely averaged, which reflects the rapid exchange of the Al centre between all positions of the ligands even at low temperatures (about –110 °C). The results of *ab initio* calculations at the RHF/3-21G* level for model compounds, *viz.*, cyclopentadienylaluminium derivatives, are indicative of the flat potential energy surface in the region of existence of isomers with different modes of η -binding (η^1 , η^2 , η^3 and η^5). Thus, the energy differences between the η^2 and η^5 structures are in the range of 1–2 kcal mol^{–1}.

III. Mechanisms of circumambulatory rearrangements

The structural diversity of cyclopolyenyl compounds of Group 13–17 elements is a prerequisite for their fluxional behaviour. The choice between different mechanisms of rearrangements of a particular compound is determined by the relative stabilities of intermediate or transition state structures with different modes of η -binding as well as by the ease of ionisation of the cyclopolyenyl–M bond. We classify the possible pathways of circumambulatory rearrangements according to the modes of η -binding for energetically favourable transition state structures, including the η^1 – η^2 (η^1 – η^3 , ... η^n) and η^2 – η^3 (η^2 – η^3 , ... η^n) rearrangements, where n is the coordination number of the central atom in the transition state. In addition to haptotropic rearrangements (this term is used for generalisation of all types of $[i, j]$ -sigmatropic rearrangements and isomerisation processes in multicentre π complexes **7–9**¹⁹), an intramolecular shift of the migrating group around the periphery of the cyclopolyene ring can occur due to successive events of the cleavage and recombination of the cyclopolyenyl–M bonds within a tight ion pair generated upon ionisation of this bond. We restrict ourselves to a brief discussion and characteristic examples of each specific mechanism responsible for circumambulatory rearrangements of derivatives of main-group elements in conjugated cyclopolyene systems.

1. Ionisation–recombination mechanism

The ionisation–recombination mechanism is most common to cyclopropene derivatives **2** and cycloheptatriene derivatives **3**, whose ionisation is facilitated by the formation of stable aromatic cations. This mechanism has been proposed for the first time in the study³³ as an explanation of rapid randomisation of the position of the chlorine atom in 3-chlorocyclopropene molecule **2** (M = Cl, R = H). More recent studies of migrations of the azido group (M = N₃) in 3-azido-1,2,3-trimethyl-³⁴ and 3-azido-1,2,3-tri-*tert*-butylcyclopropenes³⁵ demonstrated that the rate of these rearrangements is independent of the concentration of the solution, but it is substantially influenced by the polarity of the solvent. For instance, the energy barrier to the rearrangement of compound **2** (M = N₃, R = Bu^t) in non-polar tetrachloromethane is 16.5 kcal mol^{–1}, whereas this barrier in polar deuteriomethanol is lower by 4.5 kcal mol^{–1}.³⁵ These data provide evidence supporting the ionic mechanism (formation of a tight ion pair), which can be represented as a disordered (random) circumambulatory rearrangement of migrating groups in molecules **2**.



The dependence of the ¹H NMR spectrum of tropylium azide **3** (M = N₃, R = H) on the temperature and solvent was also accounted for by the intermediate formation of the ion pair, *viz.*, tropylium azide ion.³⁶ Randomisation of the position of the isothiocyanate group in the cycloheptatriene ring was also observed in solutions of compound **3** (M = NCS, R = H) in CD₃CN.³⁷

Unlike the cyclopropenyl and cycloheptatrienyl ions, the aromatic cyclopentadienyl ions bear a negative charge. Hence,

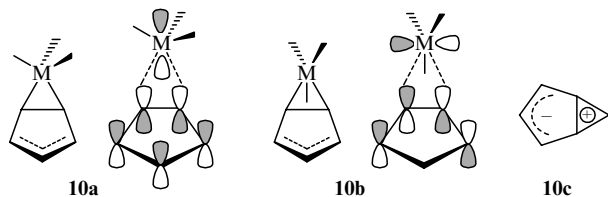
the electronic requirements for the ionisation mechanism of shifts of migrating groups *M* around the five-membered cyclopentadiene ring differ from those typical of three- and seven-membered cyclopolyenes **2** and **3**. Ionisation of the Cp–*M* bond is favoured by the presence of substituents, which facilitate delocalisation of the negative charge in the ring, as well as by the presence of groups *M*, which form stable cations *M*⁺. This combination occurs in 5-aryloxy-1,2,3,4,5-pentamethoxycarbonylcyclopentadienes. The latter compounds are the first cyclopentadiene derivatives for which the ionisation–recombination mechanism was observed (see Section VI.3.a).^{38,39}

2. 1,2-Shifts of migrating groups

The migration of the substituent *M* to the adjacent position of the cyclopolyene ring is the most common pathway of circumambulatory rearrangements of compounds **1**–**5** proceeding through a series of successive 1,2-shifts. In terms of sigmatropic rearrangements, 1,2-shifts are classified as [1,*j*]-sigmatropic shifts, where *j* = *n* (*n* is the ring size).

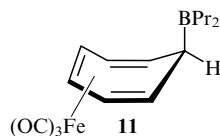
Until recently, examples of 1,2-shifts for sigmatropic rearrangements of cyclopropenyl compounds **2** remained unknown. The evidence supporting this mechanism was presented in the study of the rearrangements of *S*-substituted 1,2,3-triphenylcyclopropenes⁴⁰ (see Section IV.3). By contrast, the 1,2-shift ([1,5]-sigmatropic shift) is the most common and well-studied mechanism of circumambulatory rearrangements of cyclopentadiene derivatives **1**. The 1,2-shift of the hydrogen atom in the cyclopentadiene ring was first described in 1963.⁴¹ Two years later, rapid migrations of Si-, Ge- and Sn-centred groups around the Cp ring were discovered.⁴² Ustynyuk and co-workers^{43,44} made a considerable contribution to investigations of [1,5]-sigmatropic shifts in cyclopentadienylsilanes, -germanes and -stannanes. In the cited studies, it was demonstrated that the shifts of Si-centred groups around the five-membered ring are accompanied by the competitive migration of the hydrogen atom, which should be taken into account to gain a precise estimate of the kinetics of these rearrangements. The cited studies gave impetus to investigations of cyclopentadienes containing methyl, phenyl or methoxycarbonyl substituents in all positions of the ring in view of the fact that their migration ability is lower than that of the hydrogen atom.

According to the Woodward–Hoffmann rules, the [1,5]-sigmatropic shifts in cyclopentadienylsilanes, -germanes and -stannanes proceed with retention of stereochemical configuration of the central atom of the migrating group.⁴⁵ Consequently, transition state structure **10a** should be energetically more favourable than structure **10b** corresponding to inversion of stereochemical configuration of the central atom of the migrating group. This prediction is consistent with the results of semi-empirical calculations for the rearrangement in the cyclopentadienylsilane molecule.⁴⁶ The transition state for 1,2-shifts in cyclopentadiene derivatives is structurally analogous to bicyclo[3.3.0]hexatriene (**10c**), which is the lowest homologue of azulene. The electron density distribution in molecule **10c** gives a clue to an explanation of the influence of the nature of migrating groups and substituents in the ring on the kinetics of rearrangements.⁴⁷

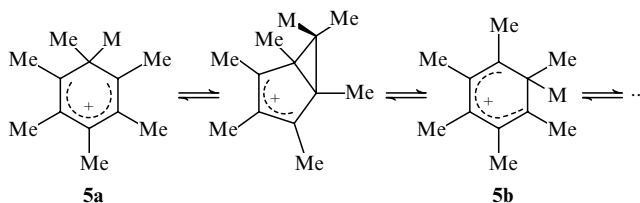


In the case of migrating substituents formed by elements of Groups 13 (B, Al) and 15 (P, As, Sb), the rearrangements also proceed predominantly as 1,2-shifts (see Sections VI.1, VI.3.b and c).

Thermal rearrangements of various cycloheptatriene derivatives caused by 1,2-shifts of the hydrogen atom, which correspond to the mechanism of [1,7]-sigmatropic shift, were described in sufficient detail.¹⁷ In the presence of bulky substituents in the ring, symmetry-allowed suprafacial [1,5]-shifts of hydrogen atoms become energetically more favourable (see Section III.4). However, theoretical and experimental studies demonstrated⁴⁸ that photochemical rearrangements of monosubstituted cycloheptatrienes associated with the migration of the hydrogen atom around the ring proceed as the [1,7]-sigmatropic shift. This mechanism was established also for rapid migrations of the Re(CO)₅ and RuCp(CO)₂ groups around the cycloheptatriene ring.⁴⁹ Recently, ¹H and ¹³C 2D EXSY NMR spectroscopic studies revealed⁵⁰ rapid 1,2-shifts ([1,7]-sigmatropic shifts) of the dipropylboryl group in the [1-4-η⁴-*exo*-7-(dipropylboryl)cycloheptatriene]tricarbonyliron molecules (**11**) (*E*_a = 17 kcal mol^{−1}), which were accompanied by the simultaneous 1,2-shift of the Fe(CO)₃ group.



For the 1,2-shifts of the hydrogen atom and various migrating substituents formed by Group 13–17 elements to occur in rings containing an even number of carbon atoms, it is requisite that the unsaturated portion of the ring should be either ionic or radical. In the four-membered ring of compound **4**, such migrations can be assigned to the η²–η³ type (see Section III.5), whereas the rearrangements in benzenium ions **5** proceed as a series of successive 1,2-shifts to form cations **5a**, **5b**, etc. The kinetics and stereochemistry of this type of rearrangement were studied in detail.^{51–53}

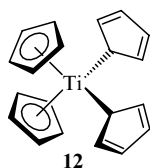


3. 1,3-Shifts

According to the principle of conservation of orbital symmetry for [1,3]-sigmatropic shifts, the suprafacial pathway of the reaction with inversion of stereochemical configuration of the central atom of the migrating group is preferable. The transition state structures for these rearrangements are substantially sterically hindered, and this mechanism is untypical of circumambulatory rearrangements of migrating substituents formed by Group 13–17 elements. As a result, the 1,3-shift of the migrating group generally involves two successive 1,2-shifts (symmetry-allowed suprafacial [1,5]-sigmatropic shifts).^{17,54} As an example we refer to the major mechanism of the rearrangement of tris(3-indenyl)-allylsilane studied by dynamic two-dimensional NMR spectroscopy.⁵⁵ The exceptions are the 1,3-shifts of the dipropylboryl group in 9-cyclononatetraenyldipropylborane⁵⁶ and compound **11**.⁵⁰ In the latter case, the rearrangement, which is presumably accompanied by the inversion of configuration of the boron atom, proceeds more slowly than the 1,2-shifts of the dipropylboryl group.

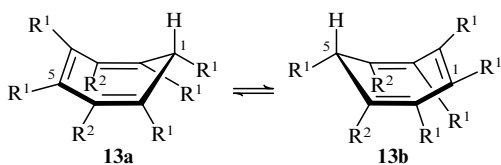
Studies by ¹³C CP/MAS NMR spectroscopy and the results of magnetisation transfer experiments showed that the 1,3-shifts of the Ti(η⁵-Cp)₂(σ-Cp) group occur in the σ-bound cyclopentadiene rings of the Ti(η⁵-Cp)₂(σ-Cp)₂ compound (**12**) both in the solid state and solution at 165 K.⁵⁷ However, 1,2-shifts

($E_a \approx 7.9 \text{ kcal mol}^{-1}$) are still the major pathway of this rearrangement.



4. 1,4-Shifts and 1,5-shifts

As mentioned in Section III.2, the migration of hydrogen atoms in sterically hindered cycloheptatrienes proceeds according to the mechanism of [1,5]-sigmatropic shifts, *i.e.*, as the 1,4-shift. For this rearrangement to occur, the migrating group must be present in the axial position. This rearrangement proceeds at a higher rate than the ring inversion in cycloheptatrienes **13** whose energy barrier is higher by 25 kcal mol^{-1} .⁵⁸

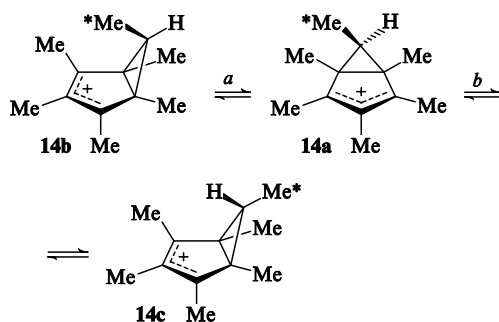


$R^1 = \text{Ph}; R^2 = \text{Me}, 4\text{-MeC}_6\text{H}_4$.

According to the data from dynamic ^{13}C NMR spectroscopy, the migrations of the triphenylsilyl, -germyl and -stannyl groups in the cycloheptatriene ring also proceed as successive [1,5]-sigmatropic shifts.^{59, 60} In 7-triphenylstannylcycloheptatriene adopting a boat conformation, the $\text{Sn}\cdots\text{C}(5)$ distance ($3.61 \text{ \AA}$)⁶¹ is approximately $0.3 \text{ \AA}$ smaller than the sum of the van der Waals radii of the tin and carbon atoms, which is indicative of the presence of strong attractive interaction between these centres even in the ground state. Recently, the ^1H 2D EXSY NMR spectroscopic study provided evidence that the mechanism of circumambulatory rearrangements in 7-trimethyltin- and 7-chlorodimethyltin-cycloheptatrienes involves a series of rapid successive 1,5-shifts of the tin-centred groups.⁶²

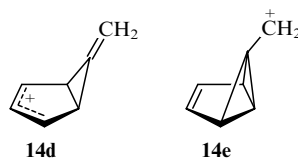
5. η^2 – η^3 -Shifts

Compounds with bicyclic structures **6** (η^2 structures) are prone to undergo [1,3]-sigmatropic shifts resulting in the circumambulatory migration of the group M. One of the first examples of such shifts was presented in the elegant study of the low-barrier ($\Delta G_{25}^\ddagger = 10.1 \text{ kcal mol}^{-1}$) rearrangement of hexamethylbicyclo[3.1.0]hex-3-en-2-yl cation **14a**.⁶³ The major reaction pathway (*a*) corresponds to retention of stereochemical configuration of the migrating carbon centre to form cation **14b**, whereas the pathway involving the inversion of configuration (*b*) to give cation **14c** is energetically less favourable (the energy difference is $4.6 \text{ kcal mol}^{-1}$).



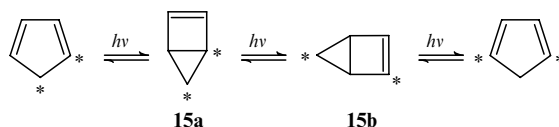
In the transition state structure for the rearrangement, the migrating group is bound to three adjacent atoms of the ring. Hence, this rearrangement can be assigned to the η^2 – η^3 type. It should be noted that an analogous rearrangement in 6-methyl-

idenebicyclo[3.1.0]hexenyl cation **14d** (its energy barrier is $10.6 \pm 0.2 \text{ kcal mol}^{-1}$) proceeds more than 10^7 times faster than that in cation **14a**. This was accounted for by the fact that intermediates with the structures of η^3 -dicyclopropylcarbinyl cations **14e** are readily formed.⁶⁴



The η^3 -transition state structure for the rearrangement of Dewar thiophene derivatives, which leads to a rapid exchange between the positions of the sulfur atom or the $\text{S}=\text{O}$ group in the four-membered ring (see Section V),⁶⁵ was confirmed by semi-empirical calculations using the PRDDO method.⁶⁶

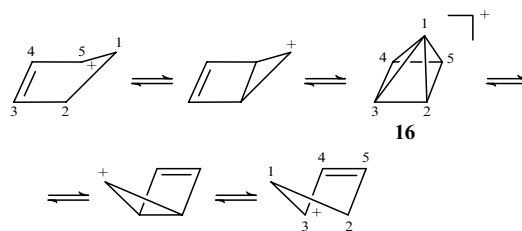
In uncharged systems, the ring-walk η^2 – η^3 rearrangements proceed rather slowly and do not satisfy the condition $\Delta G_{25}^\ddagger \leq 25 \text{ kcal mol}^{-1}$. One way of increasing the rate of such rearrangements is to irradiate a solution with UV light. For example, the photoinduced rearrangement of doubly ^{13}C -labelled cyclopentadiene was attributed⁶⁷ to the migration of the cyclopropane fragment around the four-membered ring in bicyclo[2.1.0]pentene (**15**).



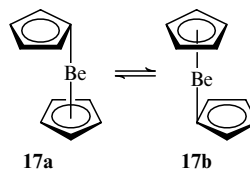
It is believed that many photoinduced migration processes in aromatic five-membered heterocycles proceed as η^2 – η^3 -rearrangements.^{68, 69}

6. σ, π Rearrangements

The mechanism of bond switching in η^1 or η^2 structures with the intermediate formation of isomeric π complexes (η^n structures at $n \geq 3$) belongs to the σ, π type.^{5, 53} However, this mechanism of exchange between the positions of the carbon atoms in antiaromatic cyclopentadienyl cation **16** was not confirmed, although a series of derivatives of the pyramidal $(\text{CH})_5^+$ cation, which has been predicted by Stohrer and Hoffmann,⁷⁰ were prepared (see the study³⁰ and references cited therein).



It should be noted that the σ, π rearrangements resulting in the shift of the migrating group around the cyclopolyene ring are known for cyclopentadienyl complexes of alkaline-earth metals. For example, the beryllium atom in beryllocene is equally disordered over two positions both in the solid state and the gas phase. This corresponds to unique asymmetric structure **17** in which very rapid ligand exchange takes place (see the study^{26, 71} and references cited therein).

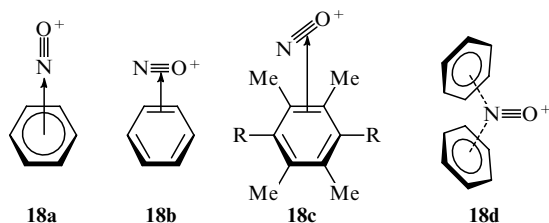


Analogous rearrangements were also observed for di(1,2,3,4,5-pentamethylcyclopentadienyl)zinc, which has a 'slip sandwich' structure. In solutions, this compound undergoes very rapid reversible ligand exchange. The ^1H NMR spectrum of this compound has only one sharp singlet common to all methyl groups even at -135°C .⁷² Apparently, this process is controlled by two concerted isomerisation mechanisms with energy barriers of $\sim 1.2\text{ kcal mol}^{-1}$ (for rotation of the ring, which is displaced from the axis passing through the centre of another Cp ring; the so-called gear mechanism) and $\sim 2\text{ kcal mol}^{-1}$ (for the σ,π rearrangements; molecular inversion).

7. π,π Rearrangements

In asymmetric π complexes with the cyclopolyene ligands, the coordination centre can undergo reversible shifts above the plane of the ligands, which is associated with interconversions of isomeric or topomeric π complexes. Haptotropic rearrangements of this type are well-known for transition metal complexes.⁷³ A few examples of such shifts for π complexes of Group 13–17 elements were also described. Of the latter processes, the rearrangements of π complexes of the nitronium cation with arenes have received the most study (see the comprehensive review⁷⁴). High-symmetry (C_{6h}) structure **18a**, which was expected based on experimental data⁷⁵ and *ab initio* calculations,⁷⁶ was in doubt because, according to the results of semiempirical calculations⁷⁷ and calculations by the density functional theory,^{78,79} this structure corresponds not to a minimum but to a hilltop on the potential energy surface of $\text{C}_6\text{H}_6\text{NO}^+$. Structure **18b** with the symmetry C_s is a stable form of the π complex. This structure undergoes rapid topomerisation (the calculated energy barrier is $< 3\text{ kcal mol}^{-1}$) due to sliding of the nitronium cation above the plane of the six-membered ring.

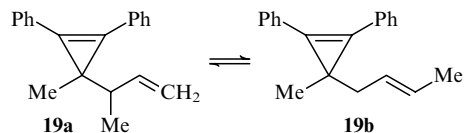
X-Ray diffraction studies of the $\text{NO}^+\text{AlCl}_4^-$ complexes with durene and hexamethylbenzene, the $\text{NO}^+\text{AsF}_6^-$ or $\text{NO}^+\text{SbCl}_6^-$ complexes with hexamethylbenzene and toluene⁷⁴ and the NO^+PF_6^- complex with hexamethylbenzene⁸⁰ demonstrated that the nitroso group in these complexes does not lie on a sixfold symmetry axis. The structure of π complex **18c** corresponds to the η^2 arrangement although the nitroso group deviates from the plane of the ring by approximately 50° . The ^{13}C CP/MAS NMR spectrum⁷⁴ and ^{13}C NMR spectrum of the complex of the nitronium cation with durene revealed a rapid rearrangement ($E_a = 10.2\text{ kcal mol}^{-1}$). This process was described as the rotation of the six-membered ring about the nitroso group.⁸¹ Analogous π complexes of the nitronium cation with fluorene, methyl-substituted naphthalenes⁸² and 1,2-bis(pentamethylphenyl)bicyclo[2.2.2]octene (the latter is called a 'Venus flytrap')⁸³ as well as the triple π complex of the cene type **18d** (see Ref. 84) were prepared and structurally characterised.



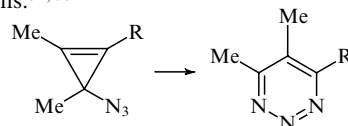
18c: R = H, Me.

8. [3,3]-Sigmatropic shifts

If a migrating group consists of three atoms with a terminal π bond, circumambulatory rearrangements can proceed by a mechanism involving concerted [3,3]-sigmatropic shifts of this group around the cyclopolyene ring. This mechanism is supported by the transformations of 3-allylcyclopropene derivative **19a** into isomer **19b** upon heating,⁸⁵ which is indicative of the [3,3]- rather than [1,3]-sigmatropic shift of the migrating group.



The mechanism of [3,3]-sigmatropic shifts is considered as an alternative to the ionisation–recombination pathway for the circumambulatory migrations of the azido group in the cyclopropene ring (see Section III.1). This mechanism is confirmed by the fact that a series of 3-azidocyclopropene derivatives **2** ($M = \text{N}_3$) were transformed into *v*-triazines under mild conditions.^{34,86}



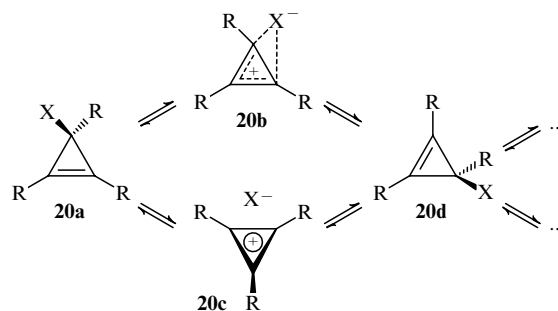
Direct evidence for [3,3]-sigmatropic shifts as a mechanism of migration of the azido group around the seven-membered cycloheptatriene ring was obtained^{87,88} by dynamic ^{15}N NMR spectroscopy (see Section VIII.6).

Rapid circumambulatory migrations of the heteroallyl groups $\text{X}-\text{C}(\text{R}^1)=\text{X}$ ($\text{X} = \text{NR}^2, \text{O}, \text{S}$) around three- and five-membered rings proceeding as successive [3,3]-sigmatropic shifts of these groups are considered in Sections IV.2, VI.3.a, VI.4.a and b.

IV. Circumambulatory rearrangements of cyclopropene derivatives

1. Rearrangements proceeding by the ionisation–recombination mechanism

Section III.1 covers the circumambulatory rearrangements of chloro- and azido-substituted cyclopropenes, involving heterolysis of the $\text{C}-\text{Cl}$ and $\text{C}-\text{N}$ bonds followed by recombination of the resulting ion pairs. Rapid degenerate and non-degenerate intramolecular migrations of the isothiocyanate groups around the three-membered ring in 1,2,3-triphenyl- and 1-(4-methoxyphenyl)-2,3-diphenylcyclopropene derivatives (**20a**) are other examples of this type of rearrangement.⁸⁹ According to the data from ^{13}C NMR spectroscopy in the temperature range of $10-80^\circ\text{C}$, the activation free energies ($\Delta G_{25}^\ddagger$) of the rearrangements of compound **20a** ($\text{X} = \text{NCS}$, $\text{R} = \text{Ph}$) in benzene and chlorobenzene are 15.6 and $14.4\text{ kcal mol}^{-1}$, respectively. The reaction pathways corresponding to the non-dissociative [1,3]-sigmatropic shift and the ionisation–recombination mechanism were simulated^{89,90} by semiempirical AM1 and MNDO/PM3 methods taking into account solvation (polarisation continuum model).⁹¹ It was demonstrated that transition state structure **20b** ($\text{X} = \text{NCO}$, $\text{R} = \text{H}$) for the 1,3-shift is energetically less favourable than tight ion pair **20c** even in non-polar solvents.



The energy barrier ($15.4\text{ kcal mol}^{-1}$; estimated as the relative energy of ion pair **20c**) which was calculated for the randomisation of the position of the isothiocyanate group in the course of the rearrangement $\text{20a} \rightleftharpoons \text{20d} \rightleftharpoons \dots$ ($\text{X} = \text{NCS}$, $\text{R} = \text{Ph}$) in chloroform, is in good agreement with the experimental value $\Delta G_{25}^\ddagger$. The calculations carried out in the studies^{89,90} demonstrated that in

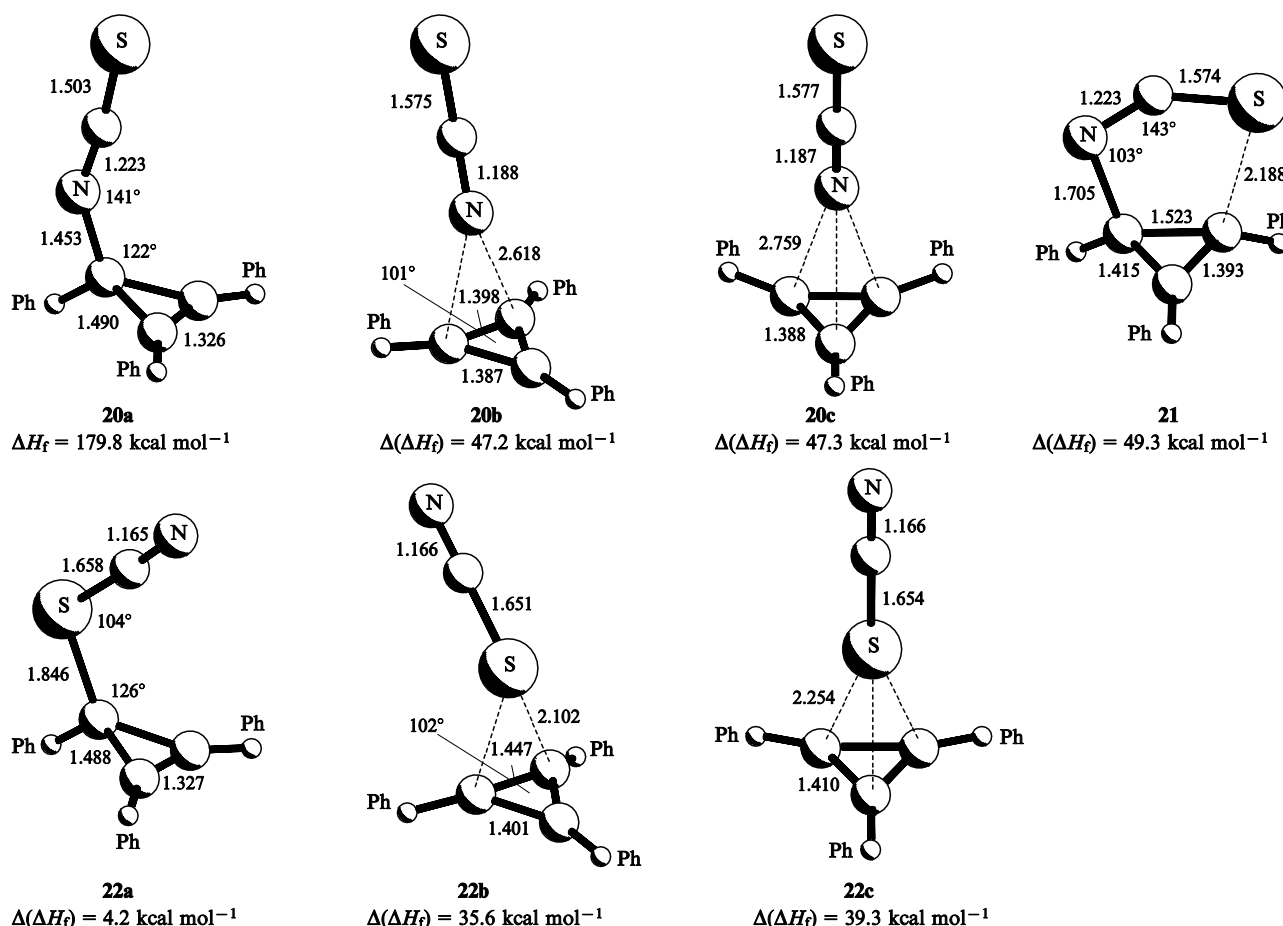


Figure 1. Geometric parameters and heats of formation of the ground state structures of 1-isothiocyanato-1,2,3-triphenylcyclopropene (**20a**) and 1,2,3-triphenyl-1-thiocyanatocyclopropene (**22a**), the transition state for the [1,3]-sigmatropic shift of the isothiocyanate (**20b**) and thiocyanate groups (**22b**), tight ion pairs (**20c** and **22c**) and transition state **21** for the interconversion $20a \rightleftharpoons 22a$ via [3,3]-sigmatropic shifts calculated by the MNDO/PM3 method.⁹⁰

Hereinafter, the bonds in the figures are given in Å; the bond angles and dihedral angles are also presented.

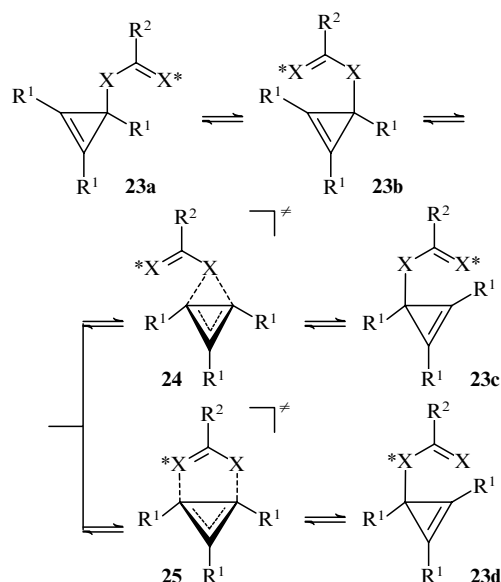
addition to the above-considered reaction mechanisms, the pathway through transition state **21** (Fig. 1) is also possible. The latter pathway corresponds to the [3,3]-sigmatropic shift in the course of interconversions of isomeric isothiocyanate **20** and thiocyanate **22**. Although MNDO/PM3 calculations demonstrated that compound **21** is less stable than isothiocyanate (the energy difference is $4.2 \text{ kcal mol}^{-1}$), it was detected⁸⁹ (0.4%) in the gas phase by mass spectrometry. The calculated relative energy of transition state structure **21** ($49.3 \text{ kcal mol}^{-1}$) is too high and its value depends only slightly on the polarity of the solvent. Therefore, in this case the [3,3]-sigmatropic shift seems to be unlikely.

2. Rearrangements via [3,3]-sigmatropic shifts

For cyclopropene derivatives, rapid circumambulatory rearrangements proceeding through a series of successive [3,3]-sigmatropic shifts were first discovered in the study of the migration of the dithioacyl group $[S-C(OEt)=S]$ around the three-membered ring of 1,2,3-triphenylcyclopropenyl *O*-ethyl dithiocarbonate **23a** ($X = S$, $R^1 = Ph$, $R^2 = OEt$).⁹²

According to the results of X-ray diffraction study, molecule **23a** ($X = S$, $R^1 = Ph$, $R^2 = OEt$) in the crystal is characterised by the *exo* conformation of the dithioacyloxy group with respect to the three-membered ring. Based on the results of MNDO/PM3 calculations, this conformation is energetically more favourable (by $0.7 \text{ kcal mol}^{-1}$) than *endo* form **23b**. The transformation into the latter form requires the migration event. According to the data from NMR spectroscopy, the energy barrier to interconversion of the conformers in solutions is lower than 12 kcal mol^{-1} . The

kinetic parameters of the degenerate rearrangement (Scheme 1), which were determined based on analysis of line shapes in the ^{13}C NMR spectra, are as follows: $\Delta G_{25}^\ddagger$ ($\text{C}_6\text{D}_5\text{CD}_3$) = $17.8 \text{ kcal mol}^{-1}$, $\Delta H^\ddagger = 14.8 \pm 0.2 \text{ kcal mol}^{-1}$, $\Delta S^\ddagger = -10.0 \pm 0.3 \text{ cal mol}^{-1} \text{ deg}^{-1}$, $k_{25} = 0.43 \text{ s}^{-1}$. These parameters



Scheme 1

are virtually independent of the concentration of the solution, which is indicative of the intramolecular character of the migration of the dithioacyloxy group around the cyclopropene ring.

To decide between two possible competitive mechanisms of migration, *viz.*, [3,3]- and [1,3]-shifts, the rearrangements of model compounds **23** ($X = \text{NH}, \text{O}, \text{S}$; $R^1 = R^2 = \text{H}$) were calculated by the semiempirical MNDO/PM3 method^{90,92} and the *ab initio* MP2/6-31G** method.⁹³ Selected results of these calculations are given in Table 1 and Figs 2 and 3.

Table 1. Relative energies ($\Delta E/\text{kcal mol}^{-1}$) and relative heats of formation ($\Delta H_f/\text{kcal mol}^{-1}$) of the structures of intermediates and transition states (TS) compared to the parameters of ground state structure **23a** for the hetero-Cope rearrangements of cyclopropene derivatives **23** ($R^1 = R^2 = \text{H}$).^{90,93}

Structure	X = NH		X = O		X = S	
	ΔE (see ^a)	ΔH_f (see ^b)	ΔE	ΔH_f	ΔE	ΔH_f
24 (TS for [1,3]-shift)	64.9	64.4	47.4	58.2	46.4	43.9
25 (TS for [3,3]-shift)	27.2 ^c	19.9	26.5	42.4	14.5	10.8
26	27.6	19.3	see ^d	see ^d	13.6	9.3
27	25.5	10.8	38.9	34.8	-5.0	-9.2

^a Energies calculated by the *ab initio* MP2 (fc)/6-31G** method.

^b Heats of formation were calculated by the MNDO/PM3 method.

^c Without consideration of zero-point vibrations, the structure of TS **25** ($X = \text{NH}$) is energetically less favourable than structure **26** ($X = \text{NH}$); the energy difference is 0.3 kcal mol⁻¹.

^d The structure was not localised on the corresponding potential energy surface.

It should be noted that the energy barriers predicted for the [3,3]-sigmatropic shifts of the dithioacyloxy group in molecule **23a** ($X = \text{S}$, $R^1 = R^2 = \text{H}$; see Table 1) are in good agreement with the barriers determined experimentally for compound **23a** ($X = \text{S}$, $R^1 = \text{Ph}$, $R^2 = \text{OEt}$), whereas the energies calculated for the migration mechanism involving the [1,3]-shift (with transition state structure **24**) are approximately 30 kcal mol⁻¹ higher and seem to be inconsistent with the results of dynamic NMR spectroscopy. The conclusion that the [3,3]-sigmatropic shift is

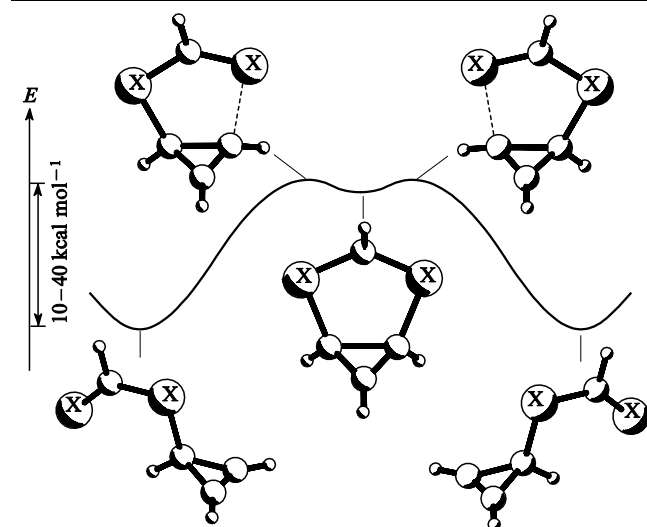


Figure 2. Energy profile of the pathway of [3,3]-sigmatropic shifts for the migrations of the allyl and heteroallyl groups around the cyclopropene ring in compound **23** ($X = \text{CH}_2, \text{O}, \text{NH}, \text{S}$).

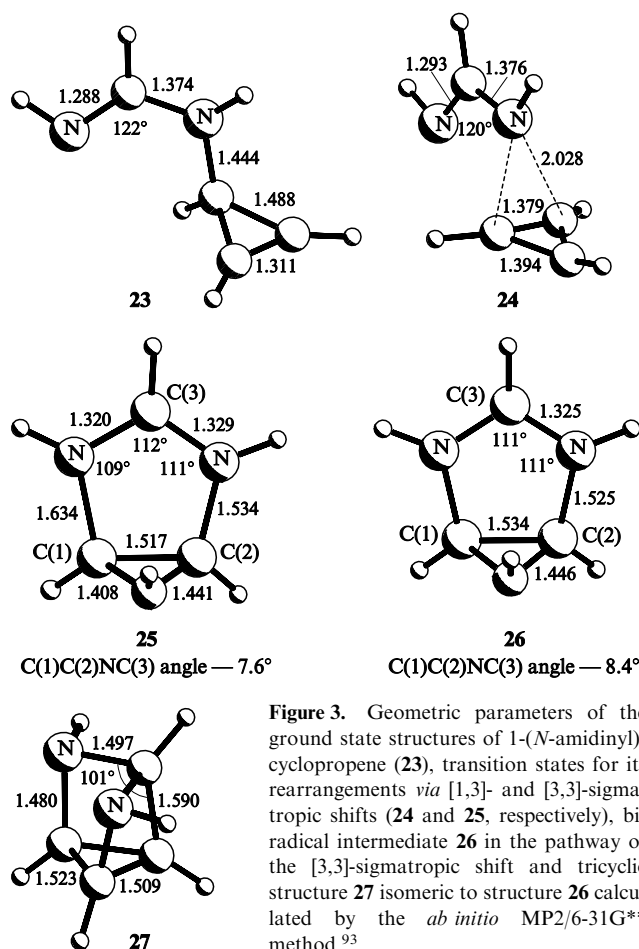
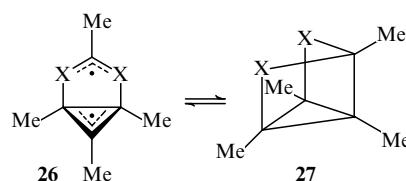


Figure 3. Geometric parameters of the ground state structures of 1-(*N*-amidinyl)cyclopropene (**23**), transition states for its rearrangements via [1,3]- and [3,3]-sigmatropic shifts (**24** and **25**, respectively), biradical intermediate **26** in the pathway of the [3,3]-sigmatropic shift and tricyclic structure **27** isomeric to structure **26** calculated by the *ab initio* MP2/6-31G** method.⁹³

energetically more favourable is also true for circumambulatory migrations of other heteroallyl substituents in the cyclopropene ring. The energy barriers calculated for this reaction pathway (transition state structure **25**) are 15–45 kcal mol⁻¹ lower than the barriers to the [1,3]-shifts.^{90,93} According to the results of calculations, the Cope rearrangement ($X = \text{CH}_2$) and its hetero-analogue ($X = \text{NH}, \text{O}, \text{S}$) proceed in cyclopropene derivatives **23** as two-step reactions to give stable singlet biradical intermediates **26** (see Fig. 3). Unlike transition state structures **25**, biradical intermediates **26** have the symmetry C_s . The typical energy profile of the reaction pathway for [3,3]-sigmatropic shifts is shown in Fig. 2. Figure 3 presents the geometric parameters of the structures, *viz.*, the starting structure, the transition state structure and the structure of the biradical intermediate, generated through the [3,3]- and [1,3]-sigmatropic shifts in the course of the circumambulatory rearrangements of 1-(*N*-amidinyl)cyclopropene **23** ($X = \text{NH}, R^1 = R^2 = \text{H}$).

Calculations predicted that biradicals **26** should readily be transformed into more stable tricyclic structures **27**.

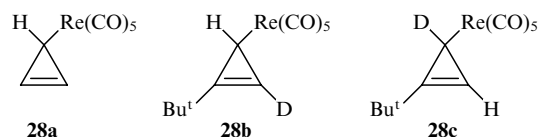


Actually, the investigation of thermolysis of 3-allylcyclopropene derivatives **19** (see Section III.8 and Refs 94 and 95) demonstrated⁸⁴ that the equilibrium mixture of products contained > 50% of the corresponding tricyclo[2.2.0.0]hexane derivative **27** ($X = \text{CH}_2$). The interconversion $\mathbf{26} \rightleftharpoons \mathbf{27}$ can be

considered as an example of isomerisation of the bond-stretching type.^{70, 96}

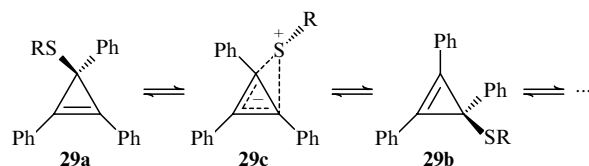
3. Rearrangements proceeding by a mechanism of [1,3]-sigmatropic shifts

The non-dissociative rearrangement pathway involving the forbidden suprafacial [1,3]-sigmatropic shift is untypical of cyclopropene derivatives, even of those containing organometallic groups, which exhibit very high ability to undergo circumbulatory migrations in the cyclopentadiene ring. For example, 3-(pentacarbonylrhenium)cyclopropene (**28a**), like its derivatives **28b,c**, is a structurally rigid compound. The transformations **28b** $\rightleftharpoons$ **28c** do not proceed in solution even at high temperature.⁷³



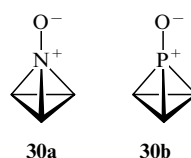
There is a high energy barrier (~ 32 kcal mol⁻¹) to the migration of the trimethylsilyl group in the 1,2-dimethyl-3-phenyl-3-trimethylsilylcyclopropene molecule.⁹⁷ By contrast, 3-phenylthio-1,2,3-triphenylcyclopropene **29a** (R = Ph) and di(1,2,3-triphenylcyclopropenyl) sulfide **29a** (R = C₃H₅) possess dynamic properties, and the ¹H and ¹³C NMR spectra of their solutions in C₂D₂Cl₄ are temperature-dependent (but are concentration-independent).⁴⁰

The energy barriers ($\Delta G_{25}^\ddagger$) to the migration of the phenylthio- and triphenylcyclopropenylthio groups calculated based on analysis of the line shapes of indicator signals in the ¹³C NMR spectra are 24.4 and 24.1 kcal mol⁻¹, respectively, which are 5–10 kcal mol⁻¹ higher than the barrier to migration of the phenylthio group in the cyclopentadiene system (see Section VI.4.b). This can be attributed to unfavourable conditions for delocalisation of the negative charge in the three-membered fragment of transition state structure **29c**.

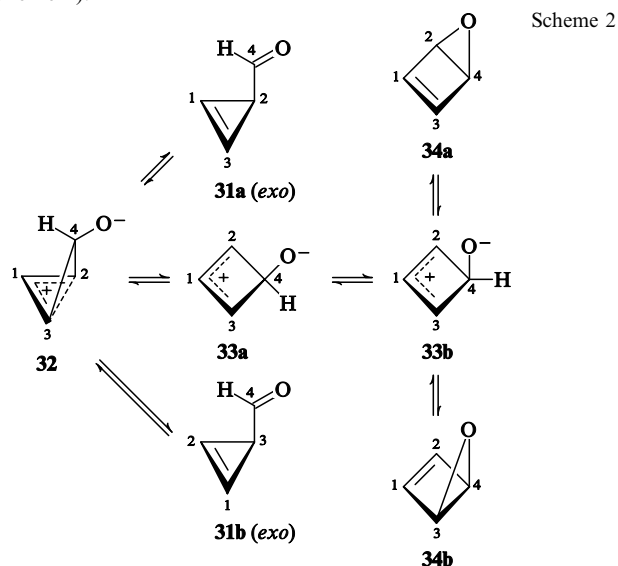


R = Ph, C₃H₅.

The rearrangements of cyclopropene derivatives containing π bonds in the migrating groups M = X = Y are of interest. Semi-empirical (MINDO/3, MNDO/PM3 and AM1)⁹⁸ and *ab initio*⁹⁰ calculations demonstrated that the potential energy surfaces for C₃H₃NO and C₃H₃PO involve several alternative pathways of intramolecular rearrangements due to secondary orbital interactions between the migrating groups of this type and the ring; however, the relative energy of bicyclic structure **20b** (X = NO, R = H) corresponding to the transition state or intermediate for the 1,3-shift of the nitroso group around the cyclopropene ring is very high [35.3 kcal mol⁻¹; MP2(full)/6-31G**]. After the replacement of the nitrogen atom in the migrating group by the phosphorus atom, the local minimum of structure **20b** (X = PO, R = H) on PES calculated by the RHF/6-31G** method is only 5.1 kcal mol⁻¹ higher than the minimum of structure **20a** (X = PO, R = H). Interestingly, calculations^{90, 98} revealed local minima corresponding to rather stable pyramidal azatetrahedrane oxide **30a** [ΔE (RHF/6-31G**) = 89.0 kcal mol⁻¹] and pyramidal phosphatetrahedrane oxide **30b** [ΔE (RHF/6-31G**) = 55.4 kcal mol⁻¹]. However, these highly strained structures are not involved in the rearrangements of the η^1 isomers **20a** $\rightleftharpoons$ **20d**.



The possibility of the circumbulatory intramolecular migration for formylcyclopropene **31**, which is another isoelectronic analogue of nitrosocyclopropene, was considered theoretically at the MP2/6-31G** level⁹⁹ using the intrinsic reaction coordinate calculations¹⁰⁰ for the identification of reaction trajectories. It was found that η^2 structure **32** is a high-energy intermediate ($\Delta G_{25}^\ddagger > 42$ kcal mol⁻¹) for this rearrangement (Scheme 2).



It was expected that *exo* conformer **32** would undergo isomerisation into the *endo* form via ring inversion. However, it appeared that the transformation of structure **32** into the planar form involves the formation of two successive transition states **33a** and **33b**, and the local minimum corresponds not to *endo* conformer **32** but to the energetically more favourable isomers of Dewar furan **34**. It should be noted that conformer **33b** corresponds to the transition state structure for the circumbulatory $\eta^2 - \eta^3$ rearrangement of compound **34** involving the migration of the oxygen atom around the four-membered ring. An analogous rearrangement is also known for derivatives of Dewar thiophene (see Section III.5) but this rearrangement was not observed for derivatives of Dewar furan **34** (see Scheme 2). Therefore, the results of these calculations⁹⁹ led to the conclusion that the formyl group in the cyclopropene ring possesses low migration ability. Hence, it is beyond reason to expect that the rearrangement of compound **31** or its derivatives, unlike the rapid migration of the formyl group around the cyclopentadiene ring (see Section VI.2), is detectable by dynamic NMR spectroscopy.

4. Rearrangements of acylcyclopropenes catalysed by protonation

The intramolecular migration of acyl groups in cyclopropene derivatives is substantially accelerated under conditions of general or specific acid catalysis.^{5, 101} The complex formation with Lewis acids has the same or an even stronger effect (see Section VI.2).

According to MP2/6-31G** calculations,⁹⁹ protonation of formylcyclopropene **31** proceeds at the carbonyl oxygen atom to give four isomeric cations of which the *exo* conformer of 4-hydroxycyclobutenyl cation **35a** is most stable (Table 2, Fig. 4). The tetra-*tert*-butyl derivative of the 4-hydroxycyclobutenyl cation (**36**), which was prepared by oxidation of tetra-*tert*-butyltetrahedrane, has precisely this structure.¹⁰² It was demon-

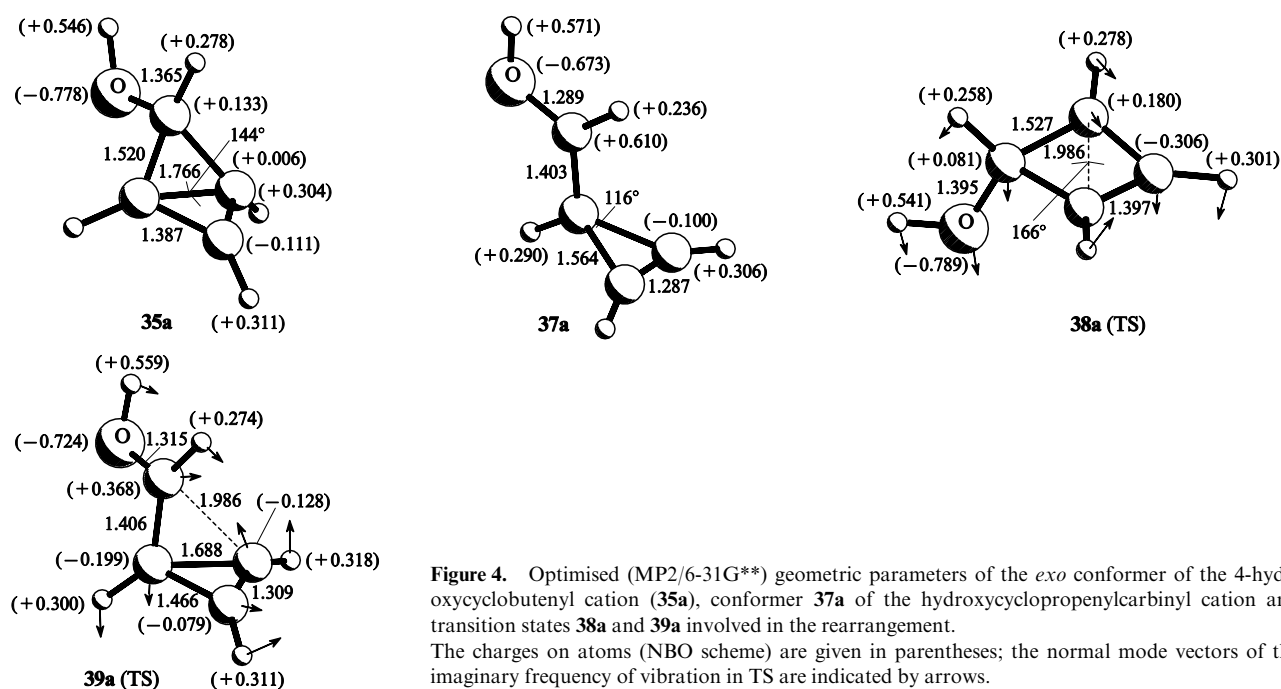


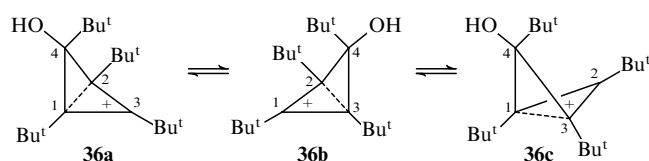
Figure 4. Optimised (MP2/6-31G**) geometric parameters of the *exo* conformer of the 4-hydroxycyclobutenyl cation (35a), conformer 37a of the hydroxycyclopropenylcarbinyl cation and transition states 38a and 39a involved in the rearrangement. The charges on atoms (NBO scheme) are given in parentheses; the normal mode vectors of the imaginary frequency of vibration in TS are indicated by arrows.

Table 2. Relative energies (ΔE) of structures 35 and 37–39 (see Ref. 99) involved in the rearrangement of the 4-hydroxycyclobutenyl cation and the values of the only imaginary frequency (ν_{im}) of normal vibrations for structures of transition states (TS).

Structure	$\nu_{\text{im}}/\text{cm}^{-1}$	$\Delta E/\text{kcal mol}^{-1}$
35a	—	0
39a (TS)	272	10.1
37a	—	3.7
35b	—	8.1
39b (TS)	431	18.4
37b	—	4.9
38a (TS)	267	13.1
38b (TS)	266	20.1

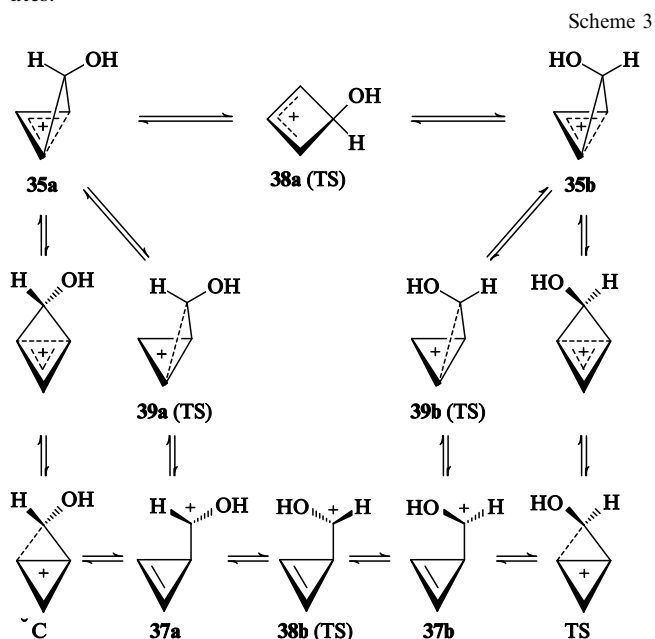
Note. The energies were calculated by the *ab initio* MP2/6-31G** method.

strated that cation 36 undergoes a low-barrier rearrangement ($\Delta G^\ddagger \approx 15 \text{ kcal mol}^{-1}$) as a result of successive 1,2-shifts of the hydroxymethylene group around the cyclopropene ring. It was found that the chemical shift of the migrating sp^3 -hybridised carbon atom in the NMR spectrum of cation 36 remains unchanged over a broad temperature range. This is indirect evidence that only *exo* isomer 36 is involved in the reaction, and, consequently, the configuration of the migrating carbon centre undergoes inversion because the reaction pathway with retention of configuration would require the interconversion between the *exo* and *endo* conformers to occur in each step of the rearrangement.



This assumption was confirmed by *ab initio* calculations,⁹⁹ which demonstrated that the rearrangement of the 4-hydroxycyclobutenyl cation 35 proceeds in two steps through the intermediate formation of classical hydroxycyclopropenylcarbinyl cations 37. All main structures corresponding to local minima on PES of the $\text{C}_4\text{H}_5\text{O}^+$ cation, which are involved in degenerate

circumambulatory rearrangements of the conformers of the 4-hydroxycyclobutenyl cation, are shown in Scheme 3. The migrations of the protonated formyl group around the three-membered ring in the *exo* (35a) and *endo* conformers (35b) of the 4-hydroxycyclobutenyl cation proceed as non-concerted two-step reactions to give the *exo* (37a) and *endo* (37b) conformers of the hydroxycyclopropenylcarbinyl cation, respectively, as intermediates.



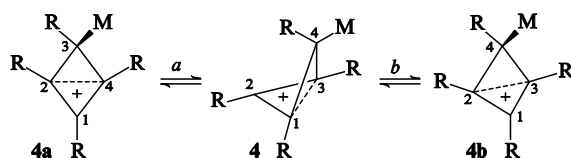
The calculated energy barriers to the 1,2-shifts of the hydroxymethylene groups (10.1 and 10.3 kcal mol^{-1} for conformers 35a and 35b, respectively) are in satisfactory agreement with the experimental activation free energy for the circumambulatory rearrangement of tetra-*tert*-butyl derivative 36 of cation 35a. The eclipsed conformer of hydroxycyclopropenylcarbinyl cation 38b, whose formation as an intermediate or transition state in the rearrangement would lead to retention of stereochemical configuration of the migrating carbon atom, lies on PES off this pathway. The intersection of the reaction pathways through the

ring inversion mechanism $35a \rightleftharpoons 38a \rightleftharpoons 35b$ requires that the higher energy barrier be overcome compared to that calculated for the rearrangement $35a \rightleftharpoons 39a \rightleftharpoons 37a$. Therefore, the two-step circumambulatory rearrangement of the *exo* isomer of 4-hydroxycyclobutenyl cation $35a$ accompanied by the inversion of configuration of the migrating carbon centre is the intramolecular rearrangement pathway corresponding to the minimum energy.

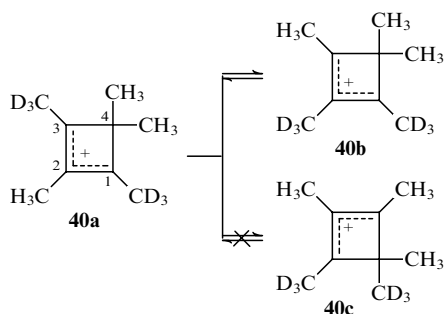
V. Circumambulatory rearrangements in a four-membered ring

High-level *ab initio* calculations^{99, 103, 104} and X-ray diffraction study¹⁰⁵ of cyclobutenyl cation **4** showed that this cation has a non-planar homoaromatic structure intermediate between the planar and bicyclo[1.1.0]butyl forms.

The migration of the group M in derivatives **4** can, in principle, proceed as a series of successive 1,2-shifts ([1,4]-sigmatropic shifts) of the migrating group around the four-membered ring (path *a*) or as [1,3]-sigmatropic shifts of the cyclopropyl fragment around the three-membered ring of the homoaromatic cyclobutenyl (homocyclopropenyl) cation (path *b*).



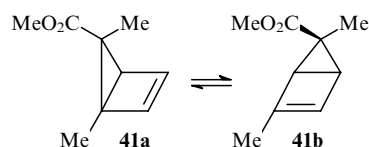
Koptug and co-workers¹⁰⁶ found that cation **40a** containing deuterated methyl groups at positions 1 and 3 underwent intramolecular exchange resulting in the distribution of the labelled groups between positions 1, 2 and 3, but not 4, of the ring. Hence, the mechanism associated with path *a* can be excluded.



The sigmatropic rearrangements of a series of other carbon-centred groups (alkyl, aryl and allyl) and the hydrogen atom around the cyclobutene ring, which are characterised by energy barriers higher than 15–25 kcal mol^{−1}, were reported.^{53, 107} By contrast, the migration of the anionic trichloroaluminium group in the permethylated σ complex of cyclobutadiene **4** (M = AlCl₃[−], R = Me) proceeded rather rapidly ($\Delta G_{25}^\ddagger < 25$ kcal mol^{−1}).¹⁰⁵ Unlike the rearrangements of the cyclobutenyl cations with the carbon-centred migrating groups, this dynamic process involves successive 1,2-shifts of the AlCl₃[−] group.

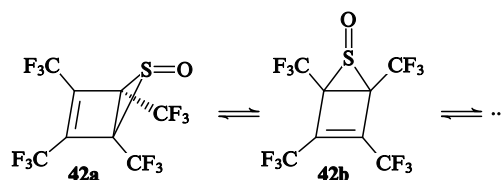
The formation of isomers of 2-azapyrylium salts in the reactions of σ complexes of dichloroethylene-, trichloroethylene- and tetraalkylcyclobutadienyldialuminium hexabromide with nitrosyl chloride¹⁰⁸ stimulated the examination of the possibility of the σ, π -mechanism for the rearrangement of nitrosocyclobutenyl cations **4** (M = NO, R = H). Semiempirical¹⁰⁹ and *ab initio*¹¹⁰ calculations demonstrated that the intermediate pyramidal cation with the η^4 -coordinated nitroso group corresponds to a local minimum on PES of the C₄H₄NO⁺ cation. However, alternative reaction pathways proceeding through the intermediate formation of structures such as N,O-substituted Dewar benzene and bullvalene are energetically more favourable.^{105, 109}

As demonstrated in Section III.5, circumambulatory rearrangements in neutral four-membered rings proceed by the η^2 – η^3 mechanism corresponding to the [1,3]-sigmatropic shift. The interconversion of isomers of bicyclopentene **41** is one of the first and most well-studied examples of this type of thermal rearrangement.¹¹¹ This rearrangement is highly stereoselective and proceeds according to the Woodward–Hoffmann rules with the inversion of stereochemical configuration of the migrating carbon atom in the cyclopropyl fragment.



$$\Delta G^\ddagger (41a \rightarrow 41b) = 21.7 \text{ kcal mol}^{-1}$$

Unlike the rearrangements of bicyclopentenes **41**, an analogous degenerate rearrangement of the *exo* conformer of the tetrakis(trifluoromethyl) oxide derivative of Dewar thiophene **42** (see Ref. 65) proceeds in solution very rapidly even at low temperatures: $\Delta G_{-124}^\ddagger = 6.8$ kcal mol^{−1}.



The possibility of the dynamic behaviour of the starting derivative of Dewar thiophene, which is the only known bicyclic isomer of aromatic five-membered heterocycles, was not examined. However, recent *ab initio* calculations (MP2/6-31 G**) and calculations at the B3LYP/6-31 G** level¹¹² demonstrated that 1,3-sigmatropic shifts of the oxygen and chalcogen atoms around the four-membered ring can occur in metastable Dewar isomers of furan, thiophene, selenophene and tellurophene **43** (X = O, S, Se, Te). The energy barriers estimated for these processes are no higher than 25 kcal mol^{−1}. The results of these calculations are given in Table 3 and Fig. 5.

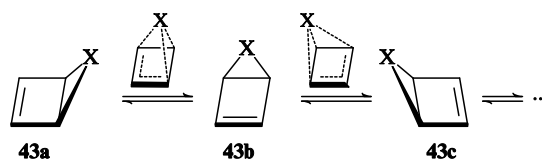


Table 3. Relative energies (ΔE) (compared to the aromatic structure) and energy barriers ($\Delta E^\ddagger$) for the rearrangements of the Dewar isomers of five-membered heterocycles **43**.¹¹²

X in 43	$\Delta E^\ddagger$ /kcal mol ^{−1}		ΔE /kcal mol ^{−1}	
	MP2/6-31G**	B3LYP/6-31G**	MP2/6-31G**	B3LYP/6-31G**
O	66.6	67.8	23.2	16.1
S	57.2	57.2	26.4	16.0
Se	50.8	52.0	21.7	13.9
Te ^a	50.0	50.3	21.2	10.2

^a The energy parameters for tellurium compounds were calculated using the LanL/2DZ orbital basis set.

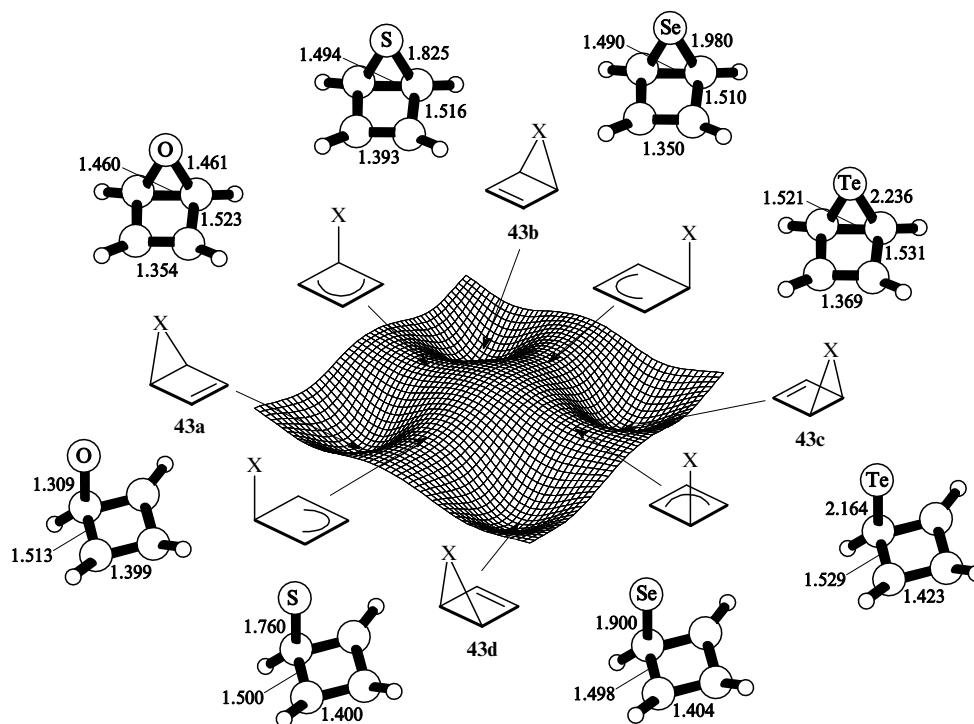


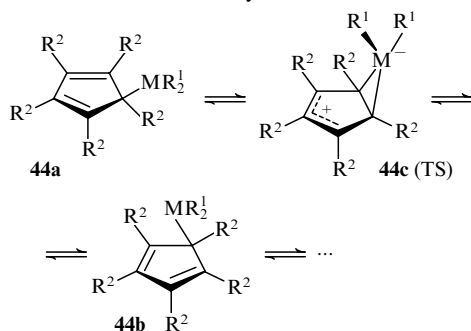
Figure 5. Topology of PES for the 1,3-sigmatropic rearrangements of Dewar isomers of furan, thiophene, selenophene and tellurophene according to the results of *ab initio* calculations (MP2/6-31G**) ¹¹² and geometric parameters of the starting (at the top) and transition (at the bottom) structures.

VI. Circumambulatory rearrangements of element-centred migrating groups in the cyclopentadiene ring

Cyclopentadiene and its derivatives belong to the most important group of ligands in the chemistry of coordination compounds. That is the reason why their structures and dynamic behaviour associated with circumambulatory rearrangements were studied in close detail. Let us consider these rearrangements by classifying them according to the position of the central atom of the migrating group in the Periodic table.

1. Migrating substituents formed by Group 13 elements

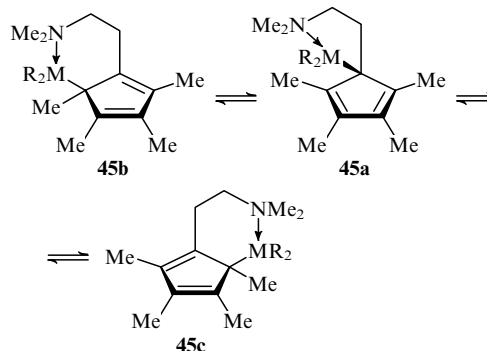
Circumambulatory rearrangements of the migrating groups BR_2 , AlR_2 , GaR_2 and InR_2 ($\text{R} = \text{Alk}, \text{F}, \text{Cl}, \text{Br}, \text{I}$) in unsubstituted and transmethyated cyclopentadiene rings proceed rather rapidly ($\Delta G^\ddagger \leq 20 \text{ kcal mol}^{-1}$). Consequently, completely averaged ^1H or ^{13}C NMR spectra of compounds **44** were recorded at normal temperatures.^{16, 20, 26, 113} Although direct experimental evidence supporting the mechanism of these rearrangements is lacking, one can say with a fair degree of assurance that each step involves the 1,2-shift ([1,5]-sigmatropic shift) of the migrating group. This conclusion was confirmed by MNDO calculations.¹¹⁴



$\text{R}^2 = \text{H}, \text{Me}.$

In the presence of electron-releasing groups R in the migrating centre, the rate of rearrangements substantially decreases. As a result, the energy barriers to migration of the $\text{B}(\text{NMe}_2)_2$, $\text{B}(\text{OMe})_2$ and $\text{B}(\text{SEt})_2$ groups in the pentamethylcyclopentadienyl ring become measurable on the NMR time scale ($\Delta G_{25}^\ddagger = 17.2$, 14.4 and 10.2 kcal mol^{-1} , respectively).¹¹⁵ In pentamethylcyclopentadienylboranes in which the boron atom is coordinated by the pyridine molecule (lone electron pair on the nitrogen atom of the pyridine ring fills the unoccupied p orbital of the boron atom), the rearrangement is completely decelerated ($\Delta G_{25}^\ddagger > 25 \text{ kcal mol}^{-1}$).

An interesting rearrangement of a series of aluminium, gallium, and indium derivatives of 1-dimethylaminoethyl-2,3,4,5-tetramethylcyclopentadiene **45** was described.¹¹⁶ The ^1H and ^{13}C NMR spectra of compound **45** have two singlets in a ratio of 1 : 1 belonging to four Me groups at the carbon atoms of the cyclopentadiene ring, the spectral pattern being temperature-independent. The presence of the intramolecularly coordinated $\text{Me}_2\text{NCH}_2\text{CH}_2$ substituent restricts the shifts of the migrating substituents formed by Group 13 elements to only the adjacent carbon atoms. Hence, the dynamic behaviour is determined by



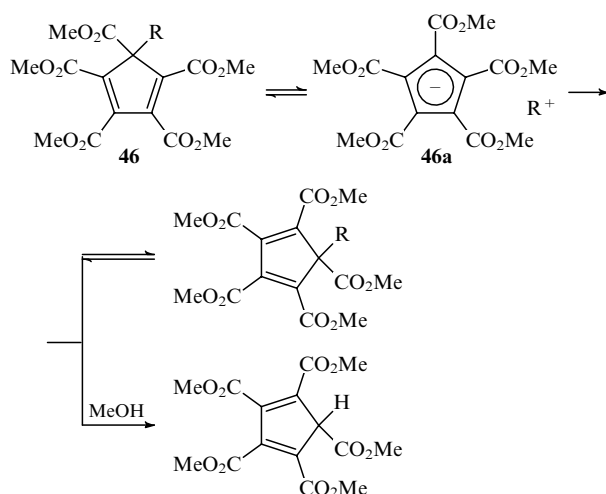
$\text{M} = \text{Al}, \text{R} = \text{H}, \text{Me}, \text{Et}, \text{Cl}, \text{Br}, \text{I}; \text{M} = \text{Ga}, \text{R} = \text{Cl}; \text{M} = \text{In}, \text{R} = \text{Cl}.$

rearrangements between isomers **45a–c**, which allowed the authors of the study¹¹⁶ to compare this mechanism with the movement of windscreen wipers.

2. Migrating substituents formed by Group 14 elements

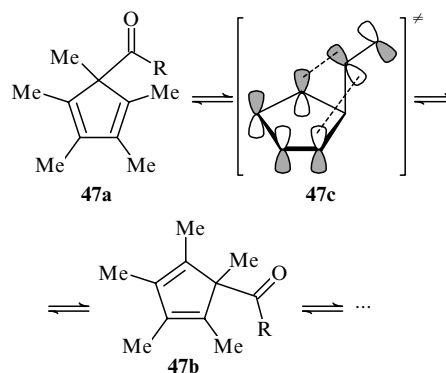
1,2-Alkyl shifts in the cyclopentadiene ring can be observed at temperatures higher than 300 °C, which corresponds to activation free energies higher than 40 kcal mol^{−1}.¹⁸ According to more accurate data obtained for the rearrangement of hexamethylcyclopentadiene containing one trideuteriomethyl group, the activation barrier to migration of the CH₃ or CD₃ group is 43.1 kcal mol^{−1}.¹¹⁷ In 5-(*p*-nitrobenzyl)-1,2,3,4,5-pentamethoxycarbonylcyclopentadiene, the migration of the *p*-nitrobenzyl group requires that the energy barrier of 30 kcal mol^{−1} should be overcome,¹¹⁸ which is close to the condition of structural non-rigidity ($\Delta G_{25}^\ddagger \leq 25$ kcal mol^{−1}).

It was hypothesised¹¹⁹ that circumambulatory rearrangements of 5-R-1,2,3,4,5-pentamethoxycarbonylcyclopentadiene derivatives **46** in polar solvents can be controlled by the ionisation–recombination mechanism involving heterolysis of the C_{sp}³–C_{Cp} bond. Actually, compounds **46** dissociate in methanol to form solvated ion pairs **46a**. Apparently, the collapse of the ion pairs giving rise to topomers **46** (degenerate circumambulatory rearrangement) can compete with the irreversible reaction with the solvent.

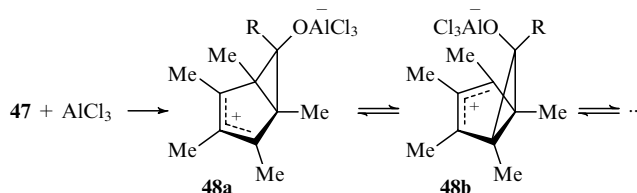


R = CH₂OMe, CHPh₂, CH₂C₆H₄OMe-4, adamantan-1-yl.

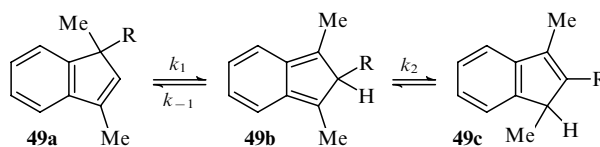
C_{sp}²-Centred groups have higher ability to migrate around the five-membered ring as compared to C_{sp}³-centred groups. The energy barrier ($\Delta G_{25}^\ddagger$) to the 1,2-shift of the phenyl group in 5-deuteriomethyl-1,2,3,4-tetramethyl-5-phenylcyclopentadiene is 37.8 kcal mol^{−1}.¹²⁰ Thermal rearrangements of a series of 5-substituted pentamethoxycarbonylcyclopentadienes^{121, 122} proceed as successive 1,2-shifts of the substituent, the energy barrier to this migration is only slightly higher than 25 kcal mol^{−1}. At 25 °C, the migration of the formyl group in 5-formyl-1,2,3,4,5-pentamethylcyclopentadiene **47** (R = H) proceeds much more rapidly ($k = 90$ s^{−1}); its energy barrier is only 14.8 kcal mol^{−1}.¹²³ This rearrangement is favoured by a secondary orbital interaction involving π -HOMO of the cyclopentadiene fragment and π^* -LUMO of the carbonyl group in transition state structure **47c**. Semiempirical calculations by the MINDO/3 method¹²⁴ confirmed that the orbital interaction of this type makes a substantial contribution to stabilisation of transition state structure **47c**.



In compound **47** (R = H), the formyl group undergoes rapid circumambulatory rearrangements in the five-membered ring, whereas other 5-acyl derivatives of 1,2,3,4,5-pentamethylcyclopentadiene are structurally rigid. To decrease the energy barrier to migration of the above-mentioned groups, powerful electron-withdrawing substituents, such as the trifluoro- or trichloromethyl group, should be introduced into the acyl fragment. The energy barriers ($\Delta G_{25}^\ddagger$) to migration of these groups around the pentamethylcyclopentadiene ring are 20.6 (hexachlorobutadiene) and 25.4 kcal mol^{−1} (DMF-d₇), respectively.¹²⁵ The coordination of the acyl oxygen atom by Lewis acid provides an alternative and more efficient way of accelerating the migration of the acyl group.¹²⁶ Upon the formation of complexes with AlCl₃, compounds **47** form bicyclic zwitterions **48**, which undergo circumambulatory rearrangement involving a series of 1,3-shifts of the cyclopropane fragment (η^2 – η^3 mechanism). The energy barriers to this rearrangement depend on the ability of the substituent R in zwitterion **48** to stabilise the positive charge and their values vary from ~ 5 (R = C₆H₄CF₃) to 10.9 (R = Me) and then to 18.2 kcal mol^{−1} (R = C₆H₄OEt).¹²⁶



Annulation of the benzene ring onto cyclopentadiene leads to an increase in the energy barrier to 1,2-shifts of carbon-centred groups by 9–11 kcal mol^{−1}. Because of this, thermal rearrangements in indene derivatives cannot be detected on the NMR time scale. In studies,^{127–129} the migration abilities of various C_{sp}³-, C_{sp}²- and C_{sp}-centred groups were examined using optically active 1,3-dimethylindenes **49**.



If the migration of the groups R proceeds more slowly than the migration of the hydrogen atom in 2*H*-indene **49b** ($k_2 > k_{-1}$), the rate of formation of compound **49c** can serve as a measure of the migration ability. If the group R undergoes more rapid migration compared to the hydrogen atom in molecule **49b** ($k_{-1} > k_2$), as in the case of R = CHO or Ar, the constant k_1 can be estimated based on the racemisation rates of optically active indenenes. The migration ability of the groups R thus estimated decreases in the following series: CHO > Acyl > H > CH=CH₂ > CO₂Me > C≡N > C≡CH > Ph > 1-naphthyl > Alk.^{127–129}

The migration ability of groups increases with increasing atomic number of the element within the same group of the Periodic table, as evidenced by a substantial acceleration of the rearrangements of the SiR_3 , GeR_3 , SnR_3 and PbR_3 migrating groups as compared to alkyl groups. Even a qualitative analysis of the ^1H NMR spectra of 5-trimethylsilylcyclopentadiene⁴² revealed the pronounced fluxional behaviour of this compound. More recent studies demonstrated that the energy barriers to migration of the trimethylsilyl group around the cyclopentadiene ring are $\sim 15 \text{ kcal mol}^{-1}$. These energies are most convenient for studying the kinetics and permutation mechanisms by dynamic NMR spectroscopy. This is the reason why the migration processes in silylcyclopentadienes have attracted particular attention in early studies of circumambulatory rearrangements (see, for example, the reviews^{15–17, 19, 20}). Generally, the 1,2-shifts of tin and lead-containing migrating groups in the five-membered ring of various cyclopentadiene derivatives proceed at very high rates, which cannot be measured directly using standard techniques of ^1H or ^{13}C NMR spectroscopy.^{130–132} The energy barriers to 1,2-shifts of substituents formed by Group 14 elements are given in Table 4.

Table 4. Energy barriers ($\Delta G^\ddagger$) to the 1,2-shifts of Si-, Ge- and Sn-centred groups (M) in cyclopentadiene derivatives $\text{C}_5\text{R}_5\text{M}$.

M	R	$\Delta G^\ddagger_{27} / \text{kcal mol}^{-1}$	Ref.
SiH_3	H	13.6	133
SiH_2Cl	H	12.9	133
SiHCl_2	H	13.5	133
SiMe_3	H	15.2	20
SiMe_2Cl	H	15.5	20
SiMeCl_2	H	15.9	20
SiCl_3	H	16.3	20
SiMe_3	Me	15.3 ^a	134
SiCl_3	Me	13.1 ^a	134
GeMe_3	H	13.9	135
GeMe_3	Me	< 11	136
GeCl_3	Me	11.9	136
SnCl_3	H	7.5	135

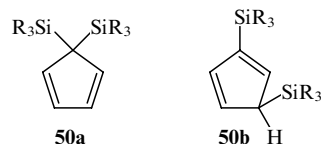
^a The activation energy (E_a).

Unlike the rearrangements of cyclopentadiene derivatives in which the migrating fragments are formed by Group 13 elements, the barriers to rearrangements of cyclopentadienylsilanes, -germanes and -stannanes are only slightly affected by substituents at the central atom of the migrating fragment. This is attributed to the absence of the low-lying unoccupied p orbital in the sp^3 -hybridised central atoms of the SiR_3 and GeR_3 groups (transition state structure **10a**), which plays an important role in stabilisation of the transition state structures of the migrating fragments of Group 13 elements.

The mechanism of rearrangements of η^1 -indenyl derivatives of main-group elements was analysed in the review,¹³⁷ where the reactivities of these compounds and indenyl derivatives of transition metals were surveyed and their use as precursors of chiral metallocene catalysts was discussed. The conclusion that migrations of the Si-, Ge-, Sn- and Pb-centred groups around the ring proceed as [1,5]-sigmatropic shifts giving rise to short-lived isoindene intermediates was demonstrated to be of general character.

Rearrangements of cyclopentadiene derivatives containing two or three SiR_3 groups in the ring were studied in detail by Ustynyuk and co-workers⁴⁴ and other researchers.²⁶ The equilibrium mixtures of di- SiR_3 -substituted cyclopentadienes bearing no other substituents in the ring can contain up to seven isomers, which are generated as a result of a series of 1,2-shifts of hydrogen atoms and SiR_3 groups in the ring. However, only two isomers,

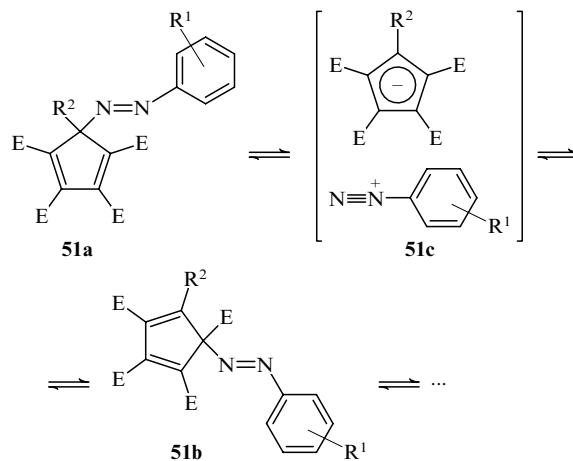
viz., **50a** and **50b**, are usually observed. These isomers are produced by successive 1,2-shifts of the SiR_3 groups, the first isomer being the major product. The high stability of compound **50a** results from the hyperconjugative π -aromaticity of 5,5-disubstituted cyclopentadienes containing electropositive groups, such as SiR_3 , GeR_3 or SnR_3 .¹³⁸



3. Migrating substituents formed by Group 15 elements

a. Nitrogen-centred migrating groups

Ionisation–recombination mechanism. Circumambulatory migrations of N-centred substituents around the five-membered ring were first studied for arylazocyclopentadienes **51** whose rearrangements proceed through the ionisation–recombination mechanism.^{38, 39}



$\text{E} = \text{CO}_2\text{Me}$; $\text{R}^2 = \text{CO}_2\text{Me}, \text{Me}$ (for notations of R^1 , see Table 5).

The design of these rearrangements is based on the strategy opposite to that used for cyclopropene derivatives (see Sections III.1 and IV.1). It was demonstrated that there is a rather fine balance between the relative stabilities of covalent (**51a**, **51b**) and ionic (**51c**) isomers of arylazocyclopentadienes. To stabilise intermediate ion pair **51c**, the negative charge of the aromatic cyclopentadienyl anion should be additionally delocalised by introducing π -acceptor substituents into the Cp ring. For example, heating of arylazopentamethylcyclopentadienes **51** ($\text{R}^1 = \text{NO}_2$, $\text{R}^2 = \text{E} = \text{Me}$) did not lead to the heterolysis of the $\text{C}_{\text{Cp}}-\text{N}$ bond; instead, the rearrangement involved the migration of the arylazo group to the adjacent carbon atom.¹³⁹ At the same time, electron-releasing substituents in the benzene ring stabilise excessively ion pair **51c**, which becomes the major form of existence of compounds **51** ($\text{E} = \text{CO}_2\text{Me}$). In the solid state, such isomers of arylazopentamethoxycarbonylcyclopentadienes prevail even in the case of $\text{R}^1 = 4'\text{-NO}_2$ (Fig. 6).

At low temperature, mono-, di- and trinitrophenylazo derivatives **51** exist in benzonitrile as covalent compounds, which readily dissociate to form ion pairs **51c** upon heating. The collapse of the latter leads to the randomisation of the position of the arylazo group in the ring and, consequently, to the circumambulatory migration around the cyclopentadiene ring. The rate constants and activation parameters for the rearrangements of compounds **51** proceeding according to the ionisation–recombination mechanism are given in Table 5. For solutions of arylazo derivatives **51** in acetonitrile, these parameters are concentration-independent in the range of $0.03\text{--}0.30 \text{ mol litre}^{-1}$, which is indicative of the intramolecular nature of these rearrangements.

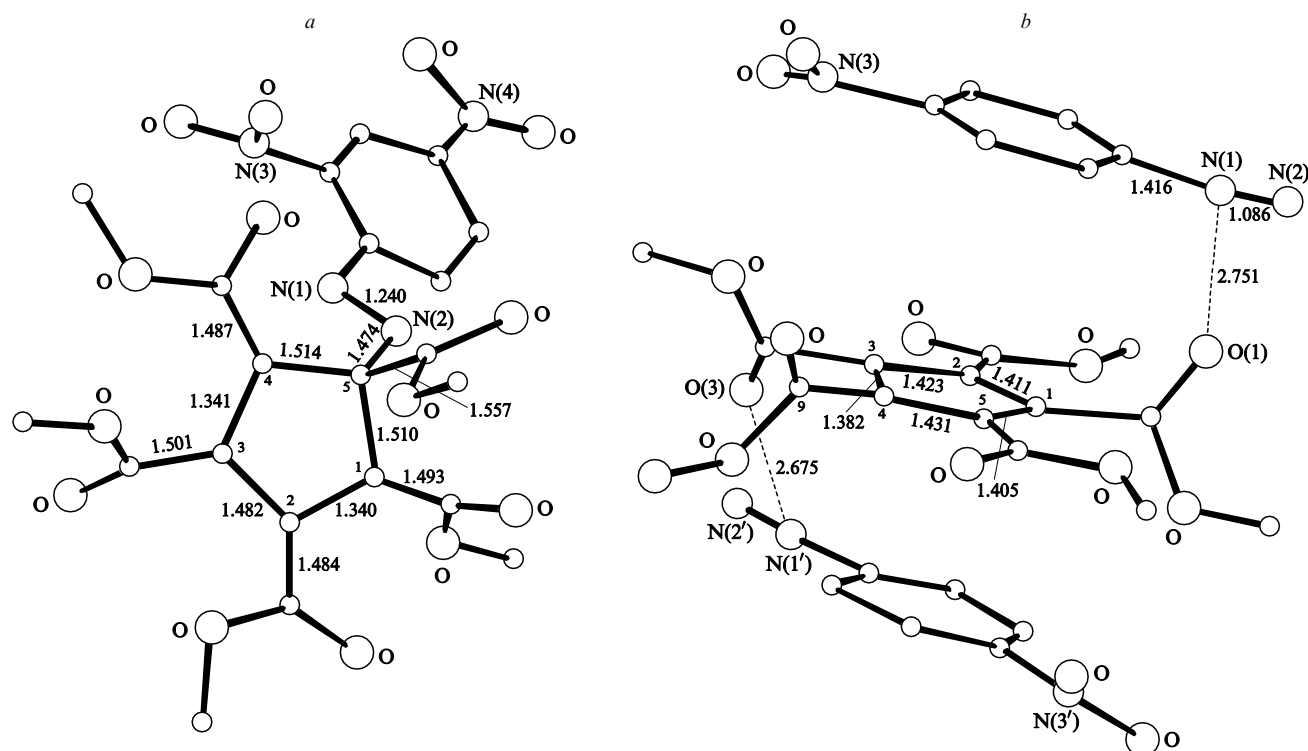
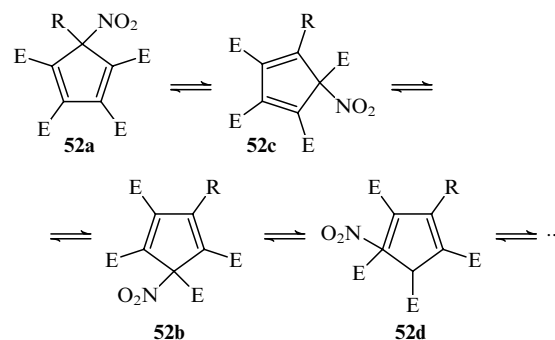


Figure 6. Molecular structures of 5-(2,4-dinitrophenylazo)-1,2,3,4,5-pentamethoxycarbonylcyclopentadiene (**a**) and 5-(4-nitrophenylazo)-1,2,3,4,5-pentamethoxycarbonylcyclopentadiene **51** (**b**) according to the results of X-ray diffraction analysis.^{38,39}

Heating of solutions of arylazopentamethoxycarbonylcyclopentadienes led to elimination of molecular nitrogen followed by rearrangements of the resulting arylpentamethoxycarbonylcyclopentadienes caused by 1,2-shifts of the methoxycarbonyl group around the five-membered ring.^{121, 122, 140}

1,2-Shifts. The slow degenerate circumambulatory rearrangements of 1,2,3,4,5-pentamethyl-5-nitrocyclopentadiene ($\Delta G_{172}^\ddagger = 25.1$ kcal mol⁻¹ in DMSO)¹⁴¹ and 1,2,3,4,5-pentamethoxycarbonyl-5-nitrocyclopentadiene ($\Delta G_{25}^\ddagger = 24$ kcal mol⁻¹ in chlorobenzene) and non-degenerate rearrangements of 5-alkyl(benzyl)-5-nitro-1,2,3,4-tetramethoxycarbonylcyclopentadienes **52a**¹⁴² proceed as 1,2-shifts ([1,5]-sigmatropic shifts) around the periphery of the cyclopentadiene ring. Compounds **52a** were prepared as mixtures with their isomers **52b** (in a ratio of ~ 1 : 1) by nitration of the corresponding cyclopentadienes in acetic anhydride at 50 °C and were then separated by chromatography. The energy barriers to the 1,2-shifts of the nitro group ($\Delta G_{25}^\ddagger = 24.0$ –26.6 kcal mol⁻¹) were determined from the

kinetics of establishment of an equilibrium between these isomers, which involves two successive 1,2-shifts of the nitro group proceeding through the intermediate formation of isomer **52c** (which was not observed by ¹H NMR spectroscopy due to its low equilibrium concentration).



R = CO₂Me, Me, CHMe₂, CH₂Ph.

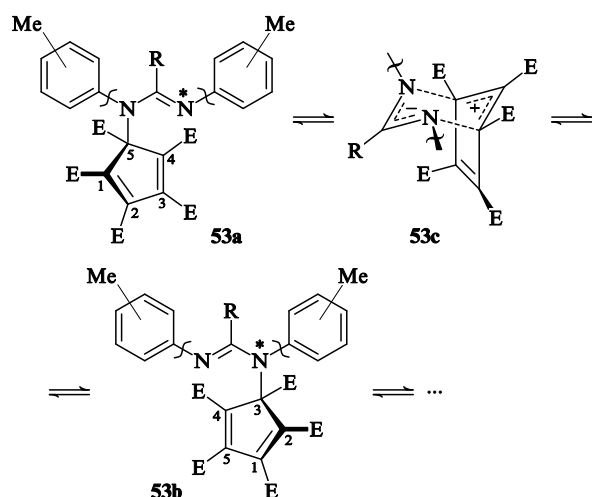
Table 5. Kinetic and activation parameters for the migration of the arylazo groups in 5-arylazo-1,2,3,4,5-pentamethoxycarbonylcyclopentadienes **51** (R² = CO₂Me) in benzonitrile.^{38,39}

R ¹ in compound 51	k_{25} /s ⁻¹	$\Delta H^\ddagger$ /kcal mol ⁻¹	$\Delta S^\ddagger$ (see ^a)	$\Delta G_{25}^\ddagger$ /kcal mol ⁻¹
4'-NO ₂	9×10^2	11.1 ± 0.8	-7.7 ± 1.2	13.4
2'-NO ₂	6.3×10^2	13.3 ± 0.7	-0.9 ± 1.0	13.6
2'-I, 4'-NO ₂	6.3×10^2	14.2 ± 0.6	-1.3 ± 1.1	13.6
2'-Cl, 4'-NO ₂	5.4×10^2	11.3 ± 0.5	-8.2 ± 1.0	13.7
2'-Br, 4'-NO ₂	4.6×10^2	11.7 ± 0.6	-7.0 ± 1.1	13.8
2',4'-(NO ₂) ₂	1.0×10^2	9.9 ± 0.5	-16.1 ± 1.0	14.7
2',6'-(NO ₂) ₂	7.2×10^1	11.5 ± 0.7	-11.4 ± 1.3	14.9
2',4',6'-(NO ₂) ₃	7.8	11.4 ± 0.7	15.4 ± 1.3	16.0

^a $\Delta S^\ddagger$ are given in cal mol⁻¹ deg⁻¹.

All attempts to synthesise nitrosocyclopentadiene derivatives failed. The rearrangements of these compounds were theoretically simulated by the semiempirical MINDO/3 method.¹⁴³ These calculations revealed two energetically almost equivalent transition state structures corresponding to the 1,2- and 1,3-shifts of the nitroso group. The relatively high stability of the latter structure is attributed to the fact that it conforms to the rules of electron calculation for pyramidal structures of this type.^{30,31}

[3,3]-Sigmatropic shifts. *N,N'*-Diaryl-*N*-(1,2,3,4,5-pentamethoxycarbonylcyclopentadienyl)amidines **53** generated by the reactions of *N,N'*-diarylamidines with compounds **52** (R = CO₂Me) underwent rapid degenerate rearrangements involving successive [3,3]-sigmatropic shifts of the amidinyl groups.^{144,145}



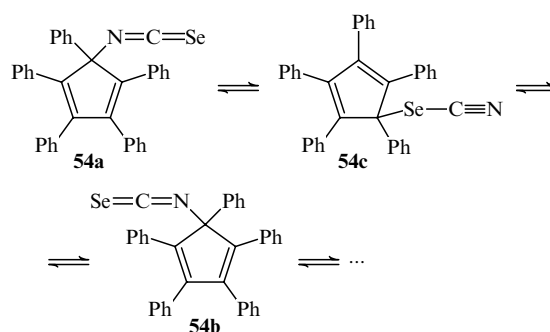
The fact that the rearrangements proceed as successive 3,3-shifts rather than as 1,2-shifts of the amidinyl groups is confirmed by the simultaneous averaging of the signals of the methyl groups of the aryl and methoxy fragments in the ^1H NMR spectra of solutions of diarylamidines **53** in hexachlorobutadiene observed at high temperatures. The kinetic parameters (Table 6) of the rearrangements, which were calculated based on analysis of full line shapes of both groups of indicator signals, are identical to each other. Quantum-chemical calculations (see Section III.8) provide additional evidence supporting the [3,3]-sigmatropic shifts (hetero-Cope rearrangement) in the amidinylcyclopentadiene molecules.

Table 6. Kinetic and activation parameters for the circumambulatory rearrangements of amidinylcyclopentadienes **53** in hexachlorobutadiene.¹⁴⁵

R, position of Me in compound 53	k_{90} /s ⁻¹	$\Delta H^\ddagger$ /kcal mol ⁻¹	$\Delta S^\ddagger$ (sec ^a)	$\Delta G_{90}^\ddagger$ /kcal mol ⁻¹
Ph, 4-Me	0.17	22.5 ± 0.4	-1.5 ± 0.5	22.7
1-Naphthyl, 4-Me	3.9	15.1 ± 0.3	-14.7 ± 0.3	20.4
1-Naphthyl, 3-Me	2.0	15.7 ± 0.4	-14.3 ± 0.9	20.9

^a $\Delta S^\ddagger$ are given in cal mol⁻¹ deg⁻¹.

The thermal rearrangement of 5-isoselenocyanato-1,2,3,4,5-pentaphenylcyclopentadiene (**54a,b**) is an example of non-degenerate circumambulatory rearrangements in the cyclopentadiene system proceeding as [3,3]-sigmatropic shifts.¹⁴⁶ In solutions, this compound is in equilibrium with isomeric selenocyanate **54c** (in ratios of 3 : 2 and 2 : 3 in CDCl_3 and toluene- d_8 , respectively). The isothiocyanate derivative of pentaphenylcyclopentadiene does not exhibit fluxional behaviour in solutions (as well as 5-isothiocyanato-1,2,3,4,5-pentamethylcyclopentadiene¹⁴⁷), whereas the ^1H and ^{13}C NMR spectra of an equilibrium mixture of selenium-containing analogues **54a–c** are temperature-dependent. This indicates that two different competitive circumambulatory rearrangements proceed simultaneously. The more rapid rearrangement involves 1,2-shifts of the selenocyanate group around the five-membered ring (see Section VI.4.3), whereas the slower rearrangement ($\Delta G_{135}^\ddagger = 22$ kcal mol⁻¹) is associated with interconversions of isomers as a series of successive [3,3]-sigmatropic shifts involving all carbon atoms of the ring.



b. Phosphorus-centred migrating groups

In the unsubstituted cyclopentadiene ring, migrations of phosphorus-centred groups and hydrogen atoms proceed at similar rates, although in most cases the rates of 1,2-shifts of the P-centred migrating groups are higher than those of the hydrogen atoms.^{26, 148} The ability of phosphorus-centred groups to migrate was estimated by studying the kinetics of circumambulatory rearrangements of compounds in which non-migrating substituents are bound to all carbon atoms of the cyclopentadiene ring. The energy barriers (E_a) to 1,2-shifts of selected phosphorus-centred groups M in the $\text{C}_5\text{Me}_5\text{M}$ molecules are given below.¹⁴⁹

M	E_a /kcal mol ⁻¹	M	E_a /kcal mol ⁻¹
P=C(SiMe ₃) ₂	< 8	PCl ₂	12.0 ± 1.6
PH ₂	31.3 ± 1.8	PBr ₂	5.2 ± 3.1
PMe ₂	23.0 ± 0.5	P(CN) ₂	16.4 ± 0.3
PMeCl	16.4 ± 1.1	P(OMe) ₂	21.2 ± 0.4
PBu ^t Cl	21.3 ± 1.5	P(SMe) ₂	17.5 ± 1.3
PPh ₂	24.3 ± 1.5	PMe ₃ ⁺	> 35
PF ₂	16.7 ± 0.7	PR ₂ Cr(CO) ₅	> 35

Compounds containing two-coordinate phosphorus atoms exhibit a pronounced fluxional behaviour, whereas compounds containing four-coordinate phosphorus atoms are structurally rigid. The migration ability of the P(III)-centred groups sharply increases with increasing electronegativities of the ligands bound to the phosphorus atom. This fact can be explained taking into account the stabilising interaction between the orbitals of the lone electron pair on the P(III) centre and LUMO of the cyclopentadiene fragment: the electronegative ligands decrease the energy level of the orbital of the lone pair, and the energy gap between the above orbitals is narrowed. According to the results of MNDO calculations,¹⁵⁰ the 1,2-shifts of P(III)-centred migrating groups can proceed either with retention or inversion of configuration at the phosphorus atom depending on the type of the ligands bound to this atom. Thus, electropositive ligands facilitate the inversion of configuration at the migrating centre, whereas electronegative ligands are favourable for the retention of configuration. The tendency to retention of configuration increases in the series P < As < Sb.

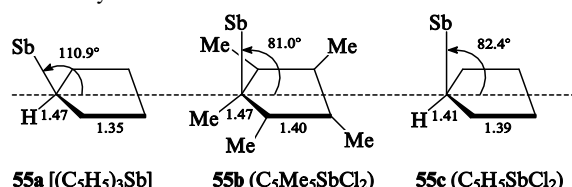
c. Arsenic- and antimony-centred migrating groups

It was found that ligands bound to Group 15 elements have an analogous effect on the ability of these elements to undergo migration in cyclopentadienyl compounds of arsenic and antimony. The 1,2-shifts of the AsMe₂ groups in $\text{C}_5\text{H}_5\text{AsMe}_2$ and the shifts of the AsCl₂ group in $\text{C}_5\text{H}_5\text{AsCl}_2$ are characterised by the energy barriers $E_a = 15.0$ kcal mol⁻¹ and $E_a < 7$ kcal mol⁻¹, respectively. There is a pronounced tendency for a substantial increase in the migration ability of the groups formed by heavier elements on going from P- to As- and Sb-centred migrating groups. The activation energies for the circumambulatory rearrangements of dimethyl(1,2,3,4,5-pentamethylcyclopenta-

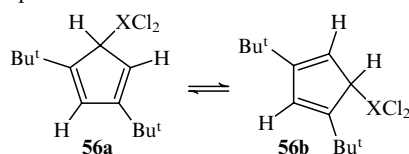
dienyl)phosphane, -arsane and -stibane are 23.0, 17.1 and 11.3 kcal mol⁻¹, respectively.²⁶

1,2,3,4,5-Pentamethylcyclopentadienyldihaloarsanes C₅Me₅.AsHal₂ (Hal = F, Cl, Br, I) are characterised by pronounced structural non-rigidity. Even at -90 °C, the ¹H NMR spectra of these compounds have only narrow singlets for the protons of the Me groups. In the ¹³C NMR spectra, the sp³- and sp²-hybridised carbon atoms and the carbon atoms of the Me groups¹⁵¹ also give common singlets. Moreover, attempts to freeze the migration of the AsHal[N(SiMe₃)₂] group in monoamide-substituted arsanes on the NMR time scale failed.¹⁵²

High rate constants of 1,2-shifts of migrating heavy Group 15 elements are attributed to the fact that there are favourable conditions for interactions between the π orbitals of the central atom and the cyclopentadienyl fragment in these compounds.^{152, 153} A comparison of the structures¹⁵³ of three fluxional stibanes **55a–c**, for which an increase in non-rigidity would be expected on going from unsubstituted compound **55a** to dichloride **55c**, showed that the mode of binding gradually changes from η¹(σ) to η³(π). In molecule **55c**, the C–C bond lengths in the five-membered ring are equalised, which is indicative of an increase in the ionicity of the compound giving rise to the symmetrical cyclopentadienyl anion. The sequence of structures **55a–55c** reflects a part of the pathway of the 1,2-shift of heavy migrating substituents formed by Group 15 elements in cyclopentadiene systems.

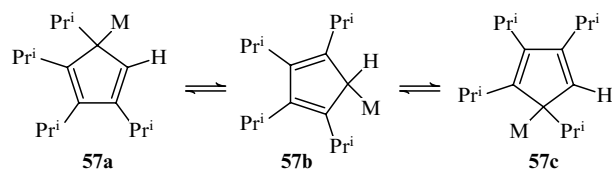


The bulky substituents in the cyclopentadiene ring influence both the relative stabilities of isomers generated in the course of circumambulatory rearrangements and the energy barriers to 1,2-shifts of the migrating groups M = XR₂ (X = P, As, Sb). For example, di-*tert*-butylcyclopentadienyl derivatives of arsanes and stibanes **56** occur primarily as isomers containing the substituent M in the allyl position and two *tert*-butyl groups in vinyl positions. The rearrangements involve shifts of the migrating groups between two vicinal carbon atoms of the ring.¹⁵⁴



X = As, Sb.

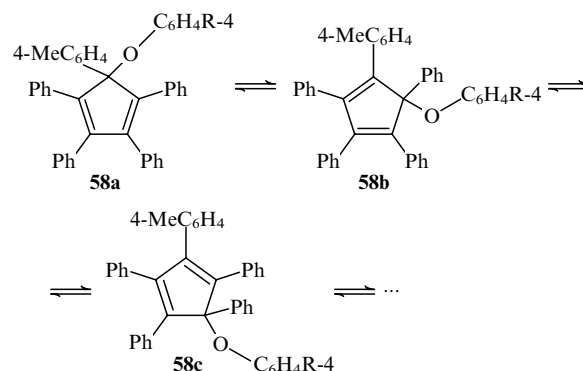
5-M-(1,2,3,5-Tetraisopropyl)cyclopentadienes **57** (M = PCl₂, PBr₂, AsCl₂ and SbCl₂) have different dynamics.¹⁵⁵ Analysis of the ¹H NMR spectra showed that the rearrangements caused by migrations of the PCl₂ (*E*_a = 13.1 ± 0.3 kcal mol⁻¹) and PBr₂ (*E*_a = 13.2 ± 0.3 kcal mol⁻¹) groups proceed as 1,2-shifts of the phosphorus atoms in space limited only by the carbon atoms of the ring adjacent to the CH centre, whereas the C(1) and C(2) atoms remain intact.



4. Migrating substituents formed by Group 16 elements

a. Oxygen-centred migrating groups

1,2-Shifts of oxygen-centred migrating groups around the cyclopentadiene ring proceed too slowly to be detected by dynamic NMR spectroscopy. Investigation of the kinetics of migrations of aryloxy groups is based on measurements of the lifetimes of individual isomers of 1,2,3,4,5-pentaaryl-5-aryloxycyclopentadienes **58**. For this purpose, a weak disturbance of degeneration of the rearrangement is required, which can be achieved, for example, by replacing one of the phenyl groups in the ring by the *p*-tolyl group.¹⁵⁶



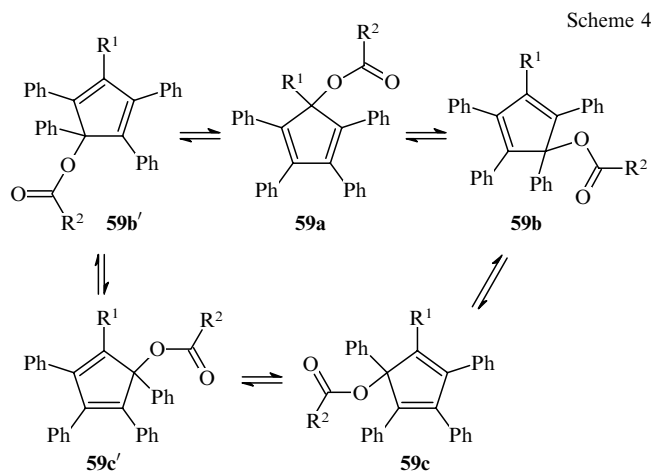
The energy barriers (averaged for the 1,2-OAr-shifts **58a** → **58b** and **58b** → **58c**) for the rearrangement of isomers of 5-aryloxy-1,2,3,4-tetraphenyl-5-*p*-tolylcyclopentadiene (180 °C, in diphenyl oxide) are given below.¹⁵⁶

R	NH ₂	OMe	Me	H	Cl	NO ₂
Δ <i>G</i> ₁₈₀ [‡] /kcal mol ⁻¹	23.8	24.6	24.8	25.5	26.3	31.6

It can be seen that the presence of electron-releasing substituents in the migrating groups facilitates this rearrangement, whereas electron-withdrawing substituents lead to its deceleration. These results provide evidence supporting polar transition state **10c**, which was proposed for [1,5]-sigmatropic shifts in cyclopentadiene molecules. Semiempirical quantum-chemical calculations¹⁴³ of the rearrangement of compound **58** also confirmed that the three-membered ring of the η²-transition state structure bears a positive charge. Semiempirical calculations showed the occurrence not only of the expected η² structure but also of the second η³-type transition state structure for the symmetry-forbidden 1,3-shift of the aryloxy group; the latter is energetically less favourable than the 1,2-OAr-shift (the energy difference is 8–10 kcal mol⁻¹).

The circumambulatory rearrangements caused by [3,3]-sigmatropic shifts of O-centred migrating groups are also characterised by high-energy barriers, which do not satisfy the conditions of structural non-rigidity.^{157, 158} The kinetic parameters for the rearrangements of acyloxycyclopentadienes **59** (R¹ = C₆H₄Me-4) were determined from the rate at which the equilibrium between isomers **59a**, **59b** and **59c** (which were prepared by treatment of a mixture of isomers of bromo-*p*-tolyltetraphenylcyclopentadiene with silver carbonates) was established in solution (Scheme 4). These parameters are given in Table 7.

The equilibrium ratios between isomers **59** correspond to the statistical distribution **59a**:**59b**:**59c** = 1:2:2. The rearrangement rate is concentration-independent. No paramagnetic intermediate species were detected in the temperature range of 25–160 °C, which is indicative of the concerted intramolecular mechanism of the reaction. The fact that the rearrangement proceeds *via* [3,3]-sigmatropic shifts, *i.e.*, as the sequence **59a** ⇌ **59b** ⇌ **59c** ⇌ **59c'** ⇌ **59b'** ⇌ **59a** (see Scheme 4), rather than *via* the alternative [1,5]-sigmatropic shift as the sequence **59a** ⇌ **59c'** ⇌ **59b** ⇌ **59b'** ⇌ **59c** ⇌ **59a** was proved in the study of the time dependence of the ¹H NMR spectra of 5-ben-



zyl-1,2,3,4-tetra-phenyl-5-trifluoroacetoxycyclopentadiene **59a** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$) (Fig. 7).

Due to the presence of the stereogenic C_{sp^3} centre in the ring of isomers **59c,c'** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$), the energetically favourable reaction pathway can be readily identified based on ^1H NMR spectra, which show diastereotopic splitting of the signals for the methylene protons of the benzyl substituent R^1 characteristic of the prochiral methylene group (AB spectrum, δ 2.88 and 3.97, $^2J = 14.5$ Hz). In the ^1H NMR spectrum of isomers **59b,b'** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$) in which the stereogenic C_{sp^3} centre is most far removed from the prochiral group, this splitting is absent. The assignment of the singlets for the methylene protons at δ 3.48 and 3.62 to isomers **59a** (symmetry C_s) and **59b**, respectively, was made after their separation and was also based on the X-ray diffraction data for compound **59a** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$).¹⁵⁷ In the course of storage of a solution of **59a** at 80 °C, a singlet (δ 3.62) assigned to the methylene protons of isomer **59b** appeared and gradually grew in its ^1H NMR spectrum. Further heating led to slow accumulation of isomer **59c** in the reaction mixture, which was detected from the appearance of the AB quartet of the methylene group. The equilibrium between interconvertible isomers of **59** (**59a** : **59b** : **59c** = 65 : 22 : 13) was established upon storage of a solution in *o*-dichlorobenzene at 80 °C for 2 h. This spectral behaviour is unambiguously indicative of a sequence of interconversions of isomers **59** corresponding to the mechanism of [3,3]-sigmatropic shifts (see Scheme 4). The activation free energies ($\Delta G_{80}^\ddagger$) of interconversions of different isomers **59** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$) calculated from the time dependence of the intensities of the signals in the ^1H NMR spectra are in the range of 26.5–27.2 kcal mol⁻¹. The difference in the mechanisms of migrations of the aryloxy and acyloxy groups around the cyclopentadiene ring is manifested also in the difference in the influence of the substituents in the migrating group on the energy barrier for the rearrangement. As can be seen from Table 7, the

Table 7. Equilibrium ratios between the isomers at 130 °C, rate constants and activation parameters for the rearrangements of compounds **59** ($R^1 = \text{C}_6\text{H}_4\text{Me-4}$) in *o*-dichlorobenzene.¹⁵⁷

R^2 in compound 59	59a : 59b : 59c	k_{130} / s^{-1}	$\Delta H^\ddagger$ (see ^a)	$\Delta S^\ddagger$ (see ^b)	$\Delta G_{25}^\ddagger$ (see ^a)
CF_3	85 : 10 : 5	1.0×10^{-2}	24.0 ± 0.5	-3.6 ± 0.7	26.6
CCl_3	85 : 5 : 10	1.7×10^{-3}	25.9 ± 0.6	-7.4 ± 0.8	28.1
CHCl_2	75 : 15 : 10	1.9×10^{-4}	28.7 ± 0.5	-5.0 ± 0.7	30.2
CH_2Cl	60 : 20 : 20	4.4×10^{-6}	31.1 ± 0.7	-6.6 ± 0.9	33.0
CH_3	55 : 30 : 15	5.9×10^{-7}	33.6 ± 0.6	-4.1 ± 0.8	34.8

^a $\Delta H^\ddagger$ and $\Delta G_{25}^\ddagger$ are given in kcal mol⁻¹.

^b $\Delta S^\ddagger$ are given in cal mol⁻¹ deg⁻¹.

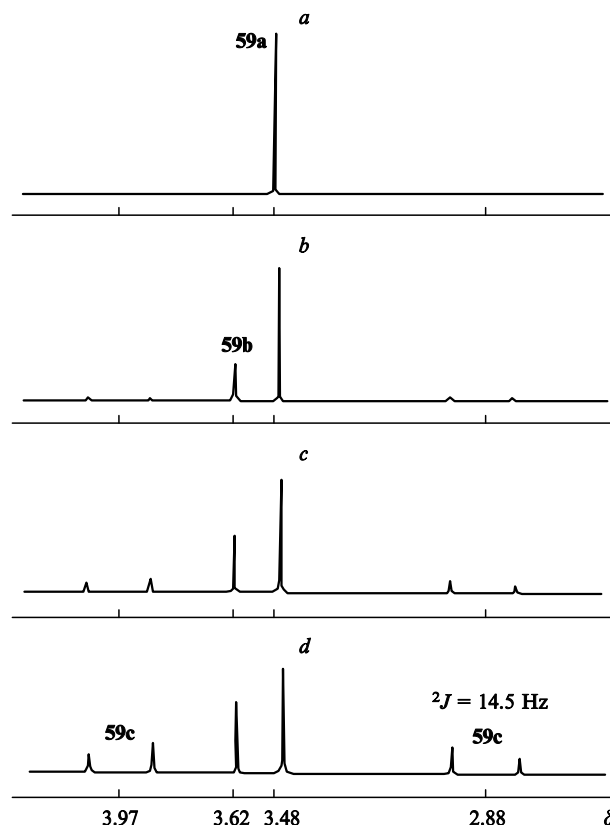


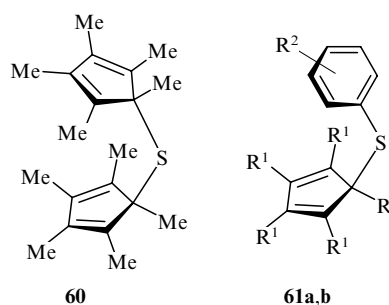
Figure 7. Time dependence of the ^1H NMR spectra of compounds **59** ($R^1 = \text{Bn}$, $R^2 = \text{CF}_3$) in *o*-dichlorobenzene in the region of signals for the protons of the benzyl group (δ 2.50–4.30) at 25 °C (a) and after heating at 80 °C for 0.5 (b), 1 (c) and 2 h (d).¹⁵⁷

rearrangements of compounds **59**, unlike the analogous rearrangements of aryloxypentaarylcyclopentadienes **58**, are accelerated upon the introduction of electron-withdrawing substituents R^2 into the migrating group.

Unlike the [3,3]-sigmatropic rearrangements of allyl acetates catalysed by mercury or palladium salts,¹⁵⁹ the circumambulatory rearrangements of their oxygen analogues **59** are rather weakly catalysed [$\Delta(\Delta G_{80}^\ddagger) = 1.3$ –2.9 kcal mol⁻¹] by $(\text{CF}_3\text{CO}_2)_2\text{Hg}$ and $[\text{PdCl}_2(\text{PhCN})_2]$. This can be attributed to steric hindrance to the formation of complexes of these salts with oxygen centres in tetra- and pentaaryl-substituted compounds **59**.

b. Sulfur-centred migrating groups

1,2-Shifts. The rearrangement of bis(pentamethylcyclopentadienyl) sulfide **60** was not observed on the NMR time scale.¹⁶⁰ However, the replacement of one pentamethylcyclopentadienyl fragment in molecule **60** by the aryl group gives rise to fluxional compounds **61a**; the energy barriers to migration of the arylthio



61: $R^1 = \text{Me}$ (a), CO_2Me (b) (for notations of R^2 , see Table 8).

group around the cyclopentadiene ring are in the range $\Delta G^\ddagger = 22\text{--}24.5\text{ kcal mol}^{-1}$.^{161, 162}

The replacement of the methyl groups in the cyclopentadienyl fragment of compound **61a** by the electron-withdrawing methoxycarbonyl groups leads to a substantial acceleration of the rearrangement.^{161, 163–166} As can be seen from Table 8, the energy barriers for degenerate rearrangements of compounds **61b** are 5–8 kcal mol^{−1} lower than the corresponding barriers for sulfides **61a** containing the same migrating groups. This observation and the fact that the electron-releasing substituents in the aryl rings of the migrating groups promote the rearrangement are consistent with polar transition state structure **10c** for 1,2-shifts in the cyclopentadiene system. Analysis of line shapes in the temperature-dependent ¹H and ¹³C NMR spectra of compounds **61a, b** and semiempirical (MINDO/3 and MNDO) calculations of the pathways of this rearrangement¹⁶⁷ demonstrated that 1,2-shifts are preferable for migrations of the arylthio groups.

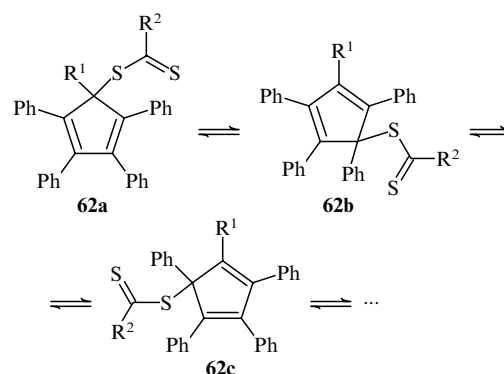
Table 8. Energy barriers ($\Delta G^\ddagger_{25}$) to 1,2-shifts of the arylthio groups in the cyclopentadiene ring of compounds **61**.

Structure	R ² in compound 61	Solvent	$\Delta G^\ddagger_{25}$ /kcal mol ^{−1}	Ref.
61a	4-OMe	<i>o</i> -dichlorobenzene	24.5	161, 163
61a	H	"	23.0	161, 163
61a	3-NO ₂	"	22.1	161, 163
61a	2,3,4,5,6-F ₅	DMSO-d ₆	23.2	162
61b	4-OMe	chlorobenzene	16.1	161, 163
61b	H	"	17.4	161, 163
61b	3-NO ₂	"	17.6	161, 163
61b	2-NO ₂	"	18.5	161, 163
61b	4-NO ₂	"	17.8	161, 163
61b	2,4-(NO ₂) ₂	"	19.0	161, 163
61b	4-CF ₃	"	20.7	161, 163

An interesting feature of compounds **61** is their half-sandwich structures, *i.e.*, the *s-cis* conformation with respect to the C_{CP}–S bond. This conformation is favourable for sulfides **60**¹⁶⁰ and, according to the results of X-ray diffraction studies, for tetra- and pentamethoxycarbonyl derivatives **61b**.^{164, 165} For the migration of the phenylthio group, not only the usual η^2 -type transition state structure **6** for the 1,2-shift but also the alternative η^3 -type transition state structure **7** were found to be possible. The latter structure is energetically less favourable (by 10 kcal mol^{−1}) than transition state structure **6** for the 1,2-shift. The opposite situation is observed for the migration of the disulfide (SSR) group. In the latter case, the transition state corresponding to the 1,3-shift is energetically more favourable (by 7 kcal mol^{−1}). This can be attributed to orbital interactions between the migrating group and the cyclic moiety of the molecule.^{167, 168} Investigation of the rearrangement of bis(pentamethoxycarbonylcyclopentadienyl) disulfide in solution by ¹H and ¹³C NMR spectroscopy demonstrated that it is characterised by a rather low energy barrier (15–17 kcal mol^{−1}).¹⁶⁴ However, no evidence in favour of the mechanisms of either 1,2- or 1,3-shifts for the migration of the RSS group was reported.

[3,3]-Sigmatropic shifts. To decide between the mechanisms of 1,2-shift ([1,5]-sigmatropic shift) and [3,3]-sigmatropic shift as the migration pathway of the dithioacyl groups around the cyclopentadiene ring, the prochiral group was introduced into the ring. The same approach was applied to acyloxycyclopentadienes (see Section VI.4.a). The circumambulatory rearrangement of *S*-(5-benzyl-1,2,3,4-tetraphenylcyclopentadienyl) *O*-ethyl dithiocarbonate **62a** (R¹ = CH₂Ph, R² = OEt) gave rise to two isomers **62b, c**. Taking into account that diastereotopic splitting of the peaks for the methylene protons in the ¹H NMR spectrum of isomer **62b** should be larger than that in the spectrum of isomer

62c because the prochiral and stereogenic centres in molecule **62b** are in close proximity, the following sequence of rearrangement steps was revealed:¹⁶⁹



R¹ = CH₂Ph, Ph, C₆H₄Me-4; R² = OEt, Ph.

In nitrobenzene-d₅, the equilibrium was established at 60 °C within 25 min; the isomer ratio **62a**:**62b**:**62c** = 45:25:30. The kinetic parameters for individual steps of the migration of the *O*-ethyl dithiocarbonate group in isomers **62** (R¹ = CH₂Ph, R² = OEt) are given in Table 9. The average rate constants and activation parameters for the slower migration of the dithiobenzoate group in solution of compound **62** (R¹ = C₆H₄Me-4, R² = Ph) in deuterionitrobenzene are as follows: $k_{130} = 1.8 \times 10^{-4}\text{ s}^{-1}$, $\Delta G^\ddagger_{130} = 30.7\text{ kcal mol}^{-1}$, $\Delta H^\ddagger = 28.9 \pm 0.7\text{ kcal mol}^{-1}$, $\Delta S^\ddagger = -4.5 \pm 1.0\text{ cal mol}^{-1}\text{ deg}^{-1}$.

Table 9. Rate constants and activation free energies for the [3,3]-sigmatropic shifts of isomers of the *O*-ethyl dithiocarbonate group in isomers **62** (R¹ = CH₂Ph, R² = OEt) in nitrobenzene-d₅.¹⁶⁹

Rearrangement	k_{60}/s^{-1}	$\Delta G^\ddagger_{60}/\text{kcal mol}^{-1}$
62a → 62b	7.5	24.3
62b → 62a	13.2	23.9
62b → 62c	8.9	24.2
62c → 62b	7.2	24.3

It can be concluded that 1,3- or 3,3-shifts, but not 1,2-shifts characteristic of the migration of the arylthio groups (see Section VI.4.b), are energetically favourable for the migration of the dithioacyl group around the cyclopentadiene ring. Although it is necessary to introduce one labelled sulfur atom to make an unambiguous choice between the mechanisms involving 1,3- and 3,3-shifts, the latter mechanism seems to be most probable, as evidenced by the results of theoretical simulation.¹⁷⁰

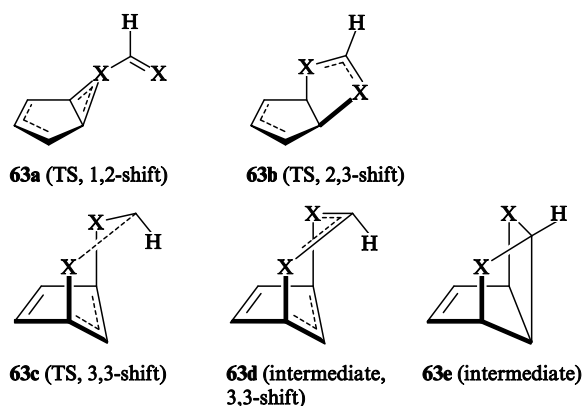
The results of calculations of the relative energies of transition state and intermediate structures for different pathways of migrations of heteroallyl groups in the cyclopentadiene ring are presented in Table 10.

Table 10. Relative (compared to the ground state structures) energies (ΔE) of the transition state and intermediate structures in different pathways of circumambulatory rearrangements of heteroallylcyclopentadienes calculated by the MINDO/3 method.¹⁷⁰

X	$\Delta E/\text{kcal mol}^{-1}$				
	63a	63b	63c	63d	63e
NH	39.3	72.7	~48.5 ^a	46.4	40.1
O	44.1	85.8	~47.9 ^a	43.6	37.0
S	19.3	37.9	17.5	see ^b	1.9

^a A saddle point was not found.

^b A biradical intermediate was not detected.



In calculations (see Table 10), the effects of the substituents in the cyclopentadiene ring and the migrating groups in compounds **53**, **59** and **62** were ignored. Nevertheless, the results of these calculations indicate with a fair degree of consistency that the [2,3]-sigmatropic shifts (structure **63b**) of the heteroallyl groups in the cyclopentadiene ring are highly improbable. As in the case of hetero-Cope rearrangements in a series of cyclopropene derivatives (see Section IV.2), the reaction pathways assuming [3,3]-sigmatropic shifts involve the transition through symmetrical biradical structures (**63d**), which can undergo isomerisation into tricyclic structures (**63e**). The energy profile of these rearrangements is analogous to that shown in Fig. 2.

c. Selenium- and tellurium-centred migrating groups

As mentioned in Section VI.3.a, 1,2,3,4,5-pentaphenyl-5-selenocyanatocyclopentadiene (**54c**) in solution undergoes two interrelated rearrangements, *viz.*, a non-degenerate rearrangement to form isoselenocyanate isomer **54a** through [3,3]-sigmatropic shifts and a rapid degenerate circumambulatory rearrangement through 1,2-shifts of the selenocyanate group around the cyclopentadiene ring. The kinetic and activation parameters for this rearrangement and another degenerate circumambulatory rearrangement of organylselenocyclopentadienes **64** *via* 1,2-shifts of Se-centred migrating groups are given in Table 11. Migrations of selenium-centred groups around substituted cyclopentadiene rings proceed more rapidly [$\Delta(\Delta G^\ddagger) = 3\text{--}4\text{ kcal mol}^{-1}$] than migrations of analogous sulfur-centred groups (see Table 8). Both electron-releasing (R^1) and electron-withdrawing (R^2) substituents facilitate acceleration of the rearrangement.

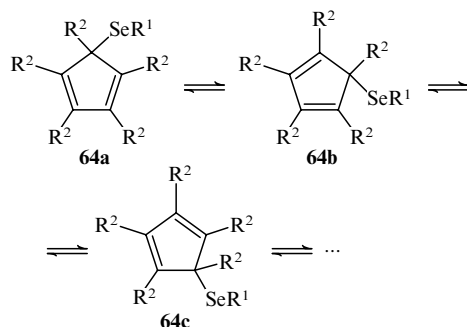
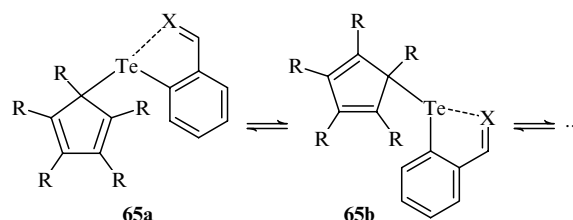


Table 11. Kinetic and activation parameters for the circumambulatory rearrangement $64a \rightleftharpoons 64b \rightleftharpoons 64c \rightleftharpoons \dots$

R^1 in compound 64	R^2 in compound 64	Solvent	k_{25}/s^{-1}	$\Delta H^\ddagger$ /kcal mol $^{-1}$	$\Delta S^\ddagger$ /cal mol $^{-1}$ deg $^{-1}$	$\Delta G_{25}^\ddagger$ /kcal mol $^{-1}$	Ref.
CN	Ph	toluene- d_8	3.4	14.2 ± 0.3	-8.4 ± 0.4	16.7	146
CF $_3$	CO $_2$ Me	<i>o</i> -dichlorobenzene	1.8	11.1 ± 0.8	-20.1 ± 1.0	17.1	164
C $_6$ H $_4$ OMe-4	Me	"	1.5×10^{-1}	15.3 ± 0.5	-10.8 ± 0.8	18.5	168
Ph	Me	"	4.2×10^{-2}	13.9 ± 0.7	-18.4 ± 0.9	19.4	168
C $_6$ F $_5$	Me	DMSO- d_6	1.1×10^{-2}	18.9 ± 0.5	-3.6 ± 0.7	20.0	171

Recently, bis(pentamethylcyclopentadienyl) selenide and bis(pentamethylcyclopentadienyl) polyselenides $Se_n(C_5Me_5)_2$ ($n = 2\text{--}4$) have been synthesised.¹⁷² Measurements of their high-temperature ^1H and ^{77}Se NMR spectra are made difficult because of thermal instability of these compounds. At room temperature, these polyselenides are structurally rigid on the NMR time scale.

High thermal sensitivity is also typical of substituted tellurocyclopentadienes. A few known representatives of this class of compounds contain intramolecular $Te \leftarrow O$ or $Te \leftarrow N$ coordination bonds, which provide substantial kinetic and thermodynamic stabilising effects in a series of organic compounds of low-oxidation-state tellurium.^{173–175} The fluxional behaviour of several tellurocyclopentadienes **65** was studied. Based on analysis of line shapes in the ^1H NMR and ^1H 2D EXSY NMR spectra recorded for solutions of compounds **65** in deuteriochloroform, their dynamic behaviour can unambiguously be assigned to rapid intramolecular rearrangements involving 1,2-shifts of the aryltellurenyl groups around the cyclopentadiene ring.^{166, 176} The migration proceeds rapidly on the ^1H and ^{13}C NMR time scale even at $-90^\circ C$, and the protons of all five methoxycarbonyl groups are manifested as the only weakly broadened peak.



$R = CO_2Me$.

X in compound 65	k_{25} /s $^{-1}$	$\Delta H^\ddagger$ /kcal mol $^{-1}$	$\Delta S^\ddagger$ /cal mol $^{-1}$ deg $^{-1}$	$\Delta G_{25}^\ddagger$ /kcal mol $^{-1}$
O	890	10.1 ± 0.7	-11.1 ± 1.0	13.4
NPh	—	—	—	7.0 ± 2.0

Therefore, the migration ability of substituents formed by Group 16 elements in the cyclopentadiene system increases in the series $O < S < Se < Te$.

5. Migrating substituents formed by Group 17 elements

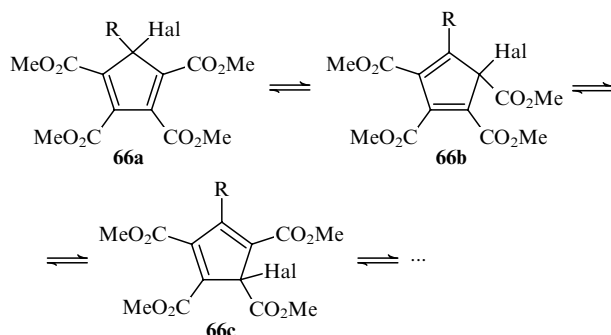
The migration of the halogen atoms around the five-membered ring cannot proceed by the ionisation–recombination mechanism because heterolysis of the $C_{Cp}\text{--}Hal$ bond would give anti-aromatic cyclopentadienyl cations. Intramolecular migrations of the chlorine and bromine atoms in a series of 5-alkyl-5-chloro(bromo)-1,2,3,4-tetramethoxycarbonylcyclopentadienes^{177–179} and 5-bromo-1,2,3,4,5-pentaphenylcyclopentadienes¹⁷⁸ proceed *via* successive 1,2-halogen shifts around the cyclopentadiene ring.

Isomers **66a–c** ($Hal = Cl$) were isolated from a mixture prepared by the reaction of 5-alkyl-1,2,3,4-tetramethoxycarbonylcyclopentadienes with *N*-chlorosuccinimide in the presence of catalytic amounts of benzoyl peroxide. Upon storage of solutions of individual isomers **66a, b** in dichlorobenzene, the equilibrium $66a \rightleftharpoons 66b \rightleftharpoons 66c$ is established, which requires the energy barriers in the range of $25.7\text{--}27.3\text{ kcal mol}^{-1}$ to be overcome

Table 12. Equilibrium concentrations of isomers **66a** and **66b** (Hal = Cl) and the kinetic parameters of their interconversions in *o*-dichlorobenzene at 80 °C.¹⁷⁹

R in compound 66	66a : 66b	k_{25}/s^{-1}		$\Delta H^\ddagger/\text{kcal mol}^{-1}$		$\Delta S^\ddagger/\text{cal mol}^{-1} \text{ deg}^{-1}$		$\Delta G_{25}^\ddagger/\text{kcal mol}^{-1}$	
		a $\rightarrow$ b	b $\rightarrow$ a	a $\rightarrow$ b	b $\rightarrow$ a	a $\rightarrow$ b	b $\rightarrow$ a	a $\rightarrow$ b	b $\rightarrow$ a
Me	11 : 89	4.3×10^{-7}	5.6×10^{-4}	25.1 ± 0.2	26.1 ± 0.2	-3.5 ± 0.3	-5.7 ± 0.3	26.1	27.3
Pr ⁱ	35 : 65	5.0×10^{-7}	2.6×10^{-7}	23.9 ± 0.4	24.1 ± 0.3	-6.9 ± 0.5	-7.6 ± 0.5	26.0	26.4
CH ₂ Ph	25 : 75	9.1×10^{-7}	3.2×10^{-7}	24.1 ± 0.3	24.3 ± 0.4	-5.5 ± 0.4	-6.6 ± 0.6	25.7	26.3

(Table 12). Although isomers **66c** are present in equilibrium mixtures in benzene in concentrations comparable to those of compounds **66a,b**, they were not detected by NMR spectroscopy in *o*-dichlorobenzene.



R = Me, Prⁱ, Bn; Hal = Cl, Br.

In molecule **66** (Hal = Br), 1,2-migrations of the bromine atom proceed more rapidly. The energy barriers for these rearrangements are in the range of 16.2–23.0 kcal mol⁻¹. In 5-bromo-1,2,3,4,5-pentaphenylcyclopentadiene, the energy barrier to intramolecular 1,2-bromine shifts is 16.7 kcal mol⁻¹ (in 1,1,2,2-tetrachloroethane). The stable pentaphenylcyclopentadienyl radical, which could exist as an intermediate in the rearrangement proceeding by a homolytic mechanism, was not detected.¹⁷⁸ As in the case of migration of the thioaryl group (see Section VI.4.b), semiempirical quantum-chemical (AM1) calculations demonstrated that not only the low-energy reaction pathway corresponding to 1,2-halogen shifts in the ring but also alternative reaction pathways involving 1,3-shifts of migrating groups can take place. However, the transition state structures corresponding to these mechanisms are energetically much less favourable than the transition state structures corresponding to the mechanism of 1,2-shifts (the energy difference is 35–40 kcal mol⁻¹).

The rapid migration of the iodine atom around the cyclopentadiene ring proceeding, apparently, *via* 1,2-shifts was also observed.¹⁸⁰ It was found that in the isomers of deuterated iodocyclopentadiene, which was prepared in an ether–benzene mixture (2 : 1) at –15 °C, the deuterium atoms are distributed over all positions of the cyclopentadiene ring. This behaviour of the label indicates that the iodine atom rapidly migrates around the ring. This conclusion was supported by the data on magnetisation transfer at ~20 °C,¹⁸⁰ which demonstrated that substantial deceleration of the rearrangement was achieved only upon a decrease in the temperature of a solution of deuterated CpI to –40 °C.

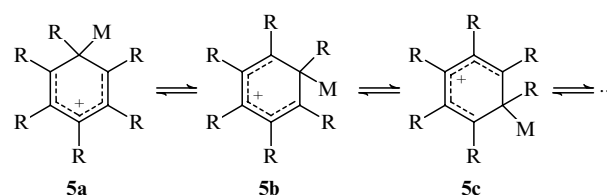
VII. Circumambulatory rearrangements in a six-membered ring

1. Rearrangements *via* 1,2-shifts

Circumambulatory rearrangements in six-membered rings in cationic systems proceed *via* 1,2-shifts (η^1 – η^2 -shifts) or η^2 – η^3 -shifts as well as *via* σ,π -shifts (see Sections III.2 and III.6). Rearrangements of the first type in a series of derivatives of the

benzenium cation are among the first cationic rearrangements proceeding on the NMR time scale, which have received the most study. These rearrangements were comprehensively surveyed in the reviews.^{17,53,181} In the present review, we briefly consider only selected, most important, results.

The mechanism of rearrangements of cations **5** involving sequences of 1,2-shifts of the migrating group M around the six-membered ring was confirmed by analysis of the line shapes in temperature-dependent ¹H and ¹³C NMR spectra, spin-echo and magnetisation-transfer experiments and data from 2D NMR spectroscopy. The elucidation of the nature of the fluxional behaviour of heptamethylbenzenium cation **5a** (M = R = Me) as a result of a series of successive 1,2-shifts of the methyl group around the ring demonstrated that 2D NMR spectroscopy is a method of choice for elucidating permutation mechanisms of exchange reactions.¹⁸²



The migration ability of various groups M in hexamethylbenzenium cations **5** (R = Me) decreases in the following series:¹⁸¹ Br > H > CH₂Ph > NO₂ > Cl > SO₃H > Et > Ph > Me > CH₂Cl > CHCl₂.

The energy barriers to migrations of some of the above-mentioned groups in compounds **5** are given in Table 13.

Table 13. Energy barriers ($\Delta G_{25}^\ddagger$) for circumambulatory rearrangements in hexamethylbenzenium cations **5** (R = Me) *via* 1,2-shifts of the migrating groups M.^{53,181}

M in cation 5	Solvent	$\Delta G_{25}^\ddagger/\text{kcal mol}^{-1}$
Me	HSO ₃ Cl	17.9
Et	HSO ₃ Cl	16.0
SO ₃ H	HSO ₃ F	15.6
Cl	HSO ₃ F	14.7
OMe	HSO ₃ F	> 11.7
NO ₂	HSO ₃ F–SO ₂ Cl ₂	12.2
H	HSO ₃ Cl	10.3
Br	HSO ₃ F–SO ₂ ClF	9.2

To correlate the migration ability of various groups in carbocations, useful semiempirical equations were deduced.^{53,181} The main equation (1)

$$\Delta G^\ddagger = a + bE_1 + cE_2 \quad (1)$$

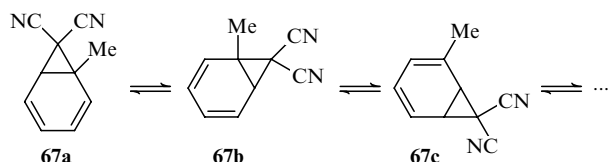
includes the following two parameters: E_1 is the energy required for the cleavage of the C(1)–M bond and deformation of the M–C(1)–C(2) bond angle and E_2 is the energy produced upon the formation of a new M–C(2) bond due to the shift of the migrating group M to the adjacent C(2) cationic centre. One approach to estimating the parameters E_1 and E_2 is to approx-

imate these parameters by the energies of the C–M bonds in the $\text{H}_3\text{C}-\text{M}$ molecule and by the affinity for the proton or methyl cation, respectively.

It was found that circumambulatory rearrangements of some cations **5** in the solid state are as rapid as in solutions. For example, the energy barrier for the rearrangement of heptamethylbenzenium cation **5** ($\text{M} = \text{R} = \text{Me}$, SbCl_6^- as the anion) in the crystal is $17.3 \text{ kcal mol}^{-1}$ (see Ref. 183), which is $0.6 \text{ kcal mol}^{-1}$ lower than that for its solution in dichloromethane. The energy barriers for the rearrangement of cation **5** in the solid state are very sensitive to the unit cell parameters. For example, the rearrangement of compound **5** ($\text{M} = \text{Ph}$, $\text{R} = \text{Me}$), which crystallises in lower-symmetry crystal lattice compared to its analogue with $\text{M} = \text{R} = \text{Me}$, is nonobservable in the solid state even at high temperature.

2. $\eta^2-\eta^3$ -Rearrangements

Migrations of the cyclopropane fragment around the six-membered ring were found by Berson,¹⁸⁴ who attributed the exchange between the deuterium positions in 2,6-dideuterio-3,7,7-trimethylcycloheptatriene at high temperatures (300°C) to the intermediate formation of norcaradiene derivatives, which undergo $[1,5]$ -sigmatropic ($\eta^2-\eta^3$) rearrangements. Migration of this type was directly observed at 77°C in the study of the rearrangement of the corresponding dicyano derivative for which norcaradiene valence tautomer **67** is energetically more favourable than the 7,7-dicyanocycloheptatriene form.^{185, 186}



Generally, such rearrangements are characterised by higher energy barriers compared to those corresponding to conditions of structural non-rigidity.^{17, 69, 186} It was found that the migration of the methylene group around the aromatic ring is accompanied by the inversion of configuration of the migrating carbon atom¹⁸⁷ (contrary to the Woodward–Hoffmann rules). This result was explained based on the results of density functional theory calculations (UB3LYP/3-21G and UB3LYP/6-31G* + ZPE) for the pathways of the rearrangement of 7-cyano-7-methylnorcaradiene.¹⁸⁸ The transition state structures for both pathways, *viz.*, both with inversion and retention of stereochemical configuration of the migrating centre, were localised, the first structure being energetically more favourable (by $\sim 1 \text{ kcal mol}^{-1}$). This difference corresponds to the 97:3 ratio between the processes occurring with inversion and retention of configuration, which is consistent with the experimental ratio of 92:8.

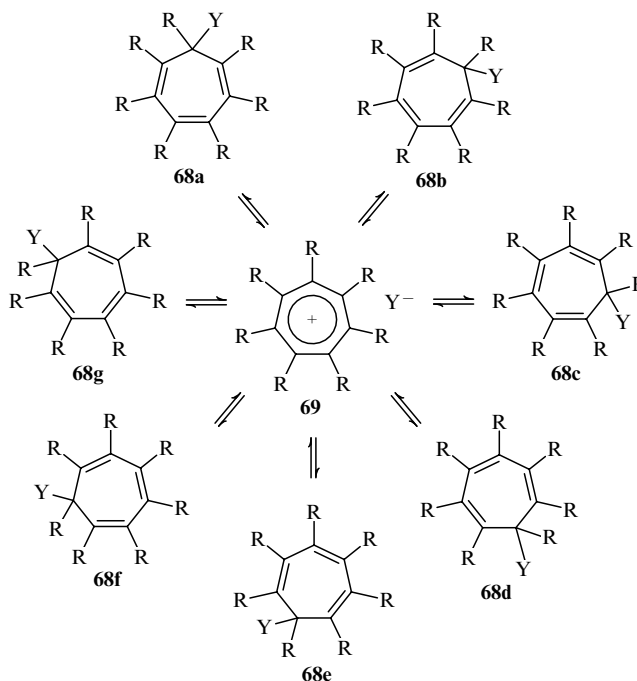
VIII. Circumambulatory rearrangements in a seven-membered ring

1. Rearrangements proceeding by the ionisation–recombination mechanism

Heterolysis of the C–M bond in 7-substituted cycloheptatriene **3** afforded the aromatic tropylium cation. This corresponds to rearrangements of compounds in which migrating groups M possess fairly high electron affinity, *i.e.*, form stable anions in the ionisation–recombination pathway. Hence, it is not surprising that circumambulatory rearrangements^{37, 189} of isothiocyanates and isoselenocyanates **68a–g** derived from cycloheptatriene proceed as random rearrangements involving preliminary ionisation of C–N bonds. The kinetic parameters of these rearrangements, which were calculated based on analysis of line shapes in temperature-dependent ^1H NMR spectra, are given in Table 14.

Table 14. Activation free energies for circumambulatory rearrangements of cycloheptatrienes **68**.

X in compound 68	R in compound 68	Solvent	$\Delta G_{25}^\ddagger$ /kcal mol $^{-1}$	Ref.
O	Ph	nitrobenzene- d_5	> 25	189
S	H	$\text{CDCl}_3-\text{CD}_3\text{CN}$ (1:3)	12.1	37
S	H	CDCl_3	14.3	37
S	H	$\text{CS}_2-\text{CDCl}_3$ (10:1)	14.8	37
S	Ph	nitrobenzene- d_5	24.3	189
Se	Ph	"	22.4	189



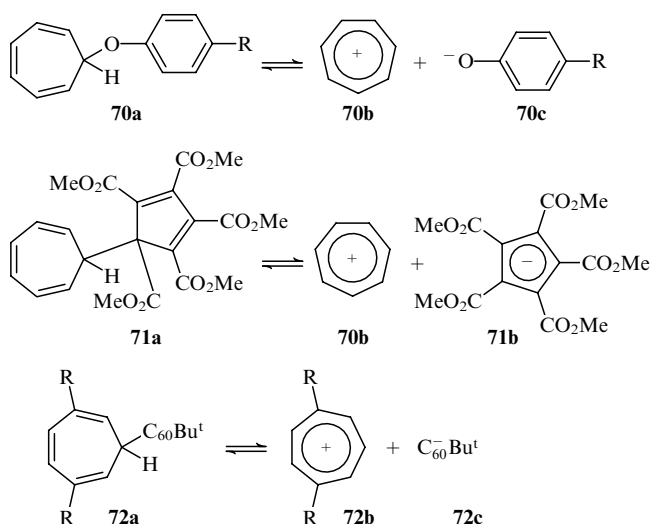
$\text{R} = \text{H}, \text{Ph}; \text{Y} = \text{NCX} (\text{X} = \text{S}, \text{Se}).$

An increase in the rate of the rearrangement of compound **68** ($\text{X} = \text{S}$, $\text{R} = \text{H}$) with increasing polarity of the solvent is indicative of the occurrence of the pre-equilibrium ionisation step. The migration of the isothiocyanate group in heptaphenylcycloheptatriene proceeds much more slowly than the analogous rearrangement in isothiocyanatocycloheptatriene, which may be associated with steric hindrance produced by the bulky phenyl groups in the recombination step. The energy barriers to hindered rotation of the phenyl groups in molecule **68** ($\text{R} = \text{Ph}$, $\text{X} = \text{O}, \text{S}, \text{Se}$) were estimated at $\sim 16 \text{ kcal mol}^{-1}$.¹⁸⁹ The migration rates of the isothiocyanate and isoselenocyanate groups are independent of the concentration of the solution, which indicates that this rearrangement proceeds through the intermediate formation of tight ion pairs **69**.

Thermally induced heterolysis of the C–N bond in *N*-(cyclohepta-1,3,5-trien-7-yl)phthalimide also led to the circumambulatory rearrangement of the phthalimide group, which migrates around the cycloheptatriene ring through the intermediate formation of the tropylium cation–phthalimide anion tight ion pair ($\text{C}_6\text{D}_5\text{NO}_2$, $\Delta G_{180}^\ddagger = 24.8 \text{ kcal mol}^{-1}$).¹⁹⁰

Examples of heterolytic dissociation of the $\text{C}_{\text{tropylium}}-\text{O}$, $\text{C}_{\text{tropylium}}-\text{C}$ and $\text{C}_{\text{tropylium}}-\text{N}$ bonds in compounds which are potentially prone to circumambulatory random rearrangements were offered.^{191–197} In these studies, the possibility of these rearrangements occurring was not discussed, but the equilibria $70\text{a} \rightleftharpoons 70\text{b} + 70\text{c}$,¹⁹¹ $71\text{a} \rightleftharpoons 70\text{b} + 71\text{b}$ (see Ref. 192) and $72\text{a} \rightleftharpoons 72\text{b} + 72\text{c}$ (see Ref. 193) were examined. The heats of

heterolysis (ΔH°) of 7-aryloxycycloheptatrienes **70a** depend substantially on the nature of substituents in the aryl ring. For example, the heat of heterolysis $\Delta H^\circ = 10.6 \text{ kcal mol}^{-1}$ for compound **70a** ($R = 4\text{-NO}_2$) is almost 10 kcal mol^{-1} lower than that for its methoxy-substituted analogue ($R = 4\text{-OMe}$). This difference is indicative of the importance of delocalisation of the negative charge in the anion favourable for ionisation of compounds **70a**. According to the dynamic ^{13}C NMR spectroscopic data, the activation free energies of heterolysis of fullerene derivatives **72a**, which dissociate into ions in dimethyl sulfoxide or the DMSO– SO_2 system, are rather low ($7.7\text{--}9.3 \text{ kcal mol}^{-1}$).

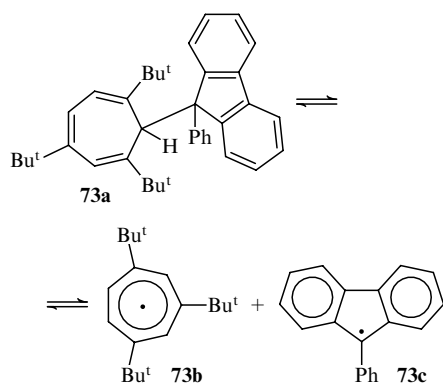


$R = \text{H, Bu}^t, \text{cyclo-C}_6\text{H}_{11}$.

Detropylation of *N,N*-dimethyltropylamine and *N*-tropylacetamide¹⁹⁸ and the dynamic equilibrium between 1-, 2- and 3-chloro-substituted 7-chlorocycloheptatrienes¹⁹⁹ are other examples of equilibria of this type involving, apparently, steps of ion recombination at an arbitrary position of the ring.

2. Homolytic reaction pathway

Thermal dissociation of C–C σ bonds in hydrocarbon molecules generally involves their homolytic cleavage. For instance, sterically overcrowded 1,3,5-tri-*tert*-butyl-7-(9-fluorenyl-9-phenyl)-cyclohepta-1,3,5-triene (**73a**) dissociates upon heating in *m*-xylene or cyclohexane to form the 1,3,5-tri-*tert*-butylpropyl (**73b**) and 9-phenylfluorenyl (**73c**) radicals ($\Delta H^\ddagger = 23 \text{ kcal mol}^{-1}$, $\Delta S^\ddagger = 22.0 \text{ cal mol}^{-1} \text{ deg}^{-1}$)²⁰⁰ detected by EPR spectroscopy. Evidently, the recombination step proceeds randomly. This reaction is a first example of cycloheptatriene rearrangements proceeding by a radical mechanism.

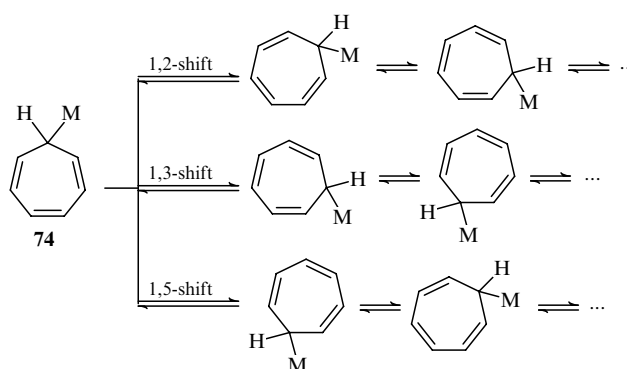


The formation of radical pairs whose subsequent recombination leads to shifts of the substituents in the ring can also be initiated photochemically, like in the rearrangements of 1-indenylcyclopropene derivatives.⁹⁵

3. Rearrangements via 1,2(2,3)-shifts

As demonstrated in Section III.2, 1,2-shifts ([1,7]-sigmatropic shifts) of the dialkylboryl group lead to the rapid rearrangement of [1-4- η^4 -*exo*-7-(dipropylboryl)cycloheptatriene]tricarbonyliron (**11**).⁵⁰ The question arises as to whether rearrangements of this type can proceed without coordination of the cycloheptatriene ring, for example, in compound **74** ($M = \text{BPr}_2$).⁶² Studies of 7-dipropylborylcycloheptatriene by ^1H 2D EXSY NMR spectroscopy demonstrated that in solutions, an equilibrium between this compound and its 7-*exo*-(dipropylboryl)norcaradiene isomer is rapidly established, and migration of the dipropylboryl group occurs, the latter process being observed at temperatures higher than 293 K. According to the results of density functional theory calculations (B3LYP/6-311+G**//B3LYP/6-31G*) for a model system, the energetically most favourable migration mechanism involves 1,2-shifts of the dipropylboryl group in the cycloheptatriene ring ($\Delta H^\ddagger = 18.4 \text{ kcal mol}^{-1}$). The calculated energy barriers for the possible 1,5- and 1,3-shifts (Scheme 5) are 27.4 and 25.7 kcal mol^{-1} , respectively.

Scheme 5



The fact that the migration of the dialkylboryl group around the cycloheptatriene ring proceeds primarily *via* 1,2-shifts was attributed⁶² to the characteristic features of the electronic structure of the transition state, which corresponds to a Möbius-type aromatic system containing eight electrons on eight active orbitals.²⁰¹ From this viewpoint, the 1,2-shift should be unfavourable for the migration of groups containing two additional electrons on active orbitals compared to boron-centred groups. However, this assumption was not confirmed in the case of rearrangements of sulfur-centred migrating groups. 7-Phenylthiocycloheptatriene **74** ($M = \text{SPh}$)^{40, 202} and cycloheptatrien-7-yl ethyl dithiocarbonate **74** [$M = \text{SC(OEt)=S}$]²⁰³ undergo circumambulatory rearrangements at rates comparable to those found for the migrations of boron-centred groups in compound **74** with $M = \text{BPr}_2$. According to the data from ^1H and ^{13}C 2D EXSY NMR spectroscopy, the phenylthio- and, probably, ethyldithiocarbonate groups migrate around the cycloheptatriene ring *via* successive 1,2-shifts ([1,7]-sigmatropic shifts). The kinetics of both rearrangements is independent of the concentrations of solutions, which is indicative of their intramolecular character. The kinetic parameters of these rearrangements are summarised in Table 15.

Since studies of the mechanisms by dynamic NMR elucidated only the type of the permutation mechanism, an alternative mechanism involving [2,3]-sigmatropic shifts for the rearrangement of compound **74** [$M = \text{SC(OEt)=S}$] cannot be excluded.

The theoretical simulation of the mechanism of rearrangement of model system **74** [$R = \text{H, M} = \text{SCH(=S)}$], which is an analogue of compound **3**, was carried out by *ab initio* calculations at the MP2/6-31G** level.⁹³ The optimised geometric parameters and energies of the transition state structures relative to the ground state of thioformylthionecycloheptatriene **74** are shown in Fig. 8. Calculations provided evidence that the 2,3-shift is the energetically most favourable channel of the rearrangement. The larger size of the cycloheptatriene ring as compared to that in lower cyclopolyenes allows more diverse pathways of circum-

Table 15. Kinetic and activation parameters for the circumambulatory rearrangements of 7-phenylthiocycloheptatriene **74** ($M = \text{SPh}$)^{40, 202} and cycloheptatrien-7-yl ethyl dithiocarbonate **74** [$M = \text{SC(OEt)=S}$]²⁰³ calculated from the data of dynamic ¹H and ¹³C NMR spectroscopy.

M in compound 74	Solvent	$\Delta G_{25}^\ddagger$ (see ^a)	$\Delta H^\ddagger$ (see ^a)	$\Delta S^\ddagger$ (see ^b)	k_{25}/s^{-1}
SPh	benzene-d ₆	19.2	18.3 ± 0.4	-4.0 ± 0.4	2.9×10^{-2}
SPh	nitrobenzene-d ₅	20.1	18.5 ± 0.5	-5.5 ± 0.4	1.1×10^{-2}
SC(OEt)=S	benzene-d ₆	17.9	16.9 ± 0.3	-3.3 ± 0.4	4.5×10^{-1}
SC(OEt)=S	toluene-d ₈	17.4	15.4 ± 0.2	-6.6 ± 0.3	1.1

^a $\Delta G_{25}^\ddagger$ and $\Delta H^\ddagger$ are given in kcal mol⁻¹.

^b $\Delta S^\ddagger$ are given in cal mol⁻¹ deg⁻¹.

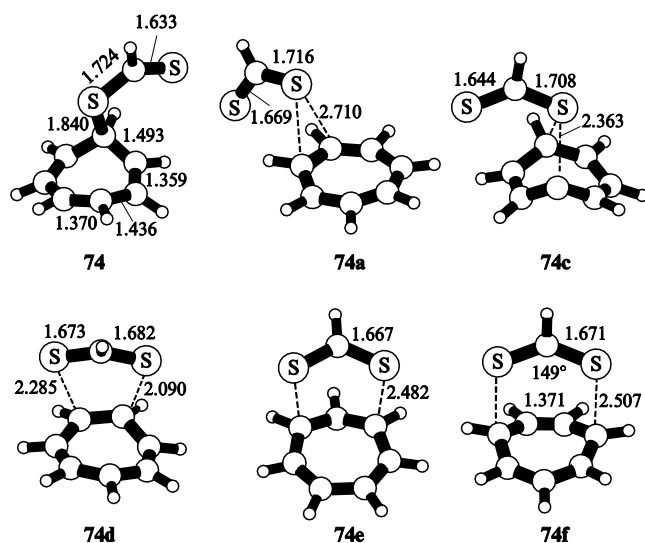
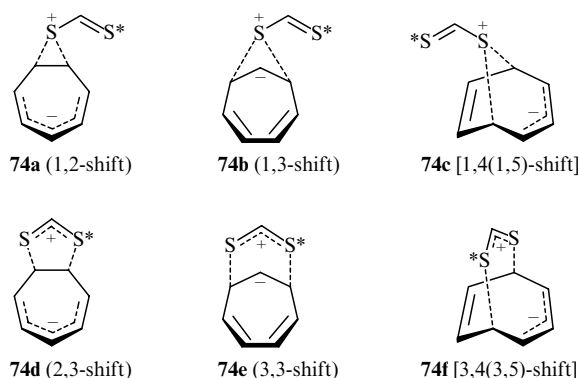


Figure 8. Optimised (MP2/6-31G**) structures of thioformylthionecycloheptatriene **74** and transition states **74a, c–f** for different mechanisms of circumambulatory sigmatropic rearrangements.⁹³

The transition state structure for the mechanism of the [1,3]-sigmatropic shift (**74b**) was not localised.

ambulatory rearrangements, including the formation of transition states **74a–f**, to proceed.



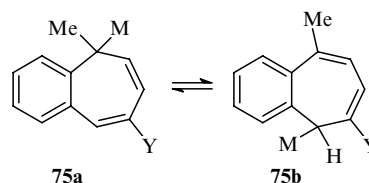
4. Rearrangements via 1,3-shifts

The presence of the $\text{Fe}(\text{CO})_3$ group in molecule **11** facilitates the 1,3-migration of the dipropylboryl group observed by dynamic NMR spectroscopy. This migration along with the main reaction channel (1,2-shift) contributes to the mechanism of the circumambulatory rearrangement.⁵⁰ In uncoordinated compound **74** ($M = \text{BPr}_2$), the 1,3-migration proceeds much more slowly and

is experimentally undetectable, although it is known that the boryl groups in polyunsaturated dialkylboranes can undergo rapid [1,3]-sigmatropic shifts.^{204, 205}

5. Rearrangements via 1,4-shifts

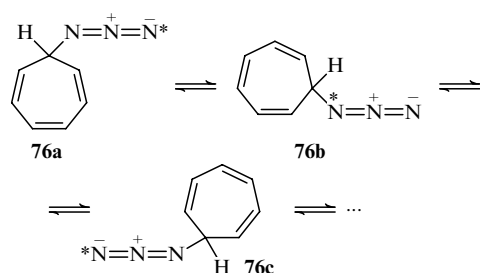
Unlike the cyclopentadiene system for which the energetically most favourable mechanism of circumambulatory rearrangements involves thermally allowed suprafacial [1,5]-sigmatropic shifts of the migrating group (1,4-shifts) (see Section VI), the rearrangements of this type in cycloheptatrienes are characterised by high energy barriers. For example, the migrations of silicon- or germanium-centred groups in compounds **74** [$M = \text{SiPh}_3$ (see Ref. 206) and GePh_3 (see Ref. 207)] are unobservable. At temperatures higher than 130 °C, [1,5]-sigmatropic hydrogen shifts take place in these cycloheptatriene derivatives. At 150 °C, the methoxy group in 7,7-dimethoxycycloheptatriene undergoes [1,5]-sigmatropic shifts characterised by fairly high activation barriers.²⁰⁸ In cycloheptatrienes, rather rapid rearrangements *via* [1,5]-shifts were observed only for migrating substituents formed by Group 14 elements of a lower period of the Periodic table, *viz.*, SnPh_3 , SnMe_3 and SnMe_2Cl (see Section III.4). This is attributed to the fact that [1,5]-sigmatropic shifts in the cyclopentadiene system proceed as 1,2-shifts along the pathways of the smallest motions of the migrating groups, whereas these shifts in the cycloheptatriene system do not correspond to this pathway (1,4-shifts). Additional arguments in favour of the 1,2-shift were obtained in calculations of the geometry of the transition state structures for various reaction pathways associated with the migration of the dimethylboryl group in compound **74** ($M = \text{BMe}_2$)⁶⁰ and the dithioformate group in its analogue with $M = \text{SCH}(\text{S})$ (see Fig. 8). If the rearrangement proceeds *via* 1,2-shifts ([1,7]-sigmatropic shift), the seven-membered ring in the transition state remains virtually planar, while the C–B and C–S bond lengths moderately increase. By contrast, the ring is forced to adopt a distorted conformation with substantially elongated C–B (1.859 Å) and C–S (2.363 Å) contacts if the rearrangement proceeds *via* 1,4-shifts ([1,5]-sigmatropic shifts). Therefore, it can be assumed that steric rather than electronic factors are predominantly responsible for fairly high energy barriers to [1,5]-sigmatropic shifts in the cycloheptatriene system. This accounts for the fact that the migration ability of various carbon-centred groups in benzocycloheptatrienes **75** depends to a much lesser extent on the nature of the migrating group compared to those in indene system **49**. The rearrangements $\text{75a} \rightleftharpoons \text{75b}$ proceed upon heating of solutions of compounds **75** in benzene in sealed tubes.²⁰⁹



The migration ability of carbon-centred groups decreases in the following series: $\text{CHO} > \text{CN} > \text{C}\equiv\text{CH} > \text{C}(\text{O})\text{Me} > \text{CO}_2\text{Me} > \text{Alk}$.

6. Rearrangements via [3,3]-sigmatropic shifts

The shifts of the isothiocyanate groups in tropyli isothiocyanate **69** belong to random processes, *i.e.*, the positions of the migrating group after ionisation of the starting molecule is randomly chosen (see Scheme 5), whereas the energetically favourable mechanism of the rearrangement of tropyli azide **76** involves the selective 1,3-migration of the azide group.⁸⁷ Dynamic ¹⁵N NMR spectroscopic studies confirmed that this migration is associated also with the exchange between the positions of the terminal nitrogen atoms in the azide group. Since the rate of this process is equal to the rate of circumambulatory migrations of the azide group around the seven-membered ring, 1,3-migrations should correspond to [3,3]-sigmatropic shifts.



Along with the [3,3]-sigmatropic shift, the following alternative reaction pathways take place: ionisation – recombination and [1,5]-sigmatropic shift. The contribution of the ionic mechanism increases as the polarity of the solvent increases (26% and 34% in THF and CD₃CN, respectively). The activation free energy barriers for various mechanisms of circumambulatory rearrangements of compound **76**, which were estimated based on analysis of line shapes in NMR spectra, are given in Table 16.

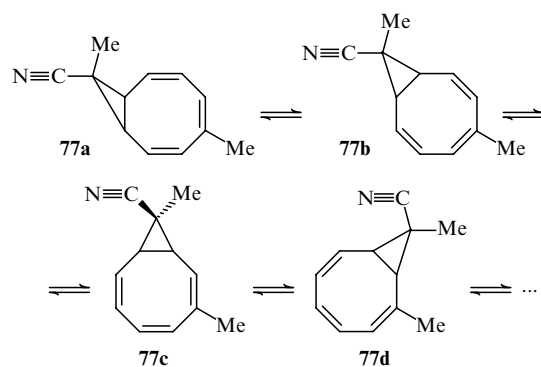
Table 16. Activation free energies ($\Delta G_{-48}^\ddagger$) for the circumambulatory rearrangements of tropyl azide **76**.^{87, 88}

Solvent	$\Delta G_{-48}^\ddagger$ /kcal mol ⁻¹		
	random shift	[3,3]-shift	[1,5]-shift
CD ₃ CN	14.8 ± 0.2	14.0 ± 0.2	16.0 ± 0.5
CDCl ₃	15.2 ± 0.5	14.9 ± 0.6	17.0
THF	16.5 ± 0.4	15.9 ± 0.4	17 ± 1

Although direct evidence of [3,3]-sigmatropic shifts of the isoselenocyanate groups in 7-isoselenocyanatocycloheptatriene **68** (Y = NCS_e) is lacking, the presence of small amounts of selenocyanate isomer **68** (Y = SeCN), which was observed in the mass spectrum of the starting isoselenocyanate,¹⁸⁹ is indicative of the possibility of this rearrangement occurring in the gas phase.

IX. Circumambulatory rearrangements in multimembered rings

Circumambulatory migrations in the eight- and nine-membered cyclopolyene rings are virtually unknown. Rearrangements in neutral eight-membered systems can proceed only in bis-hapto compounds (see Section III.5). The only known example is interconversions of the isomers of 9-cyano-4,9-dimethylbicyclo[8.1.0]nonatriene (**77**) occurring as migrations of the cyclopropyl group.²¹⁰



Compound 77	a	b	c	d
Yield at 102 °C (%)	35	33	21	11

Heating of a solution of cyclopolyene **77a** afforded a mixture of all four isomers. The activation free energy of the rearrangement **77a** → **77b** is 29 kcal mol⁻¹. Each step of the circumambu-

latory rearrangement involves the inversion of stereochemical configuration at the C(9) centre. The thermal rearrangement of isomer **77a** attended by the exchange between the positions of the cyano and methyl groups proceeds analogously.

The rapid circumambulatory rearrangement of cyclononatrienyl(dipropyl)borane **78** was studied by Bubnov and co-workers.⁵⁶ The dynamic process associated with 1,3-shifts of the dipropylboryl group in molecule **78** (R = Pr) is detected by ¹H NMR spectroscopy even at –100 °C. The activation free energy barrier for migrations of the dipropylboryl group, which was calculated based on analysis of line shapes in the ¹³C NMR spectra in the temperature range from –100 to –40 °C, is low ($\Delta G_{-78}^\ddagger$ = 8.8 kcal mol⁻¹). This value is well reproduced by calculations of model compounds **78** and **79** (R = Me) using the density functional method²¹¹ by relating this barrier to the interconversions of the most stable *cis-endo* isomers **78a** ⇌ **78b** ⇌ ... According to the results of calculations, the dialkylboryl group in the energetically less favourable *cis-exo* isomer of **79** undergoes the 1,2-shift to form *mono-trans* conformer **79a**, which, in turn, can undergo 1,3-boron shifts. These rearrangements are shown in Scheme 6.

Scheme 6

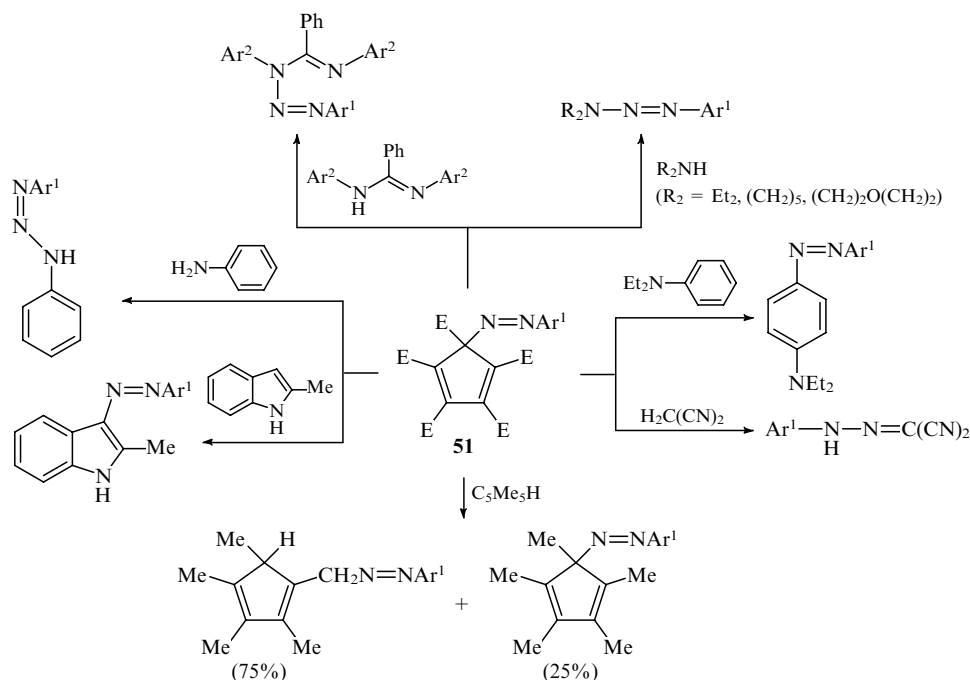
The fluxional behaviour of cyclononatrienyl(trimethyl)tin was studied in detail in the temperature range from –100 to –78 °C by ¹³C–¹³C EXSY NMR spectroscopy. The results of these studies demonstrated that the Me₃Sn group in the *exo* conformer undergoes 1,2-shifts ([1,9]-sigmatropic shifts) around the nine-membered ring.²¹² The activation energy of this process (6.0 ± 0.6 kcal mol⁻¹) agrees well with the calculated (B3LYP/3-21G*) value.

X. Fluxional compounds as efficient carriers of groups and precursors of structurally rigid chiral ligands

Compounds whose fluxional behaviour is determined by the ionisation–recombination mechanism involving dissociation into ions can serve as soft carriers of functional groups. This takes place when the rearrangement proceeds in solutions containing another substrate, which possesses a fairly high affinity for the migrating group, thus competing with the starting counterion in the recombination step. For example, arylazo derivatives of 1,2,3,4,5-pentamethoxycarbonylcyclopentadiene **51** (see Section VI.3.a) serve as efficient carriers of arylazo groups facilitating their migration to the nucleophilic carbon and nitrogen centres in various acidophobic compounds.^{38, 39, 213–216} The reactions proceed smoothly at room temperature in benzene to give various arylazo compounds in ~90% yields. The most important transformations of this type are shown in Scheme 7.

Not only ionisable arylazo compounds **51** but also 5-arythio-1,2,3,4,5-pentamethoxycarbonylcyclopentadienes **61**, which are characterised by low energy barriers to circumambulatory migrations of the arylthio groups (see Section VI.4.b), behave as

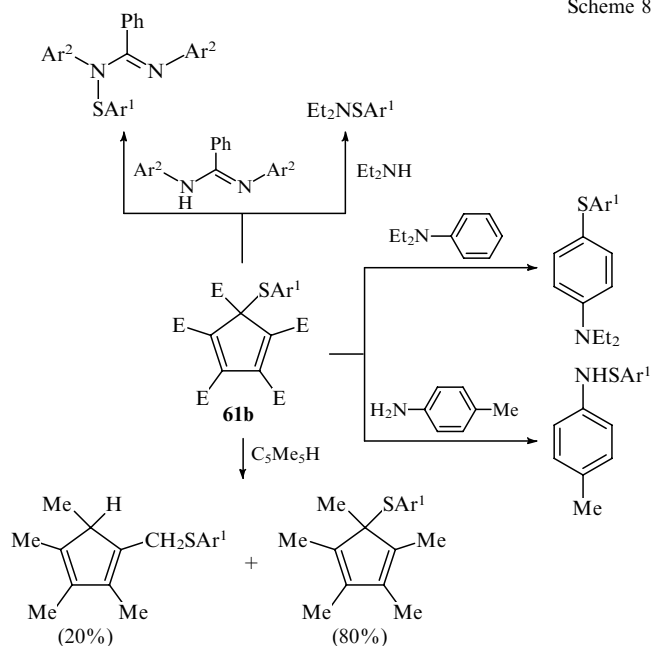
Scheme 7



$\text{E} = \text{CO}_2\text{Me}$; $\text{Ar}^1 = \text{C}_6\text{H}_4\text{NO}_2\text{-4}, \text{C}_6\text{H}_4\text{NO}_2\text{-2}, \text{C}_6\text{H}_4\text{SO}_2\text{CF}_3\text{-4}$; $\text{Ar}^2 = \text{C}_6\text{H}_4\text{Me-4}, \text{C}_6\text{H}_4\text{OMe-4}$.

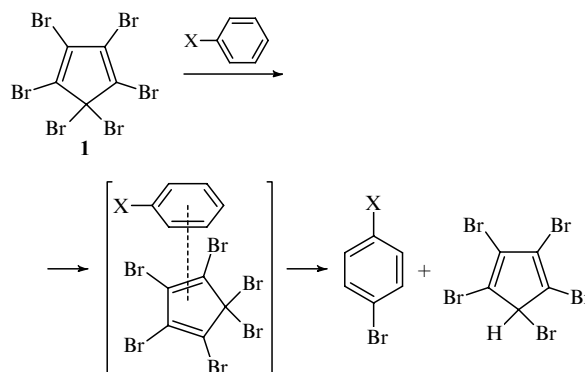
efficient carriers of these groups.^{217–220} Intermolecular migrations of the arylthio groups are illustrated in Scheme 8.

Scheme 8



$\text{E} = \text{CO}_2\text{Me}$; $\text{Ar}^1 = \text{C}_6\text{H}_4\text{NO}_2\text{-4}, \text{C}_6\text{H}_4\text{NO}_2\text{-2}$;
 $\text{Ar}^2 = \text{C}_6\text{H}_4\text{Me-4}, \text{C}_6\text{H}_4\text{OMe-4}$.

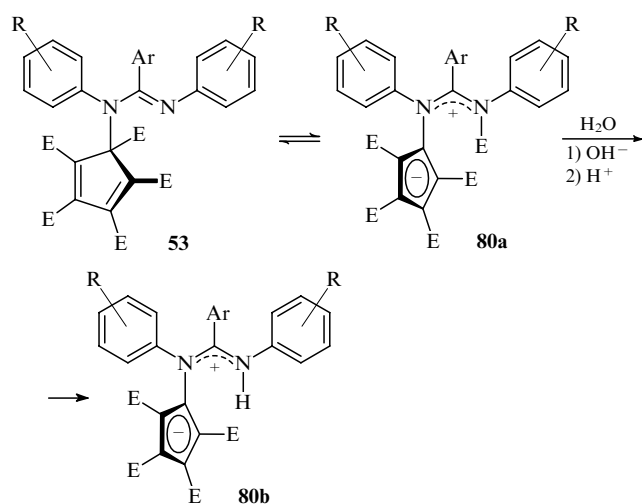
Potentially fluxional hexabromocyclopentadiene **1** ($\text{R} = \text{M} = \text{Br}$) is also able to undergo the intermolecular transfer of the bromine atom to the nucleophilic carbon centres.^{221, 222} This reagent brominates smoothly aromatic amines and alcohols, furans, thiophenes and ketones activated at the α -carbon atoms, the electrophilic substitution of aromatic compounds proceeding selectively at the *para* position due to formation of intermediate π complexes.



$\text{X} = \text{NMe}_2, \text{NMeCOMe}, \text{OH}, \text{OMe}$.

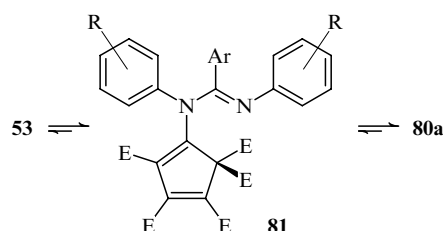
The cyclopentadienyl ligand exhibits properties of a readily leaving group in the exchange reactions of fluxional P-, Ga-, Si-, Sn- and Ge-centred pentamethylcyclopentadiene derivatives with nucleophiles.²²³

The migrations of groups analogous to those shown in Schemes 7 and 8 can also be carried out as intramolecular reactions, provided that the cyclopentadiene ring contains an additional nucleophilic centre, which can compete with the carbon atoms of the ring for the mobile migrating group bound to this ring. The correct choice of functional groups in the molecule of a fluxional compound allows one to perform the rational design of structures which are difficult to prepare according to conventional synthetic procedures. This approach can be exemplified by the new rearrangement of *N*-1,2,3,4,5-pentamethoxycarbonylcyclopentadienyl-*N,N'*-diarylamidines **53** observed in solutions at high temperatures.²²⁴ This rearrangement afforded previously unknown *N*-methoxycarbonyl-*N,N'*- α -triarylamidinium *N*-cyclopentadienides **80a**, which readily eliminated the *N*-methoxycarbonyl group upon treatment with a methanolic solution of NaOH to give (after neutralisation of the solution) amidinium *N*-cyclopentadienyl ylides **80b**. The zwitterionic structures of the ylides were confirmed by X-ray diffraction analysis of a series of derivatives **80**.^{224–226}



The rearrangement **53** → **80a** can proceed either *via* the direct 1,4-shift of the methoxycarbonyl group or as a two-step process involving an additional 1,2-shift to the carbon atom of the ring **53** → **81** followed by the 1,5-shift of this group. The possibility of the second mechanism is evidenced by rather low energy barriers to the 1,2-shifts ($E_a \approx 25 \text{ kcal mol}^{-1}$) of the methoxycarbonyl group in 5-R-1,2,3,4,5-pentamethoxycarbonylcyclopentadienes.^{119, 122} However, simulation of the mechanisms of migration of the methoxycarbonyl group for a series of amidinyl-cyclopentadiene derivatives taking into account the methoxycarbonyl and aryl substituents in the cyclopentadiene and amidine fragments, respectively, by the MNDO quantum-chemical method provided theoretical evidence for the occurrence of the 1,4-shift of the methoxycarbonyl group.²²⁷

The presence of electron-releasing groups in the C-aryl ring facilitates the shift of the equilibrium **53** ⇌ **80a** toward N-ylide (Table 17).



The non-planar molecules of N-ylides **80b** are chiral, and the presence of both the amidine and cyclopentadiene residues in these molecules provides their bifunctional character. Hence, compounds **80b** hold promise as chiral N-functionalised cyclopentadienyl ligands in the synthesis of metal complexes serving as potential catalysts for asymmetric reactions.^{228–233} In such complexes, the cyclopentadiene fragment and the nitrogen atom of the side chain coordinate the metal centre in a bidentate fashion giving rise to the rigidly coordinated chiral centre at the metal atom. Complexes of this type with N-centred functional groups, such as

the aminoethyl and pyridyl groups, were studied.^{234–237} Compounds **80b**, which contain the bulky 1-naphthyl group in the α position of the amidine triad and retain a stable chiral structure both in the crystals and solutions even upon heating to 180°C (the energy barrier to rotation about the $\text{C}_\alpha\text{--C}_{\text{Ar}}$ bond $\Delta G_{180}^\ddagger > 26 \text{ kcal mol}^{-1}$), are of particular interest. In gold(I) complexes with 1-naphthamidine N-cyclopentadienides prepared recently, the rigidity of a chiral structure is provided by additional coordination of the gold atom by the π system of the cyclopentadiene ring.²³⁸ Analogous thallium complexes retain stable chiral structures through coordination of the thallium atom both by the nitrogen atom of the side chain (N–Tl) and the π system of the cyclopentadiene ring (Tl–Cp, η^5 -binding).²³⁹

XI. Conclusion

Circumambulatory rearrangements can serve as models of many important chemical processes associated with migrations of functional groups, which allow one to prepare compounds with various structures. The elucidation of the mechanisms of such rearrangements, their driving forces and factors responsible for the energy barriers to shifts of the migrating groups around the ring helps in understanding the mechanisms and stereoelectronic requirements of a series of more complex reactions. The results surveyed in the present review demonstrate that circumambulatory rearrangements are not limited to shifts of mobile organometallic groups around the ring but involve also various migrating substituents of Group 13–17 elements. In particular cases, such Group 13–17 element-centred migrating substituents exhibit high ability to undergo intramolecular shifts comparable to the mobility of organometallic groups.

The circumambulatory rearrangements of cyclopentadiene derivatives were studied in sufficient detail. In most cases, these rearrangements proceed *via* successive 1,2-shifts ([1,5]-sigmatropic shifts) of the migrating group around the five-membered ring. The energy barriers to migrations of the substituents M whose central atoms belong to one and the same group of the Periodic table decrease with increasing atomic number of the element due primarily to a gradual decrease in the energy of the $\text{C}_{\text{sp}^3}\text{--M}$ bonds with increasing ordinal number of the period. In the presence of electron-withdrawing substituents in the five-membered ring, the migration rate increases. In the case that a migrating group can form a stable cation and the five-membered ring contains electron-withdrawing substituents, which facilitate delocalisation of the negative charge in the cyclopentadienide anion, the $\text{C}_{\text{sp}^3}\text{--M}$ bond readily undergoes ionisation and the rearrangement proceeds through the ionisation–recombination mechanism within the tight ion pair that formed. In the presence of nucleophiles possessing a higher affinity for a migrating group compared to the starting cyclopentadiene residue, the cationic migrating group can be shifted to the foreign nucleophilic centre. Such compounds serve as efficient soft carriers of functional groups.

The electronic requirements for circumambulatory rearrangements of derivatives of three- and seven-membered cyclopolyenes characterised by low energy barriers are opposite to those considered above for cyclopentadienes. Aromatic stabilisation of these cyclopolyene rings is achieved in their cationic forms and increases upon the replacement of the hydrogen atoms in the ring by electron-releasing groups. As a consequence, circumambulatory rearrangements of cyclopropene and cycloheptatriene derivatives containing electronegative migrating groups and electropositive substituents in the rings proceed by the ionisation–recombination mechanism. By contrast, the differences in the stereoelectronic requirements for migrations of heteroallyl groups in various cyclopolyenes are dictated primarily by steric factors.

The rate constants of circumambulatory rearrangements vary over a wide range characteristic of intramolecular migrations, *viz.*, from 10^6 to 10^{-8} s^{-1} at room temperature, which corresponds to energy barriers of $5\text{--}40 \text{ kcal mol}^{-1}$. Depending on the ring size,

Table 17. Equilibrium and rate constants of the rearrangement **53** ⇌ **80a** (*o*-dichlorobenzene, 120°C).²²⁴

Ar in compounds 53, 80a	$K = \frac{[\mathbf{80a}]}{[\mathbf{53}]}$	$10^3 k / \text{s}^{-1}$		$\Delta G^\ddagger / \text{kcal mol}^{-1}$	
		53 → 80a	80a → 53	53 → 80a	80a → 53
$\text{C}_6\text{H}_4\text{NO}_2\text{-4}$	0.25	0.8	3.2	28.8	27.6
$\text{C}_6\text{H}_4\text{Br-4}$	0.31	1.0	3.2	28.6	27.6
C_6H_5	0.40	1.2	3.0	28.4	27.7
$\text{C}_6\text{H}_4\text{Me-4}$	0.53	1.6	3.0	28.4	27.7
$\text{C}_6\text{H}_4\text{OMe-4}$	0.66	2.1	3.2	28.0	27.6

the nature of the migrating group, substituents in the ring and the medium, compounds **1–5** and their higher homologues can exhibit very high structural non-rigidity or, on the contrary, substantial rigidity, *i.e.*, according to the classification proposed in the study,²⁴⁰ these compounds can be assigned to both fluxional structures and structures which undergo slow rearrangements. An interesting feature of circumambulatory rearrangements is a diversity of mechanisms responsible for simple intramolecular shifts of migrating groups around the cyclopolyene ring. Among these are various sigmatropic shifts of migrating groups, haptotropic rearrangements and ionisation pathways. Very fine variations in the structure can switch the reaction between possible pathways resulting in topomerisation or isomerisation of cyclopolyene derivatives. In this respect, circumambulatory rearrangements of substituted cyclopolyenes provide a good example of the limitations of the so-called ‘principle of Ockham’s razor’,²⁴¹ which is often used as a qualitative criterion for analysis of reaction mechanisms. The Woodward–Hoffmann rules of the conservation of orbital symmetry are also non-universal for the prediction of mechanisms and stereochemistry of circumambulatory rearrangements of cyclopolyene compounds although these rearrangements belong to typical pericyclic processes. To account adequately for the electronic and steric factors, critical regions of potential energy surfaces should be calculated by quantum-chemical methods at a high level of theory.

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Condensation monomers and polymers based on 2,4,6-trinitrotoluene

A L Rusanov, L G Komarova, D Yu Likhatchev, S A Shevelev, V A Tartakovsky

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Abstract. The feasibility of conversion of 2,4,6-trinitrotoluene into condensation monomers (nitro compounds, diamines, *etc.*) and their applications in the synthesis of aromatic polymers has been analysed within the framework of a general problem of 2,4,6-trinitrotoluene conversion. The use of aromatic dinitro compounds and diamines for the preparation of oligomeric polyethers and polyamides (or polyimides), respectively, is considered. The possibility of the synthesis of polyamides and polyimides containing side aliphatic and aromatic groups and possessing better (in comparison with the corresponding unsubstituted polymers) characteristics is demonstrated. The bibliography includes 157 references.

I. Introduction

Aromatic condensation polymers belong to the most important class of thermostable high-molecular-mass compounds^{1–8} that have found wide application in the most advanced fields of science and technology.⁹ In this connection, a search for sources of raw materials for the synthesis of such polymers is the key problem, which determines further progress in this branch of chemistry.¹⁰ Of special interest is the development of methods for the synthesis of monomers from cheap and available raw materials, especially those based on compounds subject to utilisation, *e.g.*, the use of phosgene for the preparation of polycarbonates¹¹ or of dichlorodiphenyltrichloroethane (DDT) for the synthesis of a broad range of condensation polymers.^{12–16}

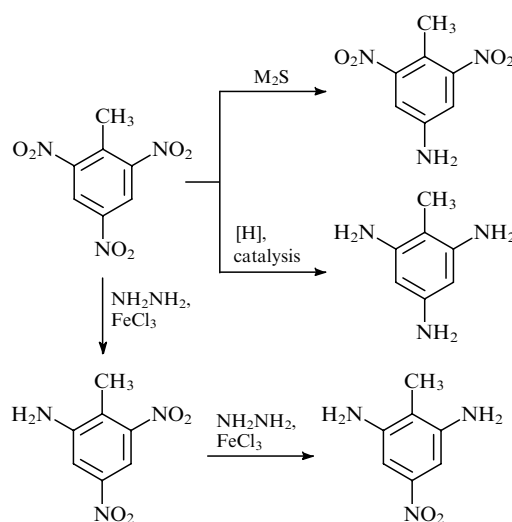
Large-scale investigations^{17–22} carried out in Russia over the past decade were aimed at the preparation of monomers and aromatic condensation polymers based on 2,4,6-trinitrotoluene

(trotyl, TNT),²³ a regnant, cheap and available product contained in large amounts in out-of-date ammunition liable to liquidation.

The simplest TNT derivatives used as monomers in the synthesis of condensation polymers include aromatic dinitro compounds (monomers for aromatic oligo- and poly-ethers^{24,25}) and aromatic di- and triamines (monomers for aromatic polyamides and polyimides^{10,26–30}). Some transformations of TNT into condensation monomers are depicted in Scheme 1.

II. Synthesis of condensation monomers based on 2,4,6-trinitrotoluene and its derivatives

Complete or partial reduction of TNT is the simplest reaction in the series of TNT transformations (Scheme 1, route *a*). Monoaminodinitrotoluenes, diaminonitrotoluenes and 2,4,6-triaminotoluene (TAT) can be obtained depending on the method and conditions for TNT reduction.



Thus reduction of TNT with sulfides of monovalent metals affords 4-amino-2,6-dinitrotoluene.³¹ Depending on the reaction conditions, the reduction of TNT with hydrazine hydrate in the presence of Raney nickel or iron chloride on activated charcoal yields either 2-amino-4,6-dinitrotoluene or 2,6-diamino-4-nitrotoluene.³² However, complete reduction of TNT resulting in TAT presents the greatest interest. Complete reduction of TNT to TAT is achieved by catalytic hydrogenation (Scheme 2, route *a*).³³ Electrochemical reduction of TNT in dilute HCl in the presence of TiCl₃ (Scheme 2, route *b*) leads to TAT · 3 HCl (yield 95%),¹⁸ which is much more resistant to oxidation than the free base.

A L Rusanov, L G Komarova A N Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, ul. Vavilova 28, 119991 Moscow, Russian Federation. Fax (7-095) 135 50 85.

Tel. (7-095) 135 63 72. E-mail: alrus@ineos.ac.ru (A L Rusanov).

Tel. (7-095) 135 93 27. E-mail: komarova@ineos.ac.ru (L G Komarova)

D Yu Likhatchev Materials Research Institute, UNAM, Circuito Exterior s/n, CU, Apdo Postal 70-360 Coyoacan, 04510 Mexico City, Mexico.

Fax (52-555) 616 12 01. Tel. (52-555) 622 45 87.

E-mail: likhach@servidor.unam.mx

S A Shevelev, V A Tartakovsky N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 119991 Moscow, Russian Federation. Fax (7-095) 135 53 28.

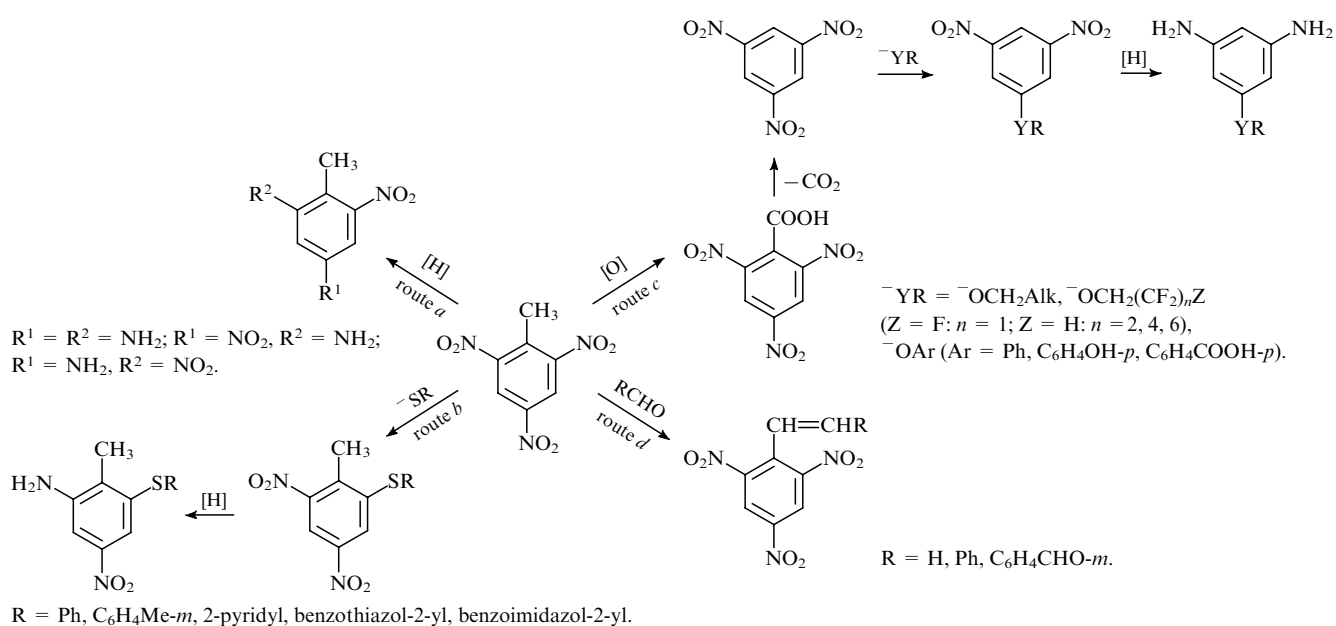
Tel. (7-095) 135 63 40. E-mail: shevelev@ioc.ac.ru (S A Shevelev).

Tel. (7-095) 135 41 11. E-mail: secretary@ioc.ac.ru (V A Tartakovsky)

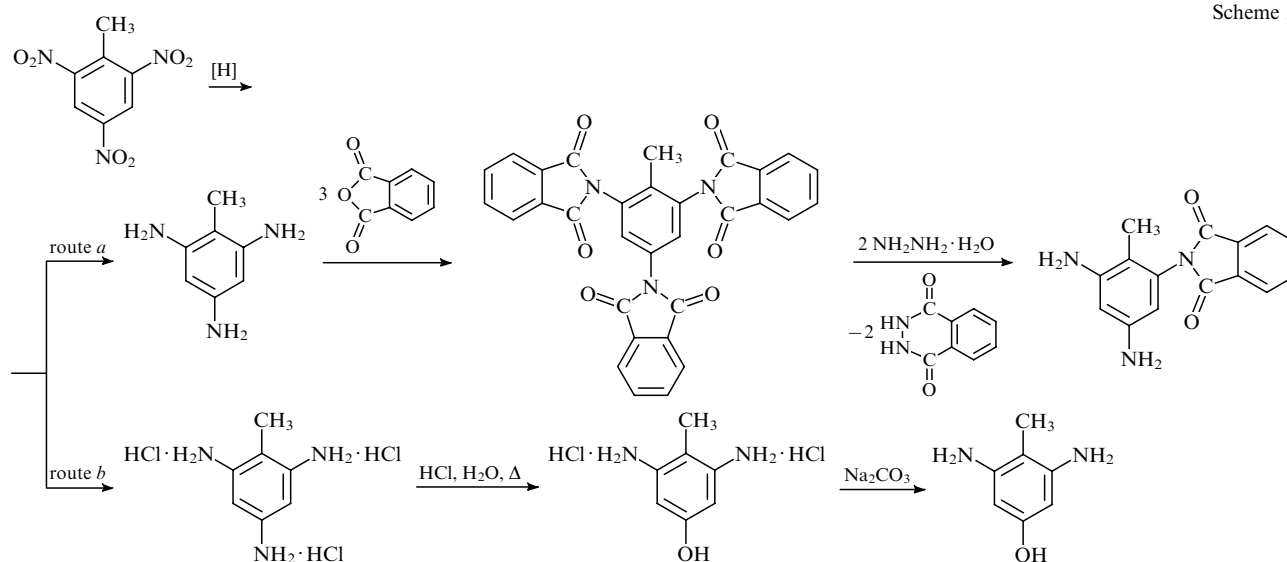
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Scheme 1



Scheme 2



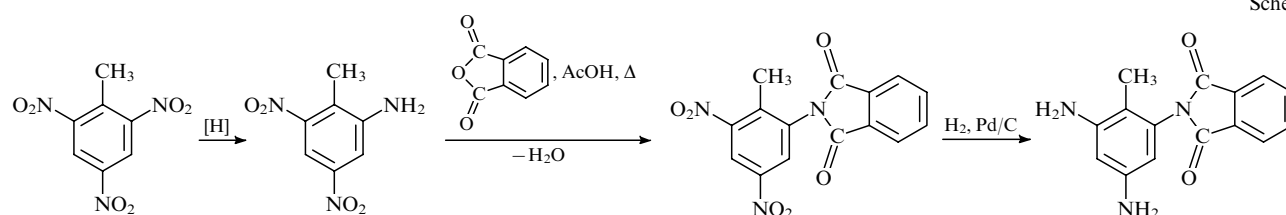
(a) catalytic hydrogenation, (b) electrochemical reduction, HCl (dilute), TiCl_3 .

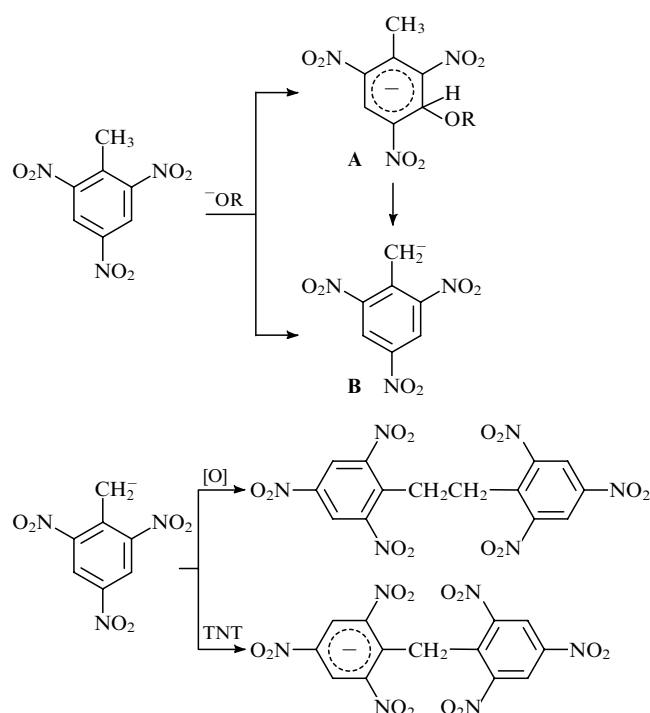
2,4,6-Triaminotoluene can be used for the synthesis of both polymers, *e.g.*, polyimides (PI) and a series of condensation monomers, substituted diamines in particular.^{34,35}

Thus partial hydrolysis of $\text{TAT} \cdot 3 \text{HCl}$ gave 2,6-diamino-4-hydroxytoluene,³⁵ whereas the reaction of TAT with a threefold molar excess of phthalic anhydride resulted in 2,4,6-tripthalimidotoluene, which was further converted into 2,4-diamino-6-phthalimidotoluene.³⁶ Since this procedure yields an isomer of 2,4-diamino-6-phthalimidotoluene (5%–10%) along with the main product, the pure monomer is prepared using the following reaction sequence (Scheme 3):³⁶

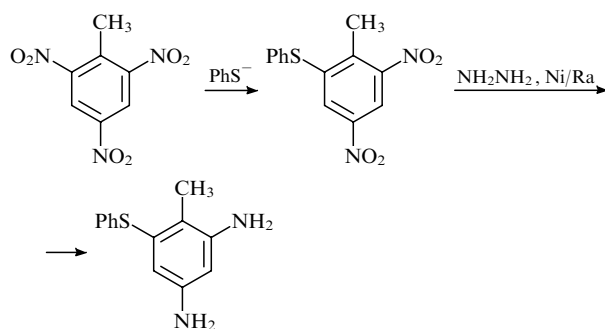
Yet another pathway for TNT conversion into condensation monomers (Scheme 1, route *b*) is based on the replacement of the nitro groups of TNT by nucleophiles under conditions of aromatic nucleophilic substitution.^{37–39} It is of note that reactions of TNT with bases are usually accompanied by the formation of an anionic 1,3- σ -complex **A**, which is further converted into a more stable 2,4,6-trinitrobenzyl anion **B** rather than the nitro groups being replaced.^{40,41} This anion can undergo further chemical transformations.

Scheme 3



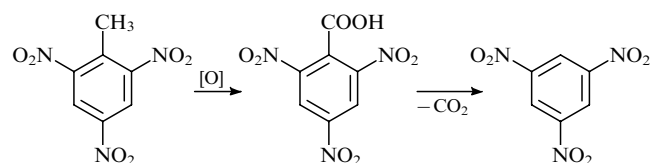


These processes can only be prevented if 'soft' nucleophiles, *e.g.*, benzenethiols and their heterocyclic analogues are used or if the reactions are carried out in dipolar aprotic solvents of the amide type.^{42, 43} Thus reaction of TNT with benzenethiol in the presence of K_2CO_3 in *N*-methylpyrrolidone (*N*-MP) (50 °C, 2 h) leads to 2-methyl-3,5-dinitrodiphenyl sulfide (yield 72%); the reduction of the latter with hydrazine hydrate results in 3,5-diamino-2-methyldiphenyl sulfide (yield 86%).

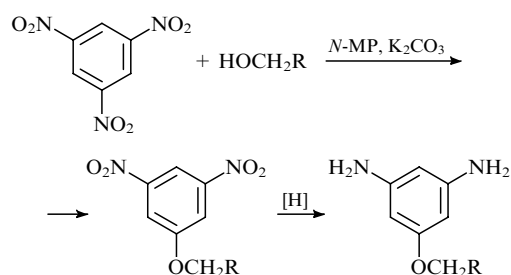


A broad range of condensation monomers was obtained following the route *c* (Scheme 1), which is based on the demethylation of TNT; this reaction yields 1,3,5-trinitrobenzene (TNB).

There are different ways to demethylate TNT; the most important includes the oxidation of the methyl group to the carboxy group and subsequent decarboxylation.^{44, 45}



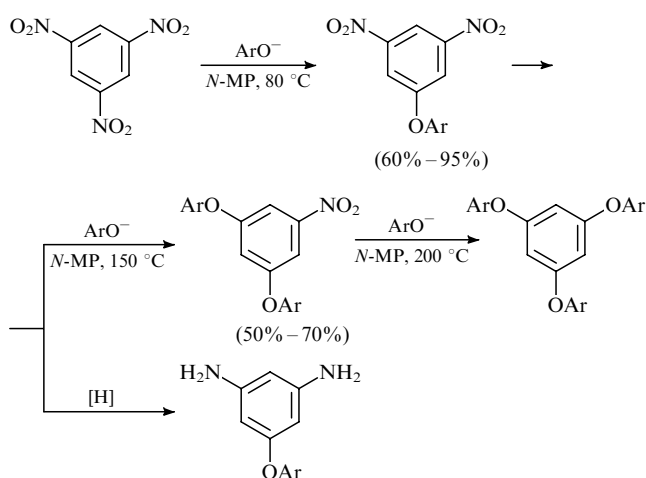
Aromatic nucleophilic substitution^{37–39} was used for the replacement of the nitro group in TNB by alkoxy-^{46–48} or perfluoroalkoxy groups.^{49–55}



$\text{R} = \text{H, Alk, (CF}_2)_n\text{X (X = F: } n = 1; \text{X = H: } n = 2, 4, 6).$

The monosubstituted dinitro compounds thus obtained were reduced to the corresponding diamines.^{46, 51–53}

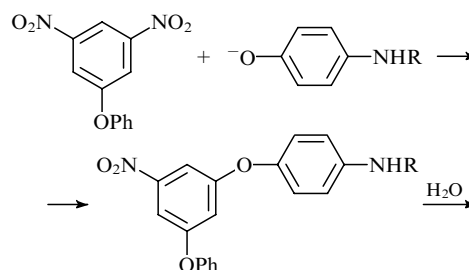
Considerable attention has been given to the replacement of the nitro groups in TNB by aryloxy groups.^{56–58} One, two or three nitro groups in TNB can be replaced using aromatic nucleophiles.

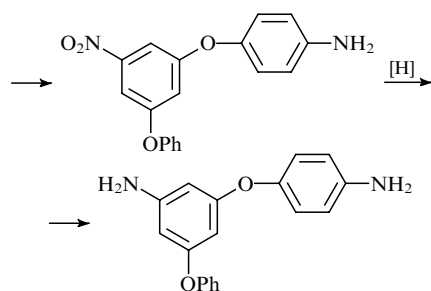


$\text{Ar} = \text{Ph, 2-MeC}_6\text{H}_4, 3\text{-MeC}_6\text{H}_4, 4\text{-XC}_6\text{H}_4$ ($\text{X} = \text{F, Br, I, OH, EtO, NH}_2, \text{CH}_3\text{C(O), COOH, NO}_2, 3\text{-ClC}_6\text{H}_4$ etc.

The replacement of the first nitro group in TNB occurs under mild conditions (80 °C) and gives high (60%–95%) yields of 3,5-dinitrodiaryl ethers^{56, 57} which are easily converted into the corresponding aryloxy-substituted diamines. The replacement of the nitro group in 3,5-dinitroaryl ethers requires more drastic conditions, *viz.*, heating to 150 °C. The yield of 3,5-diaryloxy-substituted nitrobenzenes is 50%–70%. The formation of 1,3,5-triaryloxybenzenes as a result of replacement of the nitro group in 3,5-diaryloxy-substituted nitrobenzenes is possible only at 200 °C (yield 25%–30%).

The nitro group in 3,5-dinitrodiaryl ethers can easily be replaced by a mono- or bisphenolic residue. Thus 3,5-dinitrodiphenyl ether reacts with 4-amino- or 4-acetamidophenol to give 3-nitro-5-[4-amino(amido)phenoxy]diphenyl ether. Hydrolysis of 3-nitro-5-(4-acetamidophenoxy)diphenyl ether leads to 3-nitro-5-(4-aminophenoxy)diphenyl ether; subsequent reduction of the latter gives 3-amino-5-(4-aminophenoxy)diphenyl ether.⁵⁹

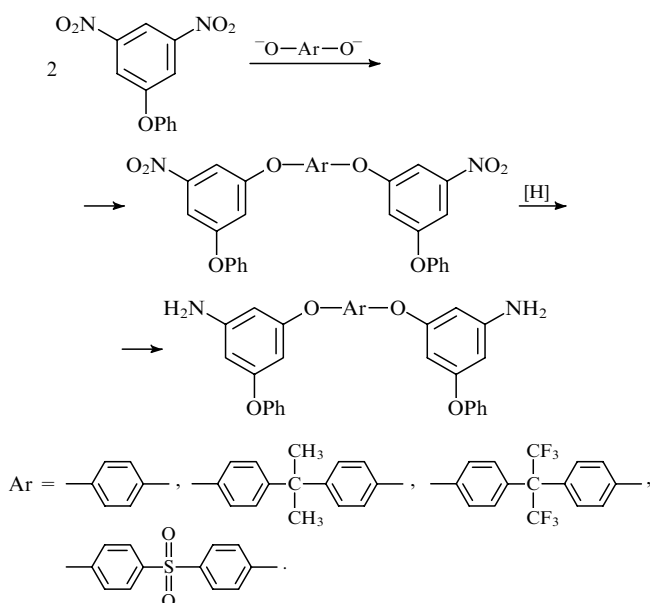




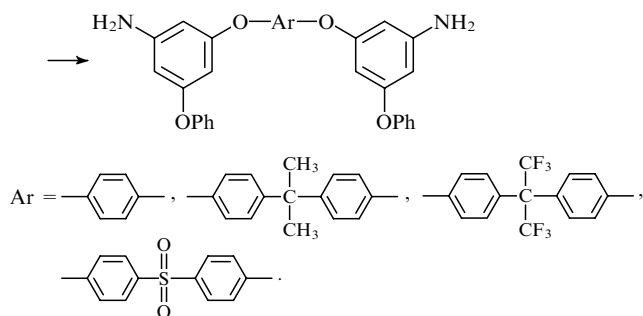
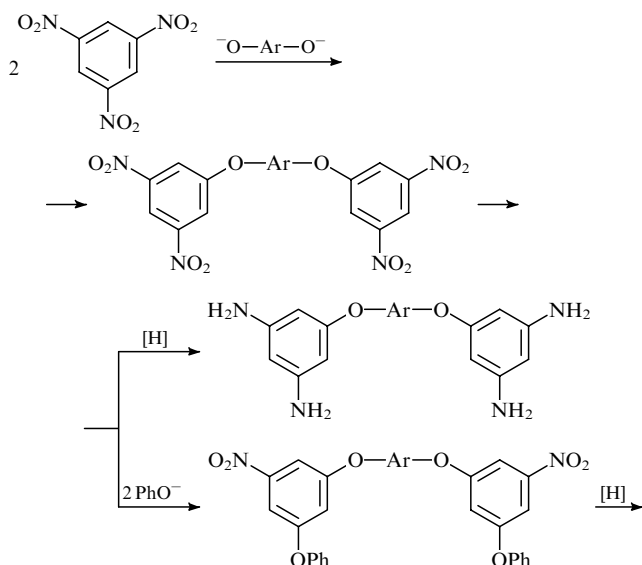
R = H, COCH₃.

It is noteworthy that 3-amino-5-(4-aminophenoxy)diphenyl ether contains an ether bond which can be incorporated into the main polymeric chain by polycondensation.

The replacement of the nitro group in dinitrophenyl ethers by bisphenolic residues yields dinitro compounds and diamines which contain no less than two ether groups; these can potentially be incorporated into the main polymeric chain.^{60, 61}

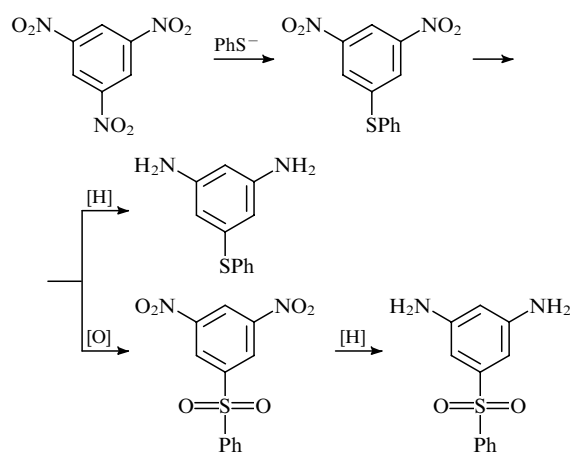


An alternative approach to the synthesis of such diamines includes the reaction of bisphenols with a twofold molar excess of TNB,⁵⁷ subsequent treatment of the tetranitro compounds formed with phenol and reduction of dinitro compounds to diamines.

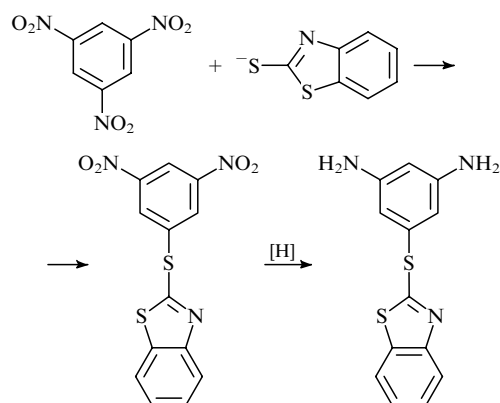


It is of note that the reduction of intermediate tetranitro compounds allows preparation of a novel type of aromatic tetraamines, viz., bis(3,5-diaminophenoxy)arylenes.

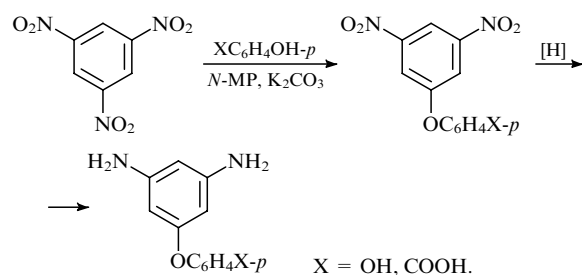
Monosubstitution of TNB is also employed in the synthesis of 3,5-dinitrodiphenyl sulfide;^{42, 62} its reduction gives the corresponding diamine. Oxidation of the sulfide group in 3,5-dinitrodiphenyl sulfide to the sulfonyl group and subsequent reduction of 3,5-dinitrodiphenylsulfone yield 3,5-diaminodiphenyl sulfone.⁶²



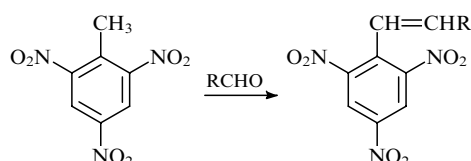
3,5-Diaminophenyl benzothiazol-2-yl sulfide was synthesised from TNB in addition to monomers containing a phenylthio group.⁶³ The former is prepared by treatment of TNB with 2-mercaptobenzothiazole (which is less expensive than benzene-thiol) and subsequent reduction of the benzothiazol-2-yl 3,5-dinitrophenyl sulfide formed.



Monomers with functionalised aryl groups were synthesised besides dinitro compounds and diamines containing non-reactive aryl substituents.⁶⁴ Among the former, aromatic diamines containing free hydroxy and carboxy groups, e.g., 3,5-diamino-4'-hydroxy- and 3,5-diamino-4'-carboxydiphenyl ethers, present special interest.^{57, 64, 65}



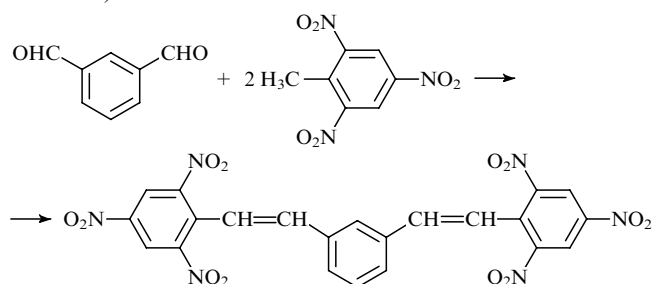
Yet another fairly interesting route of TNT conversion into condensation monomers includes reactions involving the methyl group (Scheme 1, route *d*). The methyl group of TNT, which is effectively activated by nitro groups, reacts easily with aldehydes to give trinitrophenyl-substituted alkenes.⁶⁶



$\text{R} = \text{H}, \text{Ph}.$

Such monomers can be converted into aromatic amines containing alkene substituents.

The reaction product of isophthalic aldehyde with a twofold molar excess of TNT⁶⁶ is a promising starting monomer for polycycloaddition reactions (*e.g.*, the Diels–Alder reaction^{67–70}).



III. Synthesis of polymers based on 2,4,6-trinitrotoluene derivatives

1. Polyamides and polyimides

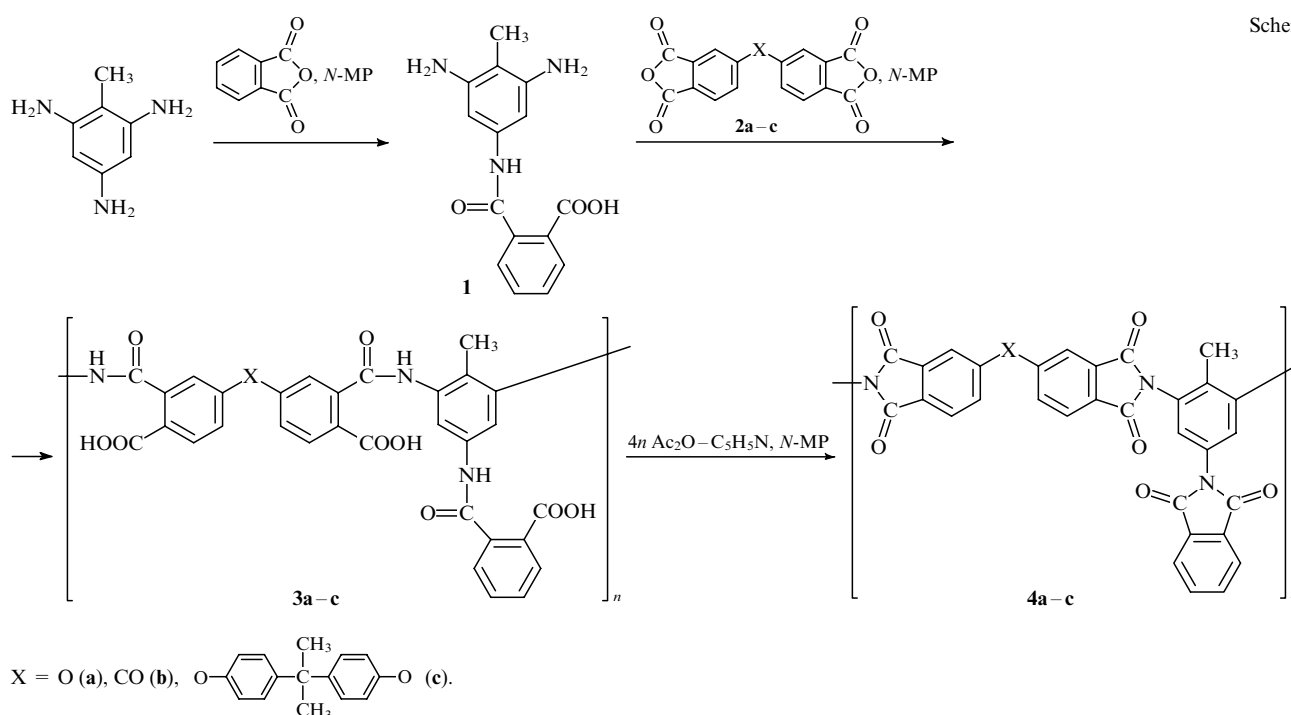
TAT presents the greatest interest among partial or complete reduction products of TNT. TAT-based phthalimido-substituted PI⁷⁵ were prepared by a selective polyacylation procedure.^{71–74}

The synthesis of phthalimido-substituted aromatic PI includes treatment of TAT with an equimolar amount of phthalic anhydride; this results in a mixture of mono-, bis- and tris(*o*-carboxybenzoyl)-substituted TAT derivatives with the predominance of the monoderivative **1**, which is due to a decrease in the activity of the free amino groups following monoacylation.⁷⁶

It is of note that the reaction of a free amino group in TAT with the carbonyl group of the substituent of the acylated amino group, due to their mutual *meta*-arrangement, is impeded in comparison with that in the reaction product of *o*-phenylenediamine with phthalic anhydride.⁷³

In order to obtain isomeric poly-*o*-carboxyamides **3a–c** (PCA) containing side *o*-carboxybenzamide groups, the acylation product of TAT with phthalic anhydride (a mixture of isomers) was treated with an equimolar amount of aromatic tetracarboxylic dianhydrides **2a–c** {3,3',4,4'-diphenyl oxide tetracarboxylic dianhydride (**2a**), 3,3',4,4'-benzophenonetetracarboxylic dianhydride (**2b**) and 2,2-bis[(3,4-dicarboxyphenyl)phenoxy]propane dianhydride (**2c**)} in *N*-MP at room temperature. The polyacylation process can be complicated due to the chemical heterogeneity of the TAT monoacylation products. Thus bis(*o*-carboxybenzoyl)triaminotoluene effects the polymeric chain termination, whereas non-acylated TAT favours the formation of branched and even cross-linked structures. Notwithstanding, homogeneous reaction solutions are formed in the synthesis of PCA **3a–c** with side *o*-carboxybenzamide substituents (Scheme 4).

Phthalimido-substituted polyimides **4a–c** are obtained from the corresponding PCA **3a–c** upon treatment with a fourfold excess of the pyridine–acetic anhydride mixture (1 : 1).⁷⁷ This is added to a solution of polycarboxyamide in *N*-MP at room temperature. The temperature is then increased to 100–110 °C and the reaction mass is kept at this temperature for 4 h. This reaction proceeds under homogeneous conditions and yields PI **4a–c** with a reduced viscosity (η_{red}) $\sim 0.3 \text{ dl g}^{-1}$ and molecular mass $\sim (22–105) \times 10^3$.



Scheme 4

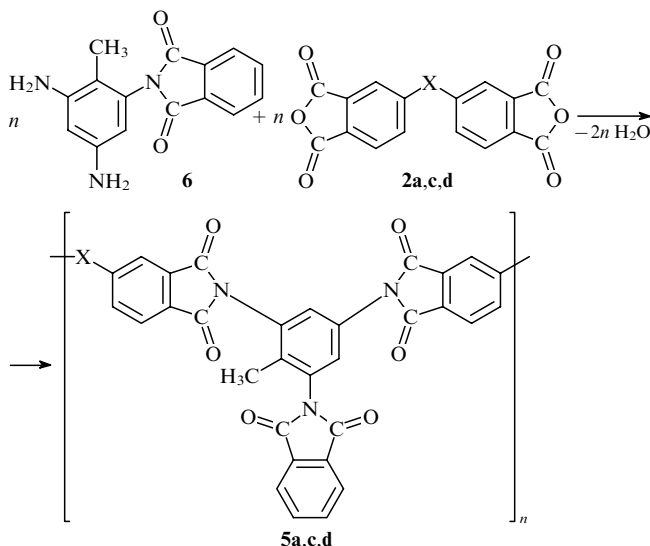
The imide structure of the products formed (the absorption maxima are around 720, 1370, 1720 and 1780 cm^{-1}) and the absence of non-cyclised units (within the limits of experimental error) were confirmed by the IR spectroscopic data.

All the PI synthesised are readily soluble in *N*-MP, DMF and a tetrachloroethane : phenol mixture (3 : 1). Good solubility of PI is due to the presence of methyl and phthalimide substituents and the isomeric character of the units in the polymer.

The softening temperatures (T_{soft}) of PI **4a–c** established by the thermomechanical method and the temperatures at which a 10% loss of the sample mass occurred ($T_{10\%}$) were determined by the dynamic thermogravimetric analysis (TGA) and found to be equal to 270–360 and 400–450 $^{\circ}\text{C}$, respectively.

The stable monomer TAT · 3 HCl is used for the synthesis of aromatic PI along with the easily oxidisable free base TAT. In the case of the former, it is first converted into a free base. To this end, a TAT · 3 HCl suspension is treated with pyridine whereupon solubilisation of the starting material occurs, which is followed by subsequent processing according to the procedure of PI synthesis from the free base (TAT) (see Scheme 4).

The polyimides **5a,c,d** having similar but more ordered structures were prepared by the reaction of 2,4-diamino-6-phthalimidotoluene (**6**) with aromatic tetracarboxylic dianhydrides **2a,c,d**.³⁶

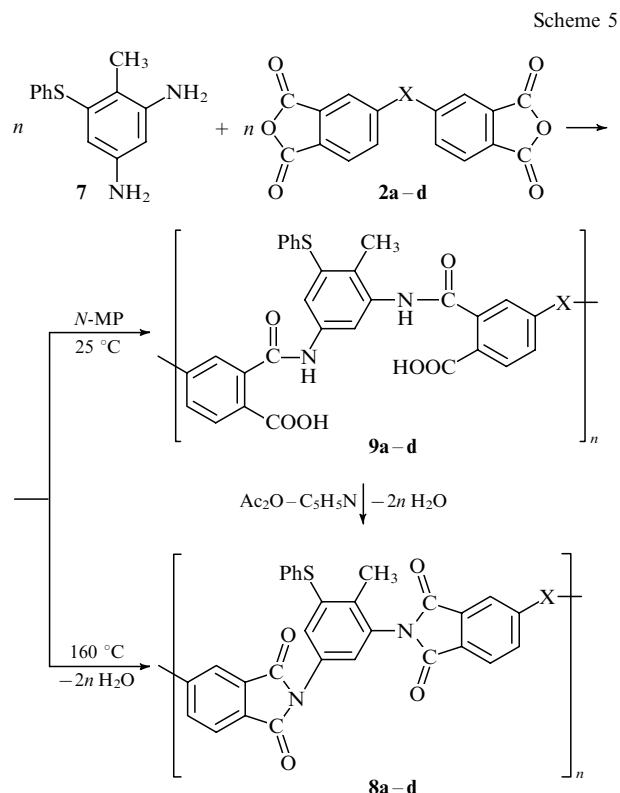


X = O (**a**), $\text{OC}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{C}_6\text{H}_4\text{O}$ (**c**), $\text{C}(\text{CF}_3)_2$ (**d**).

Polyimides **5** are synthesised by high-temperature polycyclocondensation in *m*-cresol using quinoline as a catalyst. This reaction proceeds under homogeneous conditions; the reaction products contain no non-cyclised fragments (IR spectroscopic data). All the PI synthesised are soluble in *N*-MP, *m*-cresol and butyrolactone. Polyimide **5c** is soluble in both the aforementioned solvents and THF, chloroform and cyclohexanone, and PI **5d** is also soluble in acetone. This is due to the presence in PI **5c,d** of phthalimide and methyl substituents, *m*-phenylene fragments and 'hinged' hexafluoroisopropylidene groups.

According to the data from thermomechanical analysis, T_{soft} of the polymers **5a,c,d** are 275–350 $^{\circ}\text{C}$, and $T_{10\%} = 415\text{--}465$ $^{\circ}\text{C}$ (data from TGA in air at a heating rate of 4.5 $^{\circ}\text{C min}^{-1}$). A comparison of PI synthesised from diamine **6** in accordance with Schemes 2 and 3 demonstrated that their thermal characteristics and solubilities differ slightly from one another, presumably due to the difference in their isomeric compositions.

The reaction of 3,5-diamino-2-methyldiphenyl sulfide (**7**) with aromatic tetracarboxylic dianhydrides **2a–d** is carried out in accordance with the following scheme (Scheme 5):



R = O (**a**), CO (**b**), $\text{OC}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{C}_6\text{H}_4\text{O}$ (**c**), $\text{C}(\text{CF}_3)_2$ (**d**).

Two approaches were used in the synthesis of PI **8a–d**: (1) the reaction of the diamine **7** with aromatic tetracarboxylic dianhydrides in *N*-MP at room temperature, which yields PCA **9a–d**, with subsequent imidisation of these polymers using the pyridine–acetic anhydride mixture (1 : 1); (2) high-temperature (160 $^{\circ}\text{C}$) polycyclocondensation of the starting monomers in *m*-cresol catalysed by quinoline.

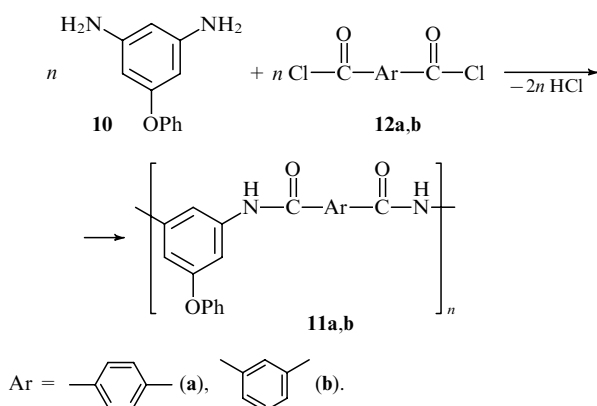
In virtually all cases, the PI **8a–d** prepared in *m*-cresol were characterised by higher values of η_{red} in comparison with the polymers of the same structures prepared in *N*-MP. For example, the η_{red} values for PI **8c** prepared in *m*-cresol and *N*-MP are equal to 0.80 and 0.30 dl g^{-1} , respectively.

High solubility in *N*-MP, DMF and *m*-cresol is a distinguishing feature of the PI under study. The polyimide **8d** is also soluble in THF, cyclohexanone, chloroform, dichloromethane and even in acetone. The presence of phenylthio substituents is one of the factors which determine high solubility of PI **8**, which is in keeping with the published data.^{78–80}

Studies of the effects of methyl substituents on the properties of PI by comparing characteristics of polymers based on 3,5-diamino-2-methyldiphenyl (**7**) and 3,5-diaminodiphenyl sulfide have shown that methyl-substituted PI possess higher solubilities. The softening temperatures of the methyl-substituted PI are 250–285 $^{\circ}\text{C}$, i.e., somewhat higher than those of the corresponding PI devoid of methyl groups. On the contrary, the decomposition temperatures of methyl-substituted PI are lower (310–370 $^{\circ}\text{C}$) than those of PI containing no methyl groups.¹⁴

Considerable attention has been given to the synthesis of heterochain polymers containing no methyl groups, especially to the synthesis of polymers based on aromatic diamines containing a phenoxy substituent, which affects favourably the solubility of aromatic condensation polymers.^{78–85} For example, polyamides **11a,b** (PA) were prepared on the basis of 3,5-diaminodiphenyl ether (**10**). (Some aromatic PA are widely known owing to their excellent thermal and mechanical properties.^{86–88}) These PA were

synthesised using terephthalic (**12a**) and isophthalic (**12b**) acid dichlorides.^{89,90}



The synthesis of PA **11a,b** was carried out using two different approaches: (1) low-temperature polycondensation in *N*-MP^{86,90} and (2) low-temperature polycondensation in chloroform in the presence of triethylamine as an HCl acceptor.^{86–90}

The polyamides **11a,b** are readily soluble in organic solvents [*N*-MP, dimethylacetamide (DMAA), DMF, *m*-cresol, etc.]; their decomposition temperatures are 350–400 °C. These characteristics are in good agreement with those obtained in earlier studies on aromatic PA containing phenoxy substituents.^{80,83} Glass-transition temperatures of the PA synthesised (236–275 °C) are lower than those of unsubstituted PA with similar structures.^{86,87} This suggests that phenoxy substituents exert a plastifying effect.

Considerable attention has been given to the synthesis of PI containing aromatic substituents. The interest in substituted PI is due to the poor processability of unsubstituted PI.^{26–30,91,92} Among PI containing aromatic substituents, phenoxy-substituted polymers are especially popular. Such PI were prepared^{58–61,90,93,94} by treatment of phenoxy-substituted amines **10, 13–16** with tetracarboxylic dianhydrides (Scheme 6).

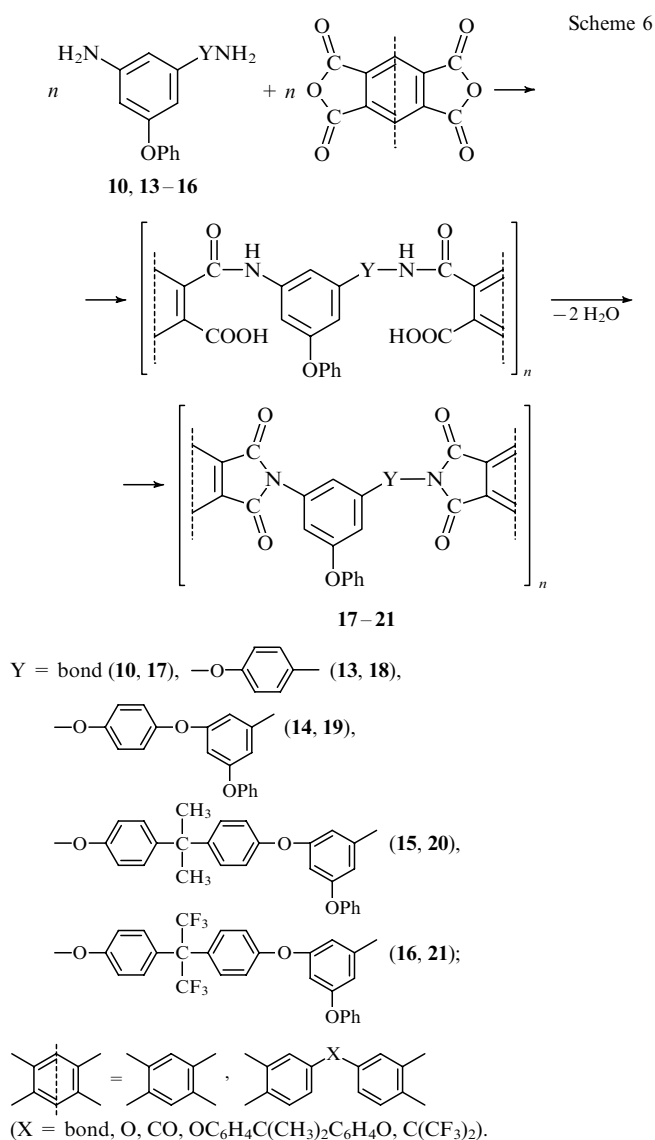
The PI **17–21** can be prepared by three routes:⁹⁵ (1) low-temperature polycondensation in *N*-MP with subsequent catalytic imidisation of the PCA formed in the reaction solution in the presence of pyridine–acetic anhydride (1 : 1); (2) high-temperature polycondensation in *N*-MP in the presence of azeotrope-forming compounds; (3) high-temperature polycondensation in *m*-cresol catalysed by isoquinoline.

A comparison of PI prepared by three different methods has demonstrated that high-molecular-mass polymers are formed in nearly all cases.

Polyimides **17** and **18** except for those PI based on pyromellitic dianhydride are soluble in *N*-MP, *m*-cresol and a tetrachloroethane–phenol mixture, which suggests a favourable influence of the phenoxy substituents on the solubility of the polymers. The values of η_{red} for these polymers in *N*-MP are equal to 0.30–0.83 dl g^{−1} ($M_w \leq 48\,000$). Some PI demonstrate good film-forming properties. The softening temperatures (T_{soft}) (180–380 °C) and $T_{10\%}$ (500–550 °C) of the polymers **17** and **18** differ significantly from one another.

Polymers **17** based on 3,5-diaminodiphenyl ether (**10**) may be considered as PI analogues based on *m*-phenylenediamine. A comparison of properties of these two groups of polymers suggests that the introduction of phenoxy substituents leads to an increase in the solubility of the polymers and a decrease in their glass-transition temperatures, indicating that phenoxy groups behave as chemical plasticisers. This finding is in good agreement with the literature data.^{78–84,96–101}

Polyimides **19–21** have $\eta_{\text{red}} = 0.22–1.00$ dl g^{−1} (*N*-MP) and M_w up to 77 000 (*N*-MP, sedimentation data). With the exception of polypyromellitimide, these polymers are soluble in organic solvents. Some of them form films. The polymers **19–21** prepared

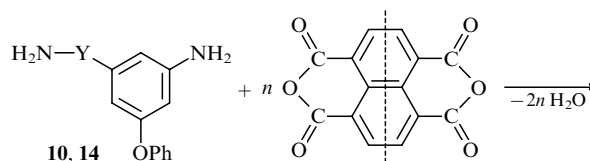


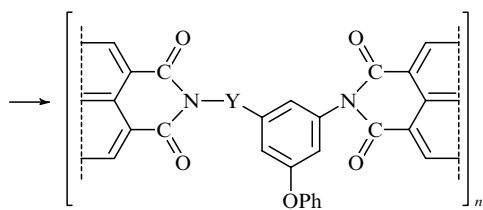
in accordance with Scheme 6 have low softening temperatures (165–213 °C) and high decomposition temperatures ($T_{10\%} = 470–550$ °C), which determines their processability into articles using solvent-free methods.

A comparison of various characteristics of these PI has shown that polymers **19** based on bis(3-amino-5-phenoxy)diphenyl bisphenol ethers manifest the best solubility; some of them are soluble even in cyclohexanone. They also have the lowest T_{soft} .

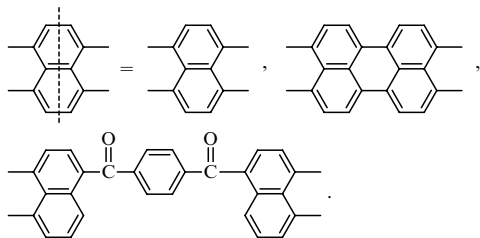
In addition to PI containing five-membered imide rings, PI with six-membered imide rings, viz., polynaphthylimides and polypyrrolenimides, have been synthesised; the latter are known to be more hydrolytically stable and thermostable than polynaphthylimides.^{102–105}

The synthesis of phenoxy-substituted polynaphthylimides and polypyrrolenimides^{90,106} was carried out as follows:



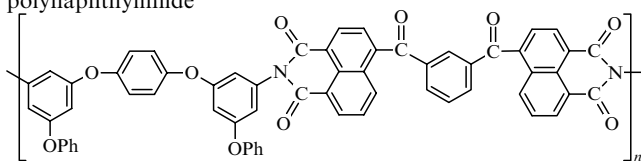


Y = bond (**10**), $-\text{O}-\text{C}_6\text{H}_4-\text{O}-\text{C}_6\text{H}_3(\text{OPh})-$ (**14**);

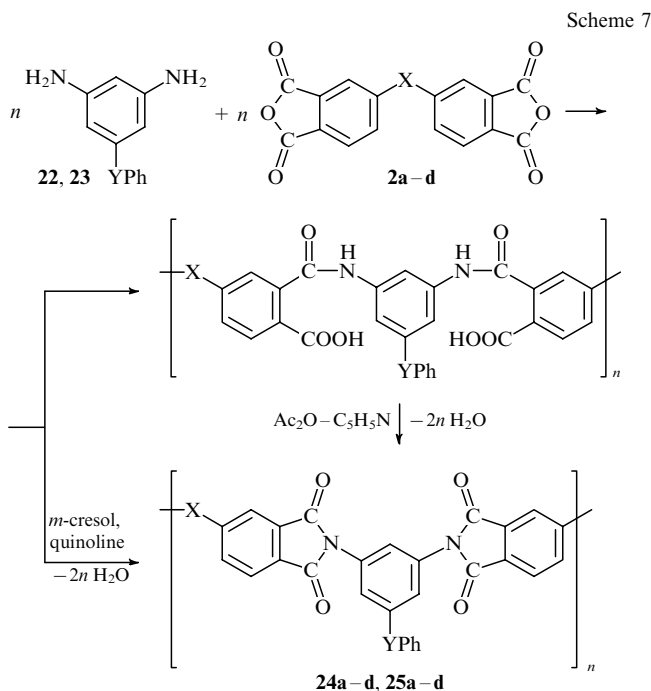


All these reactions were carried out in phenolic solvents (*m*-cresol, *m*- or *p*-chlorophenols) under high-temperature polycondensation conditions using benzoimidazole and/or benzoic acid as a catalyst. The polymerisation process is homogeneous in all cases and yields deeply coloured polymers.

Some of the polymers synthesised are well soluble in organic solvents and possess good thermal characteristics. Thus the polynaphthylimide



is soluble not only in *N*-MP and the tetrachloroethane–phenol mixture (3 : 1), but also in DMF, chloroform and, partially, in



Y = S (**22**, **24**), SO₂ (**23**, **25**);

X = O (**a**), CO (**b**), OC₆H₄C(CH₃)₂C₆H₄O (**c**), C(CF₃)₂ (**d**).

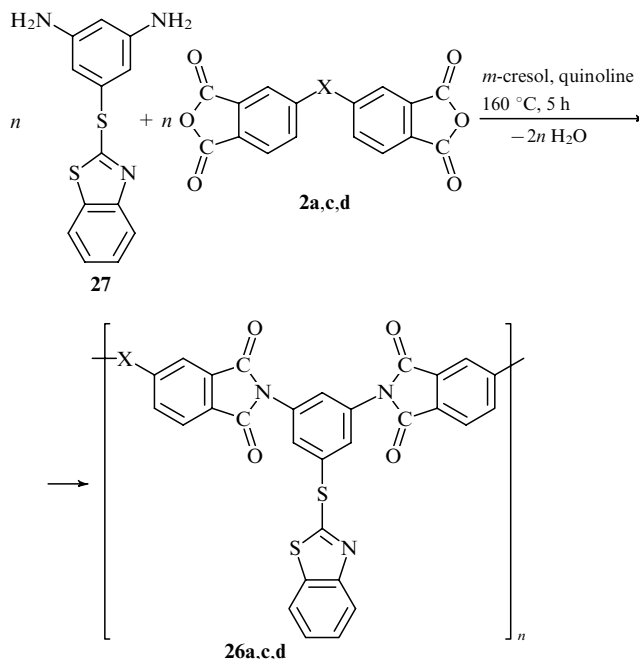
DMA. Enhanced solubility of this polynaphthylimide in comparison with the polymers prepared from the same dianhydrides and aromatic diamines containing no phenoxy substituents^{105, 107} demonstrates a positive influence of the hydroquinone bis(3-amino-5-phenoxy)diphenyl ether structure on the solubility of the polymers.

Polyimides containing phenylthio- and phenylsulfonyl side groups^{62, 94} were prepared from the diamines **22** and **23** in accordance with Scheme 7.

The polyimides **25a–d** based on 3,5-diaminodiphenyl sulfone (**23**) are characterised by lower η_{red} values (0.25 dl g^{−1}) than PI **24a–d** based on 3,5-diaminodiphenyl sulfide (**22**) (0.79–1.20 dl g^{−1}). This difference may be due to the negative effect of the electron-withdrawing phenylsulfonyl group on the reactivity of the amino groups.

The solubility of the PI **24a–d** in organic solvents strongly depends on the nature of the dianhydride used. The values of η_{red} of the polymers in *N*-MP are fairly high (0.79–1.20 dl g^{−1}), while moderate softening temperatures (210–250 °C) combine with high decomposition temperatures (400–460 °C).

The polyimides **26a,c,d** containing benzothiazol-2-ylthio groups were prepared by high-temperature polycyclocondensation of the diamine **27** with the dianhydrides **2a,c,d** in *m*-cresol.¹⁰⁸



X = O (**a**), OC₆H₄C(CH₃)₂C₆H₄O (**c**), C(CF₃)₂ (**d**).

All the PI **26** were synthesised under homogeneous conditions. These polymers have $\eta_{\text{red}} = 0.29\text{--}0.42$ dl g^{−1}, $T_{\text{soft}} = 215\text{--}265$ °C and $T_{10\%} = 325\text{--}400$ °C. The polymer **26a** is soluble in *N*-MP, the PI **26c**, in *N*-MP and THF and the PI **26d** is soluble in *N*-MP, THF and chloroform. The positive influence of benzothiazol-2-yl side groups on the solubility of the polymers has been observed previously.^{109, 110}

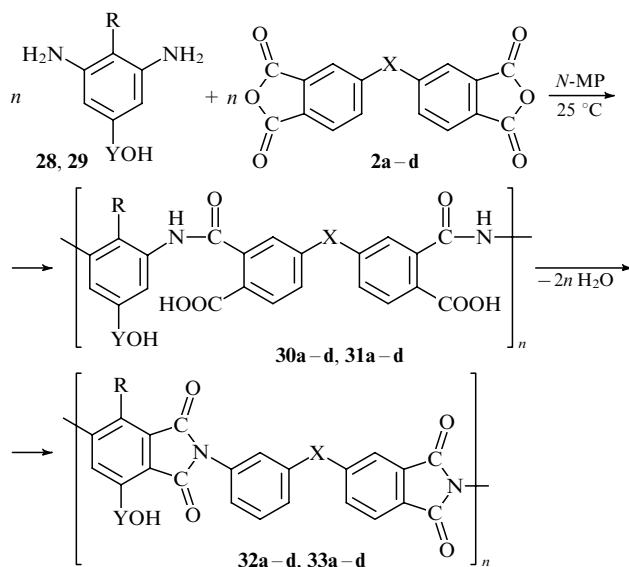
PI containing functional side groups, first of all, hydroxy groups, were synthesised along with PI prepared from TNT derivatives devoid of reactive substituents.^{65, 111}

Recently,^{112–119} PI containing free hydroxy groups have attracted the keen attention of investigators because of the possibility of forming hydrogen bonds, which increases the glass-transition temperatures of the polymers, favours their solubilities in amide solvents and enhances moisture absorption.¹¹⁶

It is noteworthy that hydroxy groups can be used as the reaction centres for the introduction of other side groups, *e.g.*,

unsaturated substituents able to form crosslinked structures;¹¹⁷ chromophores imparting nonlinear optical properties to the PI^{120–122} and thermally unstable side groups prone to thermal decomposition with the formation of low-permittivity nanofoams.^{123–125}

Polyimides based on 3,5-diamino-4'-hydroxydiphenyl ether (**28**), 2,6-diamino-4-hydroxytoluene (**29**) and the tetracarboxylic dianhydrides **2a–d** were prepared in two steps.



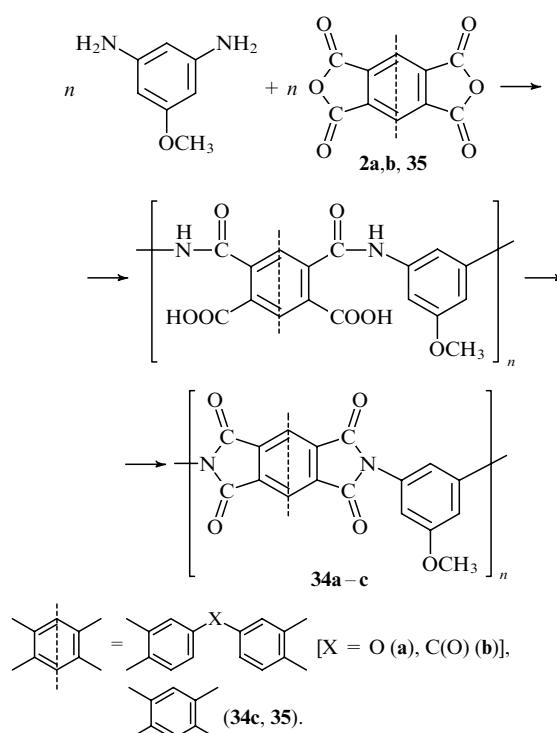
28, **30**, **32**: R = H, Y = $-\text{O}-\text{C}_6\text{H}_4-$; **29**, **31**, **33**: R = CH₃, Y = bond;
X = O (**a**), CO (**b**), OC₆H₄C(CH₃)₂C₆H₄O (**c**), C(CF₃)₂ (**d**).

The first step includes the preparation of PCA **30a–d** and **31a–d** in *N*-MP under mild conditions (25 °C). The second step, *viz.*, polycyclisation of PCA, is carried out in the absence of the pyridine–acetic anhydride mixture to prevent acylation of the hydroxy groups. After addition of toluene to the reaction mixture (for azeotropic distillation of water), the reaction temperature is raised to 180 ± 10 °C and the solution is kept at this temperature for 6 ± 1 h. This method has recently found wide acceptance in PI synthesis.^{95, 126} Cyclisation of PCA **30a–d** and **31a–d** from all the aromatic tetracarboxylic dianhydrides **2a–d** occurs under homogeneous conditions and yields PI **32a–d** and **33a–d** with moderate viscosities ($\eta_{\text{red}} = 0.28\text{--}0.80 \text{ dl g}^{-1}$) and high degrees of cyclisation.

All the PI synthesised represent amorphous polymers with glass-transition temperatures of 223–369 °C typical of flexible-chain PI and decomposition temperatures of 378–439 °C. They are well soluble in organic solvents; the PI based on the dianhydride **2d** manifest the best solubility.

The introduction of alkoxy substituents into the PI macromolecules enhances their solubilities. It is known that the presence of methoxy substituents in PI macromolecules increases their solubilities in organic solvents.⁹⁶ The methoxy-substituted PI are prepared starting from 3,5-diaminoanisole.⁴⁶

The PI **34a–c** were synthesised by the reaction of 3,5-diaminoanisole with dianhydrides **2a,b** and pyromellitic dianhydride (**35**) using three different procedures:^{90–92} low-temperature condensation of 3,5-diaminoanisole with tetracarboxylic dianhydrides in amide solvents followed by thermal (route 1) or catalytic (route 2) imidisation of the PCA formed in the presence of the pyridine–acetic anhydride mixture (1 : 1) and high-temperature (150–180 °C) condensation in *m*-cresol in the presence of a catalyst (quinoline, isoquinoline or benzoic acid) (route 3).



The reaction of 3,5-diaminoanisole with tetracarboxylic dianhydrides in amide solvents (*e.g.*, *N*-MP) is carried out at room temperature. This reaction proceeds in a homogeneous system and yields PCA with relatively high η_{red} ($0.47\text{--}1.12 \text{ dl g}^{-1}$).

Catalytic imidisation affords PI more soluble in comparison with polymers synthesised by solid-phase methods;⁹⁶ therefore, this approach presents the greatest interest. Catalytic imidisation is performed by adding the pyridine–acetic anhydride mixture to a prepolymer solution and stirring the boiling reaction mixture for several hours. In all cases studied, the imidisation was accompanied by precipitation of the polymer from the reaction mass in the form of a swollen gel. It is noteworthy that this does not prevent the cyclisation of the *o*-carboxamide fragments into imide fragments with a high degree of conversion.

Polypyromellitimide **34c** does not soften unless the decomposition temperature is reached. The softening temperatures of polyimides **34a,b** are 300 and 310 °C, respectively.

Depending on the structure of the central fragment of the dianhydride, the thermal stabilities of the PI synthesised decrease in the following order: **34c** > **34b** > **34a**. This is consistent with the generally accepted viewpoint on the correlation between the structures of the polymers and their thermal stabilities.^{127, 128}

Dynamic TGA studies of thermal stabilities of PI prepared (air, heating rate 4.5 °C min^{-1}) have shown that $T_{10\%}$ depends only insignificantly on the polymer structure: $T_{10\%}$ is ~ 400 °C for all the PI studied. The relatively low thermal stabilities of the polymers **34a–c** can be attributed to the presence of the methoxy groups.

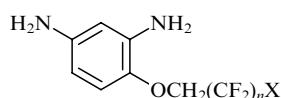
The polyimides **34b,c** are insoluble in amide-type (including *N*-MP) or any other solvents; only the PI **34a** is soluble in *m*-cresol and the tetrachloroethane–phenol mixture (3 : 1). Presumably, the ‘hinged’ groups have a more pronounced effect on the solubility of the polymers than methoxy substituents.

The high solubility of the polymer **34a** in phenolic solvents has made it possible to obtain virtually colourless films with a tensile strength of 114 MPa (at 25 °C) and elongation at rupture of 9%.

An attempt to synthesise the PI **34a** by high-temperature condensation in *m*-cresol was less successful, although this was performed in a homogeneous medium. The η_{red} value of the polymer **34a** thus prepared is much lower than that of the corresponding polymer obtained by catalytic cyclisation of PCA.

Polymers containing perfluoroalkyl side groups also present substantial interest.^{49–51} Such polymers have found wide application in aerospace and electronic engineering owing to their high thermal stabilities, mechanical strengths and good insulating characteristics.^{129–133} These technological fields have a continuing demand for transparent PI (coating of solar batteries) and low-permittivity PI (reduction of delay periods in electric circuits). The optoelectronic industry requires PI transparent at the wavelengths exceeding that of the visible light and possessing controllable refraction indices. Introduction of fluorine into polyimide materials is one of the most efficient approaches to the synthesis of such PI.^{134–136} The introduction of side fluoroalkoxy groups into the starting monomers is also widely used.

The synthesis of fluorinated PI based on diamines of the general formula

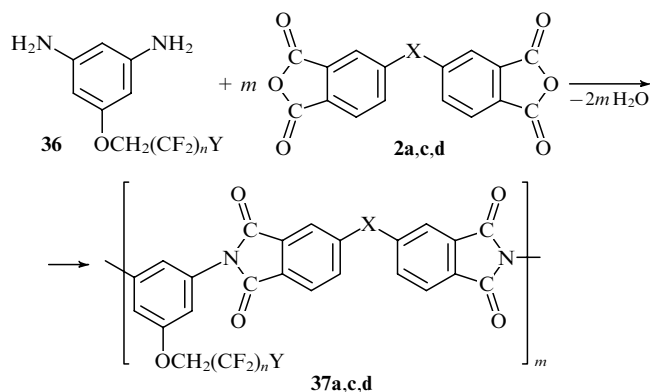


X = F: $n = 3, 6, 7$; X = H: $n = 10$.

has been described.¹³⁷

However, the values of η_{red} of the polymers thus prepared were relatively low and decreased with an increase in the length of the fluoroalkoxy group. This may be due to two reasons, viz.: (1) a decrease in the reactivities of fluorinated diamines as nucleophiles due to the presence of electron-withdrawing fluoroalkoxy groups; (2) the steric hindrance of the amino group in the *ortho*-position relative to the bulky fluoroalkoxy group. This circumstance has stimulated the search for new ways to synthesise fluorinated PI.

Some novel representatives of such PI were synthesised from perfluoroalkoxy-substituted *m*-phenylenediamines **36** based on TNT and various aromatic tetracarboxylic dianhydrides.^{51–54}



Y = F: $n = 1$; Y = H: $n = 2, 4, 6$;
X = O (**a**), $\text{OC}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{C}_6\text{H}_4\text{O}$ (**c**), $\text{C}(\text{CF}_3)_2$ (**d**).

This reaction is carried out in *m*-cresol in the presence of isoquinoline (160 °C, 5 h). The homogeneous reaction conditions favour the preparation of PI completely soluble in *N*-MP. Depending on their structures, such PI are also soluble in other organic solvents. Thus the polymers **37c** are soluble in chlorinated solvents but are insoluble in acetone, whereas the PI **37d** are soluble in acetone, but not in chlorinated hydrocarbons. High solubility of the PI **37** may be due to the presence of side perfluoroalkoxy and bridging groups^{96,136} as well as to the amorphous structure of these compounds (X-ray diffraction data).

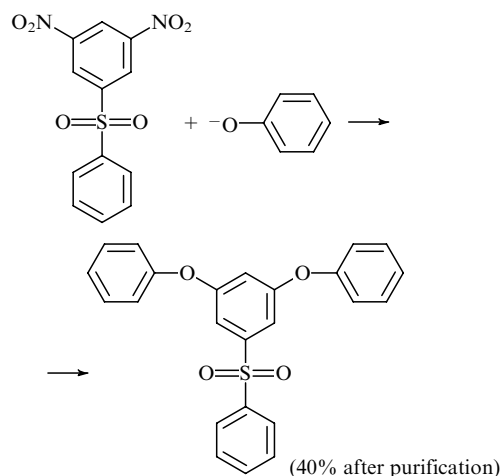
Virtually all PI **37** are high-molecular-mass compounds with $T_{soft} = 155–265$ °C (thermomechanical analysis data) and

$T_{10\%} = 400–430$ °C, which exceed those of the methoxy-substituted PI **35**. It should be noted that T_{soft} of the polymers **37** decreases with an increase in the length of the fluoroalkoxy group. Colourless strong elastic films were cast from solutions of the PI **37** in THF. Pressing of these PI at temperatures exceeding T_{soft} by 100 °C at 10 MPa produced transparent yellowish articles. The polymers **37** possess relatively low refraction indices and dielectric constants (ϵ), which is in good agreement with the known data.^{124,137}

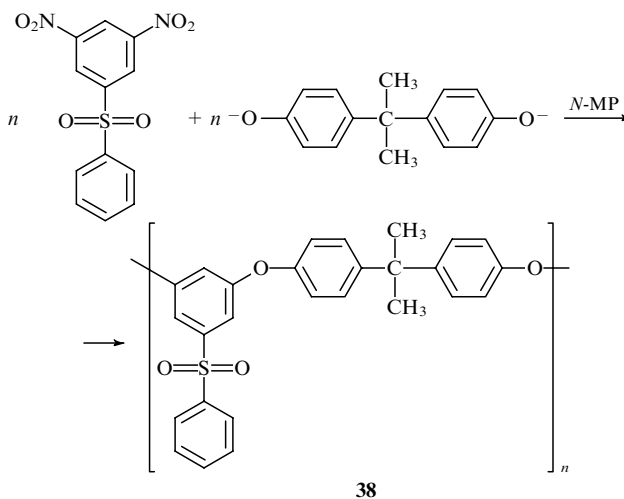
2. Aromatic oligo- and polyethers

Aromatic nucleophilic substitution of nitro groups can be employed for the preparation of aromatic polyethers,^{24,25,138} although there are few examples of such reactions.¹³⁸ A serious problem in the synthesis of polyethers from mononuclear dinitro compounds is passivation of the second nitro group following replacement of the first nitro group by a nucleophile. What is also essential is that nitro group activators usually occupy the *ortho*- and *para*-positions. Therefore, the possibility of using 3,5-dinitrodiphenyl sulfone, a TNT-based mononuclear compound containing an electron-withdrawing activating group in the *meta*-position with respect to the nitro groups, in the synthesis of aromatic polyethers is of interest for investigators.⁹⁰

The model reaction of 3,5-dinitrodiphenyl sulfone with phenol was carried out in *N*-MP (150 °C, 6 h).

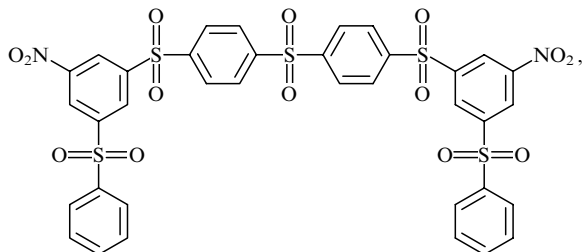


The synthesis of the polyether **38** based on 3,5-dinitrodiphenyl sulfone and bisphenol A was carried out under identical conditions.



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Although the polyether formed has low molecular mass ($n = 5$, $M_n = 1900$, $M_w = 2600$), this reaction has demonstrated the feasibility of polyether synthesis from mononuclear dinitro compounds containing an activating group in the *meta*-position with respect to the nitro groups, which is in agreement with the earlier data.¹³⁹ It seems therefore expedient to use the dinitro-compound,



which represents the reaction product of 4,4'-dimercaptodiphenyl sulfide with a twofold molar excess of 3,5-dinitrodiphenyl sulfone and subsequent oxidation of the sulfide groups to the sulfonyl groups, as a starting monomer for the synthesis of high-molecular-mass polyethers.

IV. Conclusion

The development of condensation monomers and polymers based on TNT and its derivatives offers a solution for two different problems, *viz.*, utilisation of TNT and design of cheap and accessible PI with enhanced processability into articles.

Taking into account the increasing interest in dendritic polymers in the past two decades,^{140–151} it may be expected that the progress in the chemistry of monomers and polymers based on TNT will be associated with the synthesis of such polymers. It should be noted that TAT is an ideal trifunctional core for the synthesis of novel representatives of dendritic PA and PI, while 1,4-bis(3,5-diaminophenoxy)benzene can serve as a tetrafunctional core for the preparation of dendritic PA and PI.

The A₂B-type monomers derived from TNT^{152, 153} can find application in the synthesis of superbranched polymers.^{154–157} In particular, 3,5-diamino-4'-carboxydiphenyl ether can be used for the preparation of superbranched aromatic PA containing peripheral amino groups, whereas 3,5-dinitro-4'-hydroxydiphenyl ether is a promising starting material for the synthesis of superbranched aromatic polyethers based on aromatic nucleophilic nitrosubstitution.

The novel architecture of these polymers determines their novel properties which in turn opens up new areas for their application.

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The characteristics of fractal disperse systems

V I Roldughin

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Abstract. Experimental methods of determination of the fractal dimensions of fractal aggregates are described. The results of studies on aggregation of colloidal particles in different regimes are discussed. Data on the hydrodynamics of colloid dispersions containing fractal aggregates and on the rheology of fractal gels are presented. Capillary phenomena in fractal systems as well as the structural and mechanical properties of aerogels and peculiar features of the optical properties of fractal aggregates are described. The bibliography includes 395 references.

I. Introduction

Disperse systems are of frequent occurrence in nature. The solid component of such systems represents aggregates of colloidal particles, which were among the first physicochemical objects described in the framework of fractal geometry approach. Currently, most studies on fractals are also carried out using fractal aggregates as examples. This is due to the fact that these objects can form a variety of structures, which can be identified with ease in model experiments. It was also found that fractal aggregation provides a way of simulation of many processes which at first glance have nothing to do with particle aggregation.

Fractal aggregates are constituents of a vast variety of systems. Their properties to a great extent predetermine the physicochemical characteristics of the entire systems. In this review the emphasis is placed on the physical properties of aggregates. We will discuss the experimental methods of determining the structure of aggregates and the laws of aggregation, which are based on these properties. Both widely used experimental methods and some promising original techniques for determination of the fractal dimension of aggregates are considered.

V I Roldughin Institute of Physical Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation.
Fax (7-095) 952 53 08. Tel. (7-095) 955 46 47.
E-mail: roldugin@phyche.ac.ru

In the review we will show how the fractal parameters[†] of surfaces and the properties of aerogels (systems comprised of aggregates of the primary particles) can be determined. The properties of aerogels thus implicitly reflect those of fractal aggregates. Of great importance for both aerogels and fractal surfaces are the capillary phenomena. On the one hand, they form the basis for some methods of determination of the fractal dimension of porous media. On the other hand, they affect the evolution of the structure of aerogels, especially at high temperatures.

A large part of the review is concerned with the hydrodynamic characteristics of fractal aggregates. Undoubtedly, these characteristics are of great practical value, because they are responsible for many properties of colloidal dispersions. A wide range of conditions suitable for studying the hydrodynamic behaviour of fractal aggregates is due to frequent occurrence of colloidal dispersions.

Recently, considerable progress has been achieved in studies of the optical properties of fractal aggregates. Researchers perceived that it is the fractal structure of aggregates that strongly affects the electromagnetic field distribution inside them. The fractal structure causes localisation of the electromagnetic field and a dramatic increase in its strength in some local domains. The effects revealed are of interest for all researchers who study highly dispersed metallic systems.

II. Experimental studies of the properties of fractal aggregates

1. Methods of determination of the fractal dimension

The most widely used methods of determination of the fractal dimension of aggregates include (i) sedimentation technique, (ii) electron and optical microscopy and (iii) light, X-ray and neutron scattering. The highest efficiency is provided by the third group of methods, while both microscopy techniques are most easy in use.

The methods based on optical and electron microscopy involve the determination of the dependence of the masses of aggregates on their sizes or construction of the plot of the density correlation function for an image of an aggregate.^{2–6} They can be used to study the aggregates whose fractal dimension (d_f) is at

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[†] For the definitions of the most important fractal parameters, see Ref. 1.

most two, because at $d_f > 2$ the images of a large proportion of the primary particles will overlap. Strictly speaking, some corrections⁷ for the overlap of the particle images should be included even if one deals with fractal aggregates characterised by $d_f < 2$.

Two main approaches are employed in the microscopy studies. One of them involves plotting the density correlation function determined using the image of the aggregate *vs.* the distance from the centre of the aggregate in the double logarithmic coordinates. For fractal aggregates, the plot obtained must be linear. In this case, the fractal dimension can be determined from the slope of the plot using the known relationship for the density distribution function, $\rho(r)$, in the aggregate (see Ref. 1)

$$\rho(r) \propto r^{d_f-d}, \quad (1)$$

where r is the distance from the centre of the aggregate and d is the space dimension.

Following the other approach, one should plot the dependence of the number of particles contained in a square covering the aggregate on the length of the square side (the so-called sand-box technique). This method employs the dependence of the number, N , of particles in an aggregate on the size, R , of the aggregate (see Ref. 1)

$$N = k_0 \left(\frac{R}{a} \right)^{d_f}, \quad (2)$$

(k_0 is the prefactor and a is the size of the primary particles), because the square side acts as the size of the aggregate. For a fractal aggregate, the experimental points fall on a straight line plotted in the double logarithmic coordinates ($\log N - \log R$) and the slope gives the fractal dimension.

The main advantage of the microscopy techniques is the possibility of determination of many fractal parameters, which provide versatile characterisation of aggregates (*e.g.*, a two-dimensional image of a fractal aggregate can be characterised by seven different fractal dimensions⁸). At the same time, these methods are applicable only to rather loose fractal aggregates with $d_f < 2$ (see above).

Yet another procedure for the determination of d_f of aggregates is based on the estimation of the fractal dimension of their sections. This is a useful method of studying opaque composites. It was substantiated by Miyazima and Stanley⁹ who derived an equation for the fractal dimension of the structure (d_{fs}) formed upon intersection of two fractal objects

$$d_{fs} = d_{f1} + d_{f2} - d,$$

where d_{f1} and d_{f2} are the fractal dimensions of the overlapping aggregates.

A section of a fractal object is obtained by intersecting a fractal with a plane. Therefore, the fractal dimensions of a three-dimensional object and its section are related by a simple relationship

$$d_{fs} = d_f - 1.$$

Practical evaluation showed¹⁰ that the fractal dimension of flocs determined using this technique coincided with that found from the three-dimensional structure reconstructed using electron microscopy.

In fact, similar considerations also form the basis for confocal scanning laser microscopy, which recently has been used for the determination of characteristics of fractal aggregates.¹¹ This method involves the determination of the particle distribution in the focal plane of an optical microscope, which is then used to determine the fractal dimension of aggregates. To obtain more reliable results, the fractal object is scanned in different planes.

However, the most widely used methods are small-angle X-ray^{12–15} and neutron^{16–18} scattering. The most popular technique is static light scattering,^{19–24} which involves the determination of the fractal dimension from the dependence of the

scattered intensity on the scattering vector. In the case of dynamic light scattering,^{3, 23, 25–27} the fractal dimension is found from the temporal dependence of the average size of the aggregate. Lin and co-workers²⁸ first showed that this is a power dependence with the exponent $1/d_f$.

A great body of experimental information on the determination of fractal dimensions has been accumulated to date. Therefore, the fractal dimension measurements themselves are no longer topical. Attention now focusses on the studies of the laws of structural transformations experienced by those systems whose evolution is accompanied by the growth of fractal aggregates in some stage. These investigations are mainly based on the studies of light scattering from aggregates.^{29–33}

If a system comprises N particles of the same size, the scattered intensity is given by

$$I(q) = N^2 P(q) S(q), \quad (3)$$

where q is the magnitude of the scattering vector and $P(q)$ is the form factor, which for spherical particles has the form

$$P(q) = \left[24 \frac{\sin(q/2) - (q/2) \cos(q/2)}{q^3} \right]^2, \quad (4)$$

where $S(q)$ is the structure factor

$$S(q) = \frac{1}{N^2} \sum_{j=1}^N \sum_{i=1}^N \exp[i\mathbf{q} \cdot (\mathbf{r}_i - \mathbf{r}_j)], \quad (5)$$

where $\mathbf{q}$ is the scattering vector and $\mathbf{r}_i$ and $\mathbf{r}_j$ are the particle coordinates. The structure factor can be expressed through the density correlation function, $C(r)$, of the aggregate

$$S(q) = \frac{1}{N} \left[1 + 4\pi \int_0^\infty C(r) r^2 \frac{\sin(qr)}{qr} dr \right]. \quad (6)$$

The normalising factor $1/N$ is introduced to provide $S(q=0) = 1$.

From Eqn (6) it follows that the structure factor strongly depends on the density distribution in the system under study. Suppose that the pair correlation function of fractal aggregates in the three-dimensional space is given by

$$C(r) \propto r^{d_f-3} h\left(\frac{r}{R_g}\right)$$

and that the cutoff function has a Gaussian shape

$$h(x) = e^{-x^2},$$

where

$$x = \frac{r\sqrt{d_f}}{2R_g},$$

R_g is the radius of gyration of the aggregate. Then, the structure factor can be calculated using an exact analytical expression

$$S(q) = e^{-(qR_g)^2/d_f} F_1 \left[\frac{3-d_f}{2}, \frac{3}{2}, \frac{(qR_g)^2}{d_f} \right], \quad (7)$$

where F_1 is the hypergeometric function.

The shape of the cutoff function has a rather strong effect on the structure factor. Using the exponential cutoff function

$$h(x) = e^{-\kappa_1 x}, \quad x = \frac{r}{R_g},$$

one gets

$$S(qR_g) = \left(1 + \frac{q^2 R_g^2}{\kappa_1^2} \right)^{(1-d_f)/2} \frac{\sin[(d_f-1) \arctg(qR_g/\kappa_1)]}{(d_f-1)(qR_g/\kappa_1)}. \quad (8)$$

The set of cutoff functions also includes the functions employed in the model of overlapping spheres, where

$$h(x) = 1 - \frac{3}{4}\kappa_2 x + \frac{\kappa_2^3}{16}x^3 \quad \text{at } x < \frac{2}{\kappa_2}$$

and

$$h(x) = 0 \quad \text{at } x > \frac{2}{\kappa_2},$$

and the stretched exponent

$$h(x) = e^{-\kappa_3 x^{\kappa_4}}.$$

Using these cutoff functions makes the expressions for the structure factor of a fractal aggregate more cumbersome.

Experimental studies of the effect of finite aggregate size on the small-angle light scattering intensity were reported.^{34,35} The possibility of reconstructing the cutoff function from the structure factor $S(q)$ was pointed out,^{36,37} which can also be done for polydisperse aggregates provided that the structure factor is measured for a broader interval of q values.

Fractal aggregates of complex structure and the corresponding structure factors were studied by Zhu and White³⁸ assuming an oscillating radial density distribution in the aggregate. Using such an exotic density distribution, it was found that the model correctly reproduces the experimental scattering pattern obtained for aggregates in a polydimethylsiloxane/paraffin liquid mixture.

Expressions (7) and (8) describe individual aggregates. Colloidal dispersions are always characterised by some aggregate size distribution, or particle number (s) distribution. This complicates the expressions for the structure factor³⁵ and, hence, comparison of the theoretical and experimental dependences. In particular, calculations³⁹ of various parameters, which can be determined in the static light scattering experiments, were carried out with the following aggregate size distribution

$$N_s = s^{-\tau} \exp\left[-\left(\frac{s}{\langle s \rangle}\right)^{\beta_s}\right],$$

where τ and β_s are numerical parameters and $\langle s \rangle$ is the average number of particles, and with the stretched exponential cutoff function. The expressions derived are too cumbersome and therefore not presented here.

Usually, static light scattering experiments involve intensity measurements in some range of scattering angles, $a \ll q^{-1} \ll R_g$, corresponding to the so-called small-angle scattering rather than in the whole available interval of scattering angles. In this case, the scattered intensity is given by

$$I(q) \propto (qR_g)^{-d_f}. \quad (9)$$

This relationship permits both the fractal dimension and the radius of gyration of aggregates to be determined.

In dynamic or quasi-elastic light scattering experiments information on the size of an object is obtained by analysing the relaxation times of translational, rotational and 'configuration' diffusion. The theory of dynamic light scattering has been well developed.⁴⁰ This method involves measurements of the correlation function of scattered light

$$g^{(2)}(t) = \frac{\langle I(0)I(t) \rangle}{\langle I(0) \rangle^2}, \quad (10)$$

i.e., the time-averaged product of the scattered intensities measured at instants separated by an interval t .

The second-order correlation function (10) is related to the first-order correlation function $g^{(1)}(t)$ as follows

$$g^{(2)}(t) = 1 + G|g^{(1)}(t)|^2, \quad (11)$$

where G is some function determined by the experimental conditions. The dynamical structure factor for dilute dispersion of particles of the same size is given by

$$S(q, t) = S(q)g^{(1)}(t) = S(q)\left(-Dq^2 t\right), \quad (12)$$

where $S(q)$ is the static structure factor and D is the particle diffusion coefficient. In the Stokes approximation the diffusion coefficient has the form

$$D = \frac{kT}{6\pi\eta R_h},$$

where η is the viscosity of the medium and R_h is the hydrodynamic radius of the particle.

Dependence (12) has a clear physical interpretation, namely, the relaxation time $1/(q^2 D)$ is the time taken for a spherical particle to travel the distance $1/q$. In the case of non-spherical (e.g., rod-like) objects rotation can affect the scattered intensity at $qR \gg 1$. This also holds for flexible objects (e.g., polymer chains) where conformational relaxation can contribute to the dynamical structure factor at $qR \gg 1$. For most colloidal objects (in the absence of depolarising scattering) only translational motion contributes to the dynamical structure factor at $qR \ll 1$. Usually, the experimental data allow the initial rate of change in the correlation function or the first cumulant to be found

$$\Gamma_1 = -\left.\frac{d \ln S(q, t)}{dt}\right|_{t=0} = q^2 D. \quad (13)$$

Monodispersed systems are rare in occurrence; therefore, the contribution of polydispersity to the system's dynamics should be included. Experiments with polydisperse systems permit the averaged dynamical structure factor to be determined

$$S(q, t) = \sum_{s=1}^{\infty} s^2 N_s S_s(q, t), \quad (14)$$

In this case, the averaged first cumulant is given by

$$\frac{\Gamma_1}{q^2} = \left[\sum_{s=1}^{\infty} D_s s^2 N_s S_s(q) \right] / \left[\sum_{s=1}^{\infty} s^2 N_s S_s(q) \right] \quad (15)$$

(it will be recalled that the subscript s denotes the corresponding characteristics of the aggregates composed of s particles).

Thus, the measured diffusion coefficient values are averaged over $s^2 N_s$. This complicates processing of experimental data. A more detailed consideration of the problem can be found in, e.g., a review.²⁶

Improved dynamic light scattering methods were developed. Recently,⁴¹ it was shown that the so-called time-resolved dynamic light scattering technique allows not only the gel point of the dispersion to be determined but also the critical behaviour of the system during the sol–gel transition to be studied and the mechanism of gel formation and the architecture of gel-forming clusters to be predicted. The scattering spectrum exhibits some characteristic features suitable for identification of the sol–gel transition and obtaining information on the system under study.

In conclusion of this chapter, mention may be made that both static and dynamic light scattering techniques employed in studies of fractal aggregates can be significantly improved. This can be achieved by comparing the results of model light scattering calculations with the experimental data. For this reason, numerical simulation of aggregation of colloidal particles is carried out simultaneously with calculations of light scattering by the growing aggregates. Recently,⁴² the temporal evolution of the intensity of small-angle light scattering by the system of aggregating colloidal

particles was numerically simulated. Both irreversible and reversible coagulation of primary particles and aggregates were considered. The probability for the diffusing particles and aggregates to coagulate by collisions was varied over a wide range. It was shown that irreversible aggregation can lead to growth of clusters with the fractal dimension varied from 1.78 (diffusion-limited cluster–cluster aggregation, or DLA) to 2.1 (reaction-limited cluster–cluster aggregation, or RLA). At $qR_g \gg 1$, the scattered intensity depends on the scattering vector as follows

$$I(q) \propto q^{-d_f}.$$

The plot $I(q)$ exhibits a peak which becomes higher as the particle coagulation probability decreases. This points to densification of the particles. In the case of reversible aggregation, the peak appeared in early stages is shifted towards small q values as the time passes. This is accompanied by an increase in the scattered intensity and in the fractal dimension of the aggregates present in the system. Finally, the peak disappears. The theoretical relationships derived in Ref. 42 correctly reproduce the experimental data obtained for aggregates of polystyrene latex particles reported by Giglio *et al.*^{43,44} It was pointed out that phenomenological dependences of the type⁴⁵

$$S(q) = S(0) \left(1 + \frac{2}{3d_f} R_g^2 q^2 \right)^{-d_f/2}, \quad (16)$$

which have no extrema, were obtained for the conditions characterised by the significant role of thermally induced restructuring of clusters.

2. Experimental studies of the growth of fractal aggregates

Aggregation processes are studied to solve various problems. We will consider some most important avenues of research into the kinetics of particle aggregation accompanied by growth of fractal objects.

One investigation line is to obtain complete information on the coagulating system and to compare the experimental data with the predictions made using the Smoluchowski kinetic equation. Research in this field has long been carried out. A typical example is provided by the study⁴⁶ concerned with the growth dynamics of fractal aggregates composed of 10-nm gold particles. Aggregation occurred upon adding hydrochloric acid to a hydrosol. The rate of particle coagulation was controlled by varying the amount of acid. The temporal dependence of the aggregate size was determined using dynamic light scattering. The fractal dimension of aggregates, d_f , was estimated at 1.9 rather than exactly determined. The aggregate size was found to be time dependent as follows

$$R \propto t^{z/d_f},$$

where $z = 1/(1-\mu)$ and μ is the homogeneity parameter of the coagulation kernel. At high acid concentrations, μ was equal to -0.6 . As the concentration of the acid added decreased, the μ value gradually increased to 1. It was pointed out that the limiting value of the parameter μ obtained at high acid concentrations differs from zero ($\mu = 0$ corresponds to the DLA regime). A tendency of μ to unity at low acid concentrations corresponds to the RLA regime characterised by exponential increase in the aggregate size. Hence, the study⁴⁶ demonstrated that the experimental kinetics of particle aggregation is in agreement with the predictions of the Smoluchowski theory.

‘Workability’ of the Smoluchowski equation was confirmed in a number of light scattering studies, in particular, in the experiments on aggregation of 3-nm silica nanoparticles in aqueous solutions at different pH values and temperature (d_f varied from 1.75 to 2.01)⁴⁷ and polystyrene latex particles of size 60 and 140 nm dispersed in aqueous solutions in a wide range of changes in the salt concentration in the solution.⁴⁸ Both studies revealed

good agreement between the theoretical and experimental temporal dependences of the aggregate sizes.

Yet another research avenue is to study colloidal dispersions of more complex composition and the kinetics of aggregation accompanied by growth of fractal aggregates under conditions that differ from both DLA and RLA regimes. This can be illustrated taking the results of studies^{49–52} as examples. For instance, easily restructurable aggregates characterised by low fractal dimension were grown in the experimental studies on coagulation of oppositely charged particles of different size and shape.^{49,50} Deviations from the DLA and RLA laws were found^{51,52} in those experiments where particles coagulated upon adding non-indifferent electrolytes capable of changing the surface charge of the particles. These deviations were ascribed⁵² to the short-range repulsive forces that operate in such systems (see Refs 53–55).

The growth dynamics and the fractal dimension of aggregates also depend on the presence of stabilisers (surfactants or polymers) on the particle surfaces. Surfactant modifiers can serve not only as regulators of the rate of coagulation but also initiators of the process. For such systems the laws of aggregation can be significantly different.^{56–58} Nevertheless, it should be noted that modification of the particle surface not necessarily affects the fractal dimension of aggregates.⁵⁹

Quite unexpected results were obtained⁶⁰ in studies of aggregation of polystyrene latex particles stabilised by poly(*N*-isopropyl)acrylamide. The rate of particle aggregation was controlled by varying the temperature of the system and by adding salt. It was found that the fractal dimension of aggregates increases from 1.8 to 2.7 with increasing the salt concentration and, hence, the rate of coagulation. This change could not be obtained by combining the DLA and RLA regimes. What is more, the experimentally determined laws of changes in the fractal dimension could not be explained by the restructuring of aggregates (DLA-grown aggregates were characterised by a fractal dimension of 1.7 before and of 2.1 after restructuring).

To establish the mechanism of such an unusual aggregation process, the laws of the growth of fractal aggregates of polystyrene latex particles stabilised by sodium dodecylsulfate were studied comprehensively.⁶¹ The experiments involved variation of the particle sizes and the degree of coverage by the surfactant layer. Coagulation of particles was initiated by adding salt. The fractal dimension of aggregates and the temporal dependence of the mass of aggregates were determined using static and dynamic light scattering, respectively. It was established that salt additives affect both the mechanism of aggregation and the structure of aggregates, whereas the adsorption layer of the surfactant affects only the structure of aggregates (more exactly, it mainly affects restructuring of aggregates after completion of aggregation process). Changes in the kinetics of particle aggregation and in the fractal dimension of aggregates were compared with the changes in the potential of interparticle interaction determined in the Derjaguin–Landau–Verwey–Overbeek approximation with inclusion of the adsorption layer of surfactant. It was found that the unusual mechanism of the formation of the fractal structure is governed by a rather complex procedure of particle aggregation. Namely, the primary act of aggregation corresponds to the case where particles come within a distance which is nearly equal to twice the thickness of the adsorption layer. This allows particles to retain lateral mobility, which is responsible for restructuring of aggregates. Only after some time do the particles begin to contact one another, thus losing mobility in the aggregate.

Apparently, the unexpected results obtained in Ref. 60 can be explained by the fact that the authors of this study assumed a linear dependence of the mass of aggregates on time. However, it was found that this not necessarily holds in the case of the complex mechanism of aggregation. In particular, power dependences of the mass of aggregates on time with different exponents were obtained⁶¹ and some deviations from them at certain salt concentration values were pointed out.

Aggregation of 50-nm hematite particles in the presence of adsorbing polymer (polyacrylic acid) was studied.⁶² The fractal dimension of aggregates was determined using static light scattering with different cutoff functions. The polymers used had different molecular masses (1.36×10^6 and 3.69×10^4). Three regimes of particle aggregation, *viz.*, pre-DLA, DLA and post-DLA were practically implemented. The fractal dimension determined with the exponential cutoff function was 0.1 to 0.2 larger than that found using the Gaussian cutoff function. The fractal dimensions were independent of the molecular mass of the polymer. The fractal dimension of the DLA grown aggregates was 1.84 with the exponential cutoff function or 1.73 with the Gaussian cutoff function. At low polymer content, no DLA regime was attained and the aggregation was reaction limited (growth of more compact aggregates with a fractal dimension of 2.0). Aggregation in the post-DLA regime (excess of polymer) was slow, but the structure of aggregates ($d_f = 1.8$) was similar to the structure formed in the DLA regime.

The studies carried out before Zhang's communication⁶² were concerned only with aggregation of polymer-stabilised particles initiated by salt additives^{60,63} or with flocculation using a polymer whose radius of gyration was much smaller than the hydrodynamic radius of the colloidal particles.⁶⁴ The fractal dimension greater than 3 [the exponent in the expression for $S(q)$ changed from 2.83 to 3.42] was obtained at a low content of the polymer (fulvic acids).⁶³ At a large content of fulvic acids, the fractal dimension varied from 2.03 to 2.27. Growth of looser structures was explained by the formation of polymer links despite the low molecular mass of the polymer (~ 1000).

Zhang and co-workers⁶² also studied^{65,66} aggregation of hematite particles initiated by adding polyacrylic acid using dynamic light scattering. It was found that aggregation occurs due to neutralisation of the charge on the surface of particles by the adsorbing macromolecules. The fractal dimension of aggregates (1.88) was independent of the molecular mass of the polymer.

3. Restructuring aggregates

In most systems the growth of fractal objects is almost without exception accompanied by their restructuring in different stages of aggregation. Usually, experiments are designed to allow for and to carry out a separate study of this process. Theoretical studies on restructuring of aggregates began immediately after performing the first numerical experiments on the growth of fractal aggregates. Initially, densification was treated formally, *i.e.*, assuming that particles and aggregates are free to rotate, be bent, twisted, *etc.*; more recent studies were carried out with inclusion of the relative motion of particles in aggregates.^{67–69}

Martin *et al.*²⁶ investigated the kinetics of aggregation of silica particles of radius 11 nm dispersed in aqueous solutions and reported a spontaneous increase in the fractal dimension of aggregates. In these experiments, particle coagulation was initiated by adding a salt. The temporal dependences of the radius and fractal dimension of aggregates were determined using dynamic light scattering. A power-law increase in the mean radius with time at different initial concentrations of particles and different regimes of coagulation was found, which corresponded to conventional kinetics of particle aggregation. The fractal dimension changed from 1.73 for fast (diffusion-limited) to 2.05 for slow (reaction-limited) aggregation. At the same time, it was pointed out that the fractal dimension of the system under study is determined not only by the regime of aggregation but also by some other parameters (*e.g.*, concentration and the chemical nature of the salt added). Long-term observations revealed a dramatic change in the fractal dimension of certain aggregates due to restructuring. An analogous restructuring of aggregates also occurred when the dispersion was in a shear flow.

Similar results were obtained in the experiment⁷⁰ with silica particles of size 5 and 9.4 nm (aggregation was also initiated by adding a salt). The kinetics of particle aggregation in the DLA and

RLA regimes corresponded to that predicted by the Smoluchowski equation with the relevant coagulation kernels. However, the fractal dimension of the DLA-grown aggregates increased to a value of 1.8 after passage of a long time. The change in the fractal dimension was also associated with restructuring of aggregates.

Restructuring of aggregates was also observed in studies of polymer-initiated aggregation^{71,72} (a polymer was added to the solution) and various aerosol systems.^{73,74}

4. Anisotropic aggregates

Most fractal aggregates are anisotropic.^{75,76} This opens up new prospects for studies of their structure and the kinetics of growth.

To characterise anisotropic aggregates, it is possible to introduce two fractal dimensions and the self-affinity exponent. To determine these parameters, one should obtain aggregates with pronounced anisotropy. A good example is provided by aggregates of soot particles and some other highly dispersed aerosols. Here, the prefactor and the fractal dimension can be determined with ease;⁷⁷ however, the prefactors obtained much exceeded those found for a conventional RLA model. To eliminate this problem, an extended characterisation of aggregates of soot particles was carried out.⁷⁸ The particles were found to be self-affine rather than self-similar objects. Fitting the experimental data for the entire population of aggregates gave conventional values of the fractal dimension ($d_f = 1.7$) and the self-affinity exponent¹ ($A = 0.91$).

In the case of anisotropic particles the static and dynamical structure factors can be expressed as multipole expansions⁷⁵

$$S(q) = \sum_l S_l(q), \quad (17)$$

$$S_l(q, t) = \sum_l S_l(q) \exp \left[-Dq^2 t - l(l+1)\Theta t \right],$$

where

$$S_l(q) = \sum_{m=-l}^l \left| \sum_{i=1}^N J_l(\mathbf{q} \cdot \mathbf{r}_i) Y_{lm}(\Omega_i) \right|^2 \quad (18)$$

and $J_l(\mathbf{q} \cdot \mathbf{r}_i)$ is the l th order Bessel spherical function, Y_{lm} is the lm th order spherical harmonic, Ω_i is the orientation of the vector $\mathbf{r}_i$ determining position of the i th particle with respect to the centre of mass of the aggregate; and Θ is the rotational diffusion coefficient given by

$$\Theta = \frac{kT}{8\pi\eta R_h^3}.$$

The scaling behaviour of terms of the multipole expansion (17) for the aggregates grown in the diffusion-limited and reaction-limited cluster–cluster aggregation regimes and in the diffusion-limited particle–cluster aggregation regime was studied in detail by Meakin *et al.*⁷⁵ For cluster–cluster aggregation, they found that the fractal dimension describes the q -dependence of not only the total structure factor but also the terms of the multipole expansion. By contrast, clusters formed by particle–cluster aggregation did not exhibit the same degree of scale invariance.

Relationship (15) for anisotropic aggregates is valid only in the small- q limit ($q \rightarrow 0$). However, the scaling behaviour of the second cumulant for anisotropic aggregates changes at $q \rightarrow 0$. It is an easy matter to find that the following relation holds for anisotropic aggregates at $q \rightarrow 0$

$$\frac{\Gamma_2}{\Gamma_1^2} = Q \left(\frac{\Theta}{D} \right)^2, \quad (19)$$

where Q is a constant; for spherically symmetric aggregates this ratio equals zero.

The optical method^{79,80} of investigation of fractal aggregates is based on their natural anisotropy. The essence of the technique is as follows. The scattered intensity is measured after switching on and off a constant electric field. Switching on the field causes the fractal aggregates to be oriented in space, thus changing the scattered intensity. Switching off the field is followed by disordering of aggregates and the scattered intensity changes again. By analysing the dynamics of changes in the scattered intensity and by comparing the steady-state scattered intensities in the presence and in the absence of external field it is possible to determine the diffusion coefficients of aggregates. Using a number of dispersion samples prepared by successive removal (by, *e.g.*, centrifugation) of aggregates of different sizes, it is possible to determine their fractal dimension. Experiments with silica particles gave a fractal dimension of 2.5.⁸⁰ Analysis of experimental data also revealed a linear dependence of the induced dipole moment of aggregates on their size.

Theoretical analysis^{81–83} of the laws of relaxation of orientational optical effects showed that the anisotropic structure of aggregates can make itself evident in the orientational turbidimetric effect, which is measured in unpolarized laser beam. The effect manifests itself as a difference between the optical densities of colloidal dispersions in which fractal aggregates are disordered and oriented by the external field. This effect is due to the dependence of the total extinction cross-section of anisotropic aggregates on their orientation. The theory of orientational turbidimetric effect was generalised⁸⁴ by inclusion of the interaction between dipoles in the fractal aggregate. The magnitude of the effect was calculated for fractal clusters of different size grown under specific conditions and then evaluated experimentally. Theoretical predictions (in particular, scale invariance of the structure of aggregates and turbidimetric effect) were confirmed by the experiments with 40-nm silica particles. Namely, the dependences of the magnitude of the effect on the aggregate size and on the emission wavelength specifically normalised fell on the same curve.

Yet another method⁸⁵ of studying the laws of growth of anisotropic aggregates involves the determination of the kinetics of development and relaxation of birefringence, which is observed in dispersions of fractal aggregates upon application of external electric field. The technique was evaluated taking dispersions of 9.5 nm polystyrene latex particles as examples (particle aggregation was initiated by adding a salt). The fractal dimension of aggregates and the growth rates were in agreement with the corresponding values found for these systems by dynamic light scattering.

5. Aggregation in transient regime

Particle aggregation is carried out in a particular regime. Diffusion-limited cluster–cluster aggregation causes clusters with a fractal dimension of 1.8 to grow; the fractal dimension of the RLA grown clusters can be as large as 2.1. Not only the fractal dimensions but also the functions $f(x)$ determining the cluster size distribution are different. In the case of diffusion-limited cluster–cluster aggregation one has

$$N_s(t)^2 \propto s^{-2} f\left(\frac{s}{\langle s \rangle(t)}\right),$$

and the function $f(x)$ has the form

$$f(x) \approx e^{-x}.$$

The mean aggregate size varies with time as follows

$$\langle s \rangle(t) \propto t.$$

In the case of reaction-limited cluster–cluster aggregation one has

$$f(x) \approx x^{-1.5} e^{-x}$$

and $\langle s \rangle$ exponentially increases with time. Usually, the results of theoretical studies of DLA are in good agreement with the experimental data and with the results of numerical simulation. As to RLA studies, agreement is observed only in the initial stages of the process. Deviations from the RLA regime were established in both model³³ and numerical^{86,87} experiments. Namely, the fractal dimension varied with time and the exponential growth of the aggregate size was changed by a power-law process.

Systematic studies of the transition region between diffusion- and reaction-limited cluster–cluster aggregation were carried out.^{88–92} Aggregation of polystyrene latex^{88–91} and silica⁹² particles was initiated by adding a salt. The salt concentration was chosen to deliberately perform experiments in the transient regime of aggregation. Dynamic and static light scattering studies reliably established that the transition does occur. Experimental data were confirmed by the results of calculations using the Smoluchowski coagulation equation with a time-dependent coagulation kernel (kernel parameters were chosen based on information on the interaction between latex particles in electrolyte solutions). The possibility of solving the inverse problem, namely, determination of parameters of the interaction between latex particles from the kinetics of coagulation (more rigorously, from the point of transition from one regime of aggregation to another) was also shown.

Experiments showed⁹⁰ that the aggregate size increases linearly with time and that the so-called stability factor, w_c , is related to the fractal dimension

$$d_f = 1.45 + 0.857 \ln w_c. \quad (20)$$

This dependence is valid if the stability factor varies within an order of magnitude.

Differences between the $I(q)$ dependences obtained for the DLA and RLA regimes were reported.⁹¹ Experiments on diffusion-limited cluster–cluster coagulation of polystyrene latex particles revealed that the $I(q)$ dependence passes through a maximum at a finite q value. As the process developed, the peak shifted towards small q , which corresponded to spinodal decomposition. Similarly to the results reported earlier for other systems,^{43,93} no peak was observed for the $I(q)$ dependence when the process was performed in the RLA regime. Transient aggregation studies revealed a gradual transition from the RLA to the DLA regime. The change in the regime of aggregation was accompanied by some delay in the appearance of the $I(q)$ peak; development of the coagulation process led to disappearance of the peak.

Studies of various systems using calculations with the Smoluchowski equation for transient regime of aggregation allowed one to choose the coagulation kernels, which best described the experimental kinetics of particle aggregation.^{89,94–97}

6. Anisotropic particles

Most theoretical and experimental studies are carried out using spherical particles. Aggregation of anisotropic particles also causes the formation of fractal structures.^{98,99} This process was studied¹⁰⁰ in detail by experimenting with iron(III) particles 20–30 nm long and 2–3 nm in diameter, which were electrostatically stabilised in the aqueous dispersion. Coagulation of particles was initiated by adding an electrolyte. The characteristics of aggregates were determined using dynamic light scattering, transmission electron microscopy and small-angle X-ray scattering. Experiments revealed the formation of fractal aggregates with $d_f = 1.95$. The temporal dependence of the aggregate size exhibited two linear portions; the growth rate changed after the aggregate size became as large as nearly 300 nm. A tendency to parallel orientation of particles in the aggregate was pointed out. Because of this, aggregates contain rather dense regions, the extent of densification being strongly affected by the rate of coagulation. It is the dense regions that serve as building blocks for the fractal structure of the whole aggregate.

The first theoretical study of diffusion-limited aggregation of anisotropic particles was reported by Meakin *et al.*¹⁰¹ who

analysed fast and slow rotation of particles in a two-dimensional system with substantially different coagulation probabilities for two different particle orientations. The structure of the growing aggregates was shown to be strongly dependent on the particle rotation rate. Namely, slow rotation of particles with a prescribed orientation causes needle-shaped aggregates to grow, whereas fast rotation or aggregation of disordered particles leads to branched aggregates.

The aggregation of rod-like and fibrous particles and corresponding gel formation was studied.¹⁰² Simple estimates gave expressions for the concentration of the disperse phase at the gel point, the coordinates of the maximum of the structure factor of the dispersion and for the gel density. The relationships obtained differed from the corresponding expressions for spherical particles only in that the cubic root of the particle volume was used instead of the particle radius. Experimental data on the volume fractions of the disperse phase were reported, which corresponded to transition of dispersions of iron(III) hydroxide, clay, rod-like particles imogolite (aluminosilicate fibres), boehmite and silica particles to the gel state. It was found that gel formation occurs at the volume fractions of the disperse phase that are nearly an order (sometimes, two orders) of magnitude smaller than those corresponding to random packing of rods. The fractal dimension of aggregates of rod-like particles depended on their nature and varied from 1.95 for hematite aggregates to 2.35 for boehmite ones.

The depolarised dynamic light scattering technique appeared to be convenient for studies of aggregation of optically anisotropic particles. For systems composed of such particles the depolarised component in the scattered light is independent of the extent of their aggregation. Besides, it was shown^{103, 104} that at sufficiently small q values the decay of the correlation function of photons is governed solely by the rotational diffusion coefficient. Experiments on the aggregation of crystals of a (tetrafluoroethylene-*co*-hexafluoropropene) copolymer showed that the correlation function has the form of a stretched exponent

$$g_d(t) = \exp \left[- \left(\frac{t}{\tau_d} \right)^{\beta_d} \right],$$

where τ_d is some characteristic time and the parameter β_d is related to the fractal dimension as follows

$$\beta_d = \frac{d_f}{3 + d_f}.$$

Crystals of the above-mentioned polymer (size 40 nm) were characterised by a fractal dimension of 2, which was in good agreement with the prediction based on the RLA model.

7. Polydispersed colloids

The effect of particle polydispersity on the structure of fractal aggregates was experimentally studied¹⁰⁵ taking mixtures of virtually monodispersed hematite particles of size 70 and 216 nm as examples. Mixing of two stable dispersions of particles of the same size was followed by their coagulation induced by addition of salt. At the same time, experiments on coagulation of monodispersed particles were carried out. The fractal dimension was determined using three methods based on static light scattering, namely, relationship (9) for the q dependence of the scattered intensity, the Guinier equation for very small scattering angles

$$I(q) = I(0) \left[1 - \frac{1}{3} (qR_g)^2 \right]. \quad (21)$$

and correlation of the average mass and the radius of gyration of aggregate at a given scattered intensity $I(0)$. The fractal dimensions obtained were very close (about 1.75) irrespective of whether the system was monodispersed or bidispersed.

Fractal structures are also formed in atmospheric aerosols, which can thus be treated as polydisperse colloidal systems. Atmospheric aerosols and their laboratory-born analogues were studied using various methods.¹⁰⁶ Interpretation of experimental data was complicated by the fact that atmospheric aerosols can undergo essential restructuring owing to absorption of atmospheric water. It was found that the fractal dimension of atmospheric aggregates can vary from 1.5 to 3; the structure factor (prefactor) of fractal aggregates also varied over a wide range. In some cases the fractal dimension increased as the number of particles in aggregates increased. Apparently, this was due to restructuring of aggregates.

8. Search for new systems and methods

Most recently reported experimental studies on fractal aggregates were devoted to searching for new systems suitable for aggregation. For instance, a light scattering study¹⁰⁷ showed that porphyrin molecules form fractal aggregates in aqueous solutions in the DLA regime. The fractal dimension of aggregates of humic acid particles is typical of RLA regime.¹⁰⁸ Aggregation of copper oxide particles initiated by addition of an exotic biopolymer produced by microorganisms was also investigated.⁶⁴ The results of studies on the effect of ferrocene additives on the density and fractal dimension of soot aggregates formed during combustion of methane in a laminar diffusion flame were reported.¹⁰⁹ Aggregation of fullerenes C_{60} and C_{70} in a mixed toluene–acetonitrile solution was studied.¹¹⁰ The aggregate sizes were determined using static and dynamic light scattering. The aggregation process was found to occur reversibly. Sedimentation of aggregates began after they grew to nearly 300 nm. The hydrodynamic radius and the radius of gyration of aggregates were determined. The fractal dimension was 2.1 for C_{70} and 2.9 for C_{60} clusters.

Growth of fractal aggregates from vesicles bound by a special agent (streptavidine) was studied.¹¹¹ A feature of the aggregation process was the use of a small amount of binder to provide finite sizes of the growing aggregates; the growth of aggregates ceased after consumption of the whole amount of binder introduced into the system. Static light scattering measurements of aggregates of different sizes gave the same value of the fractal dimension (2.9).

A somewhat different vesicular structure was also observed.¹¹² Vesicles 30–50 nm in diameter were formed from variously functionalised fullerene molecules. Aggregation of such vesicles led to formation of a foam-like structure with cavities of different size. Light scattering and transmission electron microscopy data showed that the growing structure was self-similar with a fractal dimension of 1.4.

A number of studies concerned the laws of the growth of fractal aggregates from particles immediately after formation of the latter in various physicochemical processes. Formation of fractal structures immediately after nucleation of hydrous ferric oxide from 10-nm particles was studied.¹¹³ It was established that the fractal dimension of aggregates of hydrous ferric oxide particles increases from 1.5 to 2 as time passes. A static light scattering study of aggregation of AgI particles formed by mixing of aqueous solutions of $AgNO_3$ and KI was reported.¹¹⁴ Depending on the salt concentration ratio (the higher the fraction of $AgNO_3$, the greater the d_f value), aggregates with fractal dimensions varied from 1.61 to 2.88 grew in solution. A rather smooth dependence of the fractal dimension on the salt concentration ratio was established. Apparently, changes in the component concentrations in the system under study were followed by changes in the particle aggregation regime from DLA to RLA. Restructuring of aggregates cannot also be ruled out. Growth of fractal aggregates from silver nanoparticles formed in γ -irradiated aqueous solutions was studied.¹¹⁵ Fractal aggregates of size 20 and 100 nm were obtained. Depending on the reaction conditions, the fractal dimension of aggregates changes from 1.7 to 1.8.

Surface-enhanced Raman scattering was proposed as a tool for studying the kinetics of aggregation of colloidal particles.¹¹⁶ Experiments were carried out with pyridine molecules adsorbed

on the silver bromide surface. Temporal dependences of the Raman scattering intensity were determined for different regimes of particle aggregation. According to the model proposed, the intensity decreases with time obeying a power law

$$I_R \propto t^{(d_f-3)/d_f} \quad (22)$$

The exponent depends on the mechanism of particle aggregation. Fitting the experimental data gave a fractal dimension of 1.81 and 2.16 for colloidal dispersions aggregated in the DLA and RLA regime, respectively.

III. Hydrodynamics of fractal aggregates and their dispersions

1. The hydrodynamic radius of a fractal aggregate

The hydrodynamic properties of fractal aggregates were studied.^{117–120} Using numerical simulation and experimental studies, it was established^{118, 121–123} that the hydrodynamic radius and the radius of gyration of an aggregate are related by a simple relation

$$R_h = \beta_h R_g. \quad (23)$$

For three-dimensional spherical aggregates, the parameter β_h can be expressed through the fractal dimension¹²¹

$$\beta_h = \left[\frac{2(2 + d_f)(d_f - 1)^2}{d_f^3} \right]^{1/2}. \quad (24)$$

For aggregates with $d_f = 2.1$, one gets $\beta_h = 1.04$. Other models (see, e.g., Ref. 124) included the dependence of β_h on the number of particles in the aggregate. However, this had little effect on the absolute values of β_h .

Some other values of the parameter β_h were also obtained. For instance, Wiltzius¹²³ reported β_h values of 1.03 and 0.62 found from calculations based on the Kirkwood–Riseman model (see Ref. 125) for rather large aggregates using a step and an exponential cutoff function, respectively. This indicates a high ‘sensitivity’ of the hydrodynamic radius to the structure of the aggregate perimeter. The experimental hydrodynamic radius of the RLA-grown fractal aggregates of 3.5-nm silica particles was found to be 0.72, thus lying between the limiting values predicted by theory. These results were considered¹²² underestimated because of ignoring possible polydispersity of aggregates in processing experimental data. The β_h value determined with inclusion of polydispersity varies in the range 0.82–0.98 depending on the type of the cutoff function.¹²² Numerical simulation¹²¹ (off-lattice RLA model) gave a β_h value of 0.97, which remained virtually constant as the aggregate size changed,¹²¹ whereas calculations¹²⁴ in the framework of Brinkman’s model assuming a uniform permeability of aggregates gave $\beta_h = 1.23$. Rogak and Flagan¹¹⁹ solved the hydrodynamic problem using the scattering method with different models of self-similar aggregates and obtained $\beta_h \approx 1$. This approach is applicable only to clusters composed of a small number of particles. The expression relating β_h to the number of particles in the aggregate was extrapolated to the case for large aggregates using a special procedure based on replacement of a group of particles in large aggregates by one spherical particle. Numerical calculations¹²⁰ in the framework of Brinkman’s model assuming a radially varying aggregate porosity allowed the dependence of the parameter β_h on the fractal dimension and aggregate size to be determined. The β_h values obtained were in agreement with the results of calculations carried out using other models and with the experimental data.

Based on dimension considerations,¹²⁶ a simple relation between the radius of gyration and the hydrodynamic radius of aggregate was established

$$\beta_h = k_0^{1/d_f} \sqrt{\frac{2 + d_f}{d_f}}.$$

The β_h values calculated using this equation correspond to the results obtained earlier. The dependence of the viscosity of dispersions containing fractal aggregates on the volume fraction of primary particles was also calculated. Viscosity calculations were performed using various models developed to determine the hydrodynamic permeability of porous media.

The hydrodynamic characteristics of a fractal aggregate were calculated numerically¹²⁷ and analytically¹²⁸ using the Brinkman model for the flow of a fluid inside the aggregate. It was shown¹²⁷ that if the fractal dimension of the aggregate is greater than two, structural inhomogeneity has no effect on the hydrodynamic characteristics and the aggregate can be treated as a particle characterised by uniform porosity.

Filippov¹²⁹ calculated the hydrodynamic radius of a fractal aggregate using the multipole expansion of the solution of the Stokes hydrodynamic equations. The expansion coefficients were found by numerically solving the corresponding system of algebraic equations. Calculations were carried out with inclusion of viscous fluid slip on the surface of spherical particles constituting the fractal aggregate. The calculated R_h values coincided with the radius of gyration of the aggregate to an accuracy of 5% to 10% for a wide range of change in the number of particles. As should be expected, taking into account the slip effect led to a decrease in R_h . The same approach was also employed for calculating the thermophoresis and electrophoresis velocities of fractal aggregates.¹³⁰ They decrease on increasing the number of particles in the aggregate, being for rather large aggregates nearly 10% lower than the corresponding velocities of a single spherical particle.

The problem of heat transfer between a fractal aggregate and its environment is related to the hydrodynamic problem.¹³¹ Calculations were carried out for free-molecular and continuum heat transfer regimes. It was shown that using the radius of gyration as the equivalent radius can introduce large errors, especially for aggregates characterised by small fractal dimension and in the case of free-molecular heat transfer.

The results of calculations of the hydrodynamic drag of fractal aggregates using different equations were compared¹³² with the experimental data on the settling velocities of aggregates of different size. The results obtained using the models with radially varying hydrodynamic permeability of aggregates were in agreement with the experimental data.

For aggregates in a gas, the hydrodynamic radius is determined by the Knudsen number

$$\text{Kn} = \frac{l}{d'},$$

where l is the mean free path of molecules and d' is the diameter of the primary particles.

Numerical calculations¹³³ showed that the collision frequency of gas molecules with a small DLA-grown aggregate is virtually independent of the Knudsen number. An increase in the aggregate size causes the effective diameter of collisions to increase in proportion to $N^{0.417}$ and $N^{0.446}$ (N is the number of particles in the aggregate) at $\text{Kn} = 2$ and $\text{Kn} = 200$, respectively.

Collisions of a point particle with fractal aggregates were studied in more detail¹³⁴ taking the DLA-, RLA- and ballistic-grown aggregates as examples (restructuring of aggregates was also considered). Scattering of a point particle by the monomer surface was described by the laws of elastic and diffuse scattering and by a cosine curve. Simulation showed that at $d_f < 2$, the collision cross-section, σ , is proportional to the number of particles in the aggregate, N . At $d_f > 2$, the following relation is valid

$$\sigma \propto N^{2/d_f}.$$

The number of collisions of a point particle with the aggregate is independent of the aggregate size at $d_f < 2$ and increases in proportion to N^{1-2/d_f} at $d_f > 2$. The momentum and the angular

momentum transferred from the point particle to the aggregate by collision were also calculated. It was shown that the drag in a rarefied gas is proportional to N at $d_f < 2$ and to N^{2/d_f} at $d_f > 2$. The angular momentum transferred to the uniformly moving aggregate is proportional to N^{1/d_f} .

A general consideration of the problem of the motion of a particle scattered by the fractal structure was reported.¹³⁵ According to calculations, the root-mean-square value of the multiple scattering angle increases with an increase in the free path of particles in proportion to l^{d_f} . This indicates that the angular distribution of particles scattered by the fractal medium is narrower than for the non-fractal medium characterised by the same mean free path of the particles. The possibility of determining the fractal dimension of the structure from the shape of the angular distribution of the scattered particles was pointed out.

2. Aggregation in shear flow

Sonntag and Russel^{136, 137} pioneered experiments on the growth of fractal aggregates in a shear flow. They experimented with polystyrene latex particles and varied the shear flow rate, particle concentration and the composition of the disperse medium, which determines the parameters of the particle–particle interaction. It was found that the fractal dimension of aggregates weakly depends on the shear rate and the particle concentration. The d_f values obtained (1.8 to 2.5) mainly depended on the particle–particle interaction. The average cluster size (R) was also shown to be related to the shear rate ($\dot{\gamma}$)

$$R \propto \dot{\gamma}^{-\kappa_R}, \quad (25)$$

where $\kappa_R = 0.35$. The aggregate size was independent of the particle concentration.

Relationship (25) can also be derived based on theoretical considerations. Let us represent an aggregate as a set of chains that transfer the mechanical stress from one end of the aggregate to the other end. The chains are characterised by the chemical dimension d_c and by the bending modulus (E)^{138–140}

$$E \approx E_1 \left(\frac{a}{r} \right)^{2+d_c}, \quad (26)$$

where E_1 is the elastic modulus of a monomer unit, r is the distance between the chain ends and a is the chain segment length (or the size of primary particles).

Numerical simulation^{141, 142} showed that the hydrodynamic stress is localised at the periphery of aggregates. This allows the limiting aggregate size corresponding to the beginning of restructuring induced by hydrodynamic forces to be determined with ease. For a flow with the shear rate $\dot{\gamma}$, the hydrodynamic force is

$$F_h \propto \eta \dot{\gamma} R^2, \quad (27)$$

and the limiting radius is given by

$$\frac{R_r}{a} \propto \left(\frac{\eta a \dot{\gamma}}{E_1} \right)^{-1/(3+d_c)}; \quad (28)$$

then one gets

$$\kappa_R = \frac{1}{3 + d_c}.$$

The parameter E_1 cannot be calculated using the known expressions for the interaction potential of colloidal particles, because this interaction depends on the interparticle distance only. Therefore, the E_1 value is usually chosen empirically as some fraction of the particle–particle interaction.

Expressions (27) and (28) were evaluated^{143–145} using numerical experiments with variation of the type of the interaction between particles in the fractal aggregates and the structural organisation of the aggregates ('rigid' and 'soft' aggregates were

studied). According to calculations, these relations are valid with a reasonable accuracy for aggregates of different nature. The parameters of the 'soft' and 'rigid' aggregates corresponded to the experimental values found for dispersions of polystyrene latex^{136, 146} and silica particles¹⁴⁶ (aggregates of these particles can be treated as the 'soft' and 'rigid' ones, respectively).

A number of theoretical studies^{147–156} (most of them involved numerical simulation) concerned the effects of the concentration^{147, 148} and Brownian motion¹⁵¹ of primary particles, walls,¹⁵⁰ hydrodynamic interaction¹⁵² and structure field flow^{153–155} on the laws of growth of fractal aggregates in non-uniform fluid flows. Particle–cluster and cluster–cluster aggregation regimes were considered.^{147–149, 153–155} The laminar flow and a weak turbulent flow with mixing of the fluid was also simulated.¹⁵⁵ The possibility of obtaining a self-similar size distribution of compact aggregates in shear flow was reported.¹⁵⁶ No self-similar size distribution was obtained for fractal clusters because of exponential growth of the average cluster size. Simulation using a model two-fraction colloidal dispersion with inclusion of shear-induced fragmentation led to steady-state distributions of fractal aggregates in shear flow.¹⁵⁷

The subject of experimental studies^{158–162} was the influence of mixing¹⁵⁸ and shear rate^{159–161} on the structure of aggregates growing under the fast and slow coagulation conditions and in the presence of intense Brownian diffusion (see Ref. 162). In the absence of Brownian motion the fractal dimension was independent of the shear rate,^{163–165} while in the presence of intense Brownian motion the aggregates exhibited¹⁶² two structural zones with different fractal dimensions, the greater fractal dimension corresponding to the longer length scale. This situation was also numerically simulated,¹⁶³ namely, particle aggregation in shear flow was studied assuming either a complete or partial restructuring of aggregates including aggregation in the absence of restructuring. Simultaneously, the intensity of small-angle light scattering by the grown aggregates was calculated in the Rayleigh–Gans–Debye approximation. The results obtained showed that the scattered intensity patterns corresponded to a fractal dimension of 1.8 on short and of 2.1 on long length scale, respectively. Therefore, the fractal dimension of aggregates in shear flow can be changed only on long length scales.

A large number of recent experimental studies were concerned with the laws of growth of fractal aggregates in turbulent flows.^{164–166} It was found that the fractal dimension increases with the stirring rate (turbulent flow intensity). This was confirmed by numerical simulation.¹⁶⁶

3. Sedimentation of fractal aggregates

The sedimentation velocity (v_s) of a dense aggregate composed of s particles is given by

$$v_s = \frac{2\Delta\rho g a^2}{9\eta} \frac{a}{R_h} s, \quad (29)$$

where $\Delta\rho$ is the density difference between the particle and the fluid, g is the free fall acceleration and η is the fluid viscosity. Since the number of particles in a fractal aggregate is related to the aggregate size by relation (2), the sedimentation velocity is

$$v_s = v_{s0} \left(\frac{R}{a} \right)^{d_f-1}, \quad (30)$$

where v_{s0} is the sedimentation velocity of a single particle.

From relationship (30) it follows that v_s increases as the aggregate size increases. Therefore, for rather small primary particles there is a critical aggregate size such that for any larger size sedimentation dominates Brownian motion in aggregation processes. The critical size, R_{cs} , can be determined with ease assuming that the times taken for the aggregate to travel the average inter-aggregate distance by sedimentation and by Brownian diffusion are equal. Simple estimation showed¹⁶⁷ that

$$R_s \propto a\varphi^{1/4d_f} \left(\frac{3kT}{4\pi\Delta\rho g a^4} \right)^{1/4d_f}, \quad (31)$$

where φ is the volume fraction of primary particles.

In the initial stage of growth, the settling aggregates are small and insensitive to hydrodynamic stress. However, after reaching a certain critical size they can undergo restructuring. There are two ways of determining the critical size. If sedimentation of already grown aggregates occurs, the critical size is found by analogy with the critical aggregate size in shear flow [see expression (28)]: in the case of sedimentation one has

$$F_h \approx 6\pi\eta R v_s$$

and the first critical radius is given by

$$R_r \propto a \left(\frac{3E_1}{4\Delta\rho g a^2} \right)^{1/(1+d_f+d_c)}. \quad (32)$$

The exponent in expression (32) equals ~ 0.25 and the critical radius weakly depends on the elastic modulus of the single unit. When comparing the calculated and experimental data, one should take into account the possibility of restructuring, which causes densification of aggregates and an increase in their fractal dimension. Restructuring of aggregates was both numerically simulated^{143, 144} and observed in model colloidal systems;^{24, 34, 136, 137, 146, 168} the fractal dimension usually varied from 1.8 to 2.4.

The second critical radius corresponds to the case where sedimentation is accompanied by growth of fractal aggregates. If attractive interparticle forces acting between two collision-coagulated aggregates are smaller than the hydrodynamic force, the resulting structure will be broken and the aggregates will move away from each other. In this case, the limiting aggregate size is determined assuming that the attractive force is equal to the hydrodynamic force. If the molecular attractive force dominates, the bonding force for two spheres (particles) separated by the distance h_s is given by

$$F_b = \frac{Ha}{12h_s^2},$$

where H is the Hamaker constant. In this case, the limiting radius of the settling aggregates is

$$R_b \propto a \left(\frac{1}{16\pi\Delta\rho a^2 h_s^2} \right)^{1/d_f}. \quad (33)$$

It can be determined from experimental data or estimated assuming that the molecular attraction force equals the steric repulsion force. The results obtained from size distribution calculations for the settling aggregates^{169, 170} and from model experiments^{171, 172} confirmed the existence of the limiting sizes defined by relationships (28) and (33).

A number of experimental procedures for determining the fractal dimension of aggregates using sedimentation analysis is based on the fact that the hydrodynamic radius differs only slightly from the radius of gyration. The deposit density

$$\varphi_s \propto R_h^{d_f-3} \quad (34)$$

was compared^{173, 174} with the viscosity of a dispersion of fractal aggregates

$$\eta_d = \frac{n}{(1 - b_v \varphi_a)^{c_v}}, \quad (35)$$

where b_v and c_v are some constants in the empirical dependence¹⁷⁵ of the dispersion viscosity on the volume fraction of the solid phase ($c_v \approx 5.2$ and $b_v \approx 0.4$) and $\varphi_a \propto R_h^3$ is the volume fraction

of aggregates in the dispersion. The radius of fractal aggregates was estimated from the data on the dispersion viscosity while the fractal dimension was evaluated from the sedimentation volume. The fractal dimension can also be determined using the aggregate viscosity and settling velocity data.^{176, 177}

The settling velocity, v_s , of a dispersion is related to the sedimentation volume, V_s as follows¹⁷⁸

$$v_s = A_0 \left(\frac{V_s}{V_0} \right)^{(d_f-1)/(3-d_f)} \left[1 - B_0 \frac{V_s}{V_0} \right]^{c_v}, \quad (36)$$

where A_0 and B_0 are some constants and V_0 is the sedimentation volume of non-aggregated particles.

Methods of determination of the fractal dimension only from the sedimentation velocity of aggregates of different size, characterised by the same d_f value were proposed.^{179, 180} They involve a special procedure for processing experimental data¹⁸⁰ followed by finding a correlation between the sedimentation velocities of two fractal aggregates and a third aggregate formed from the first two aggregates.¹⁷⁹ (It should be noted that modern methods allow the particle aggregation process to be monitored with ease and are therefore often used for practical purposes,¹⁸¹ in particular, for preparation of aerosols possessing high sedimentation stability.) Given a constant number of particles, from relationship (30) it follows that the sedimentation velocities of the three fractal aggregates must be related as follows

$$v_{s1}^{d_f/(d_f-1)} + v_{s2}^{d_f/(d_f-1)} = v_{s3}^{d_f/(d_f-1)}, \quad (37)$$

By measuring the settling velocities of the aggregates it is possible to unambiguously determine their fractal dimension. Experiments carried out following the design mentioned above gave $d_f = 1.97$ and 1.19 for aerosol particles of soot and magnesia, respectively. These values are in good agreement with those found for the same systems using electron microscopy.

It is possible to determine the fractal dimension by studying the sediment morphology.¹⁸² However, this approach can be practically implemented only when using non-destructive methods of investigation.

If aggregates are composed of small particles or if the density difference between the disperse phase and the disperse medium is small, sedimentation can slow down due to thermal motion of particles and aggregates. Since in the gravitational field the local concentration of monomers varies with height, the characteristic aggregate size will also change with height.¹⁸³ By measuring the density of the disperse phase and the aggregate sizes at different heights one can determine the fractal dimension and draw some conclusions about salient features of structural organisation of aggregates.

Sedimentation of colloidal dispersions is not completed by the formation of loose deposit. Usually, the height of the deposit layer slowly decreases with time due to densification of fractal aggregates. The consolidation dynamics were studied by Potanin and Russel¹⁸⁴ who preliminarily established that the bulk viscosity, η_v and the yield stress, P_c , of the deposit (fractal aggregates) are given by

$$\eta_v \propto \left(\frac{1 - \varphi}{\varphi_m} \right)^{-\kappa} \varphi^{\gamma_\eta}, \quad (38)$$

$$P_c \propto \left(\frac{1 - \varphi}{\varphi_m} \right)^{-\kappa} \varphi^{\gamma_p},$$

where $\varphi_m \approx 0.61$ is the limiting volume fraction of filling and κ_φ is a fitting parameter,

$$\gamma_\eta = \frac{3 + 2d_c}{1 - d_f},$$

$$\gamma_P = \frac{3}{3 - d_f}.$$

The results of calculations using relations (38) are in good agreement with the experimental data¹⁸⁵ for oleic acid stabilised by alumina particles. The best agreement with the experiment was achieved using a two-fraction model for the sedimenting dispersion, which deals with the deposit itself and the dispersion, which settles without formation of an elastic network.

4. Fractal gel rheology

Recently,¹⁸⁶ a typical example of a detailed rheological study of a gelling colloidal dispersion was reported. The subject of this investigation was a colloidal dispersion of 43-nm silica particles. Flocculation was initiated by adding a salt. The dispersion structure was determined using small-angle X-ray scattering while the storage and loss moduli were determined by oscillation shear rheometry. The scale range of surface fractality was found; however, the fractal dimension was not determined. It was shown that an elastic gel network is formed as time passes. It was established that a slow process proceeds in the system, which results in the change (namely, an increase) in the gel storage modulus but leaves the local structure of the gel virtually unchanged. Shear-induced breakdown of the gel network causes no significant changes in the local structure of the dispersion, whereas the storage and loss moduli decrease substantially. The kinetics of recovery of the moduli mentioned above, measured after shear relieving, differs from the kinetics of growth of the same moduli in the course of flocculation. The laws established are characteristic of fractal colloidal gels of different nature. In particular, the experimentally observed¹⁸⁷ rheological behaviour of a gel of protein molecules was explained only using the fractal approach.

Based on a model treating a gel as an ensemble of contacting fractal aggregates, a simple relation between the elastic modulus of gel and the volume fraction of particles was obtained¹⁴

$$E_e \propto \varphi^{(1+\zeta)/(3-d_f)}, \quad (39)$$

where ζ is the parameter responsible for the size dependence of the elastic constant of a fractal object (K_e)¹⁸⁸

$$K_e \propto \frac{K_0}{R^\zeta}. \quad (40)$$

Since then, the elastic and rheological characteristics of gels have been analysed with inclusion of the concept^{139,140} of elastic chains, which are responsible for elastic energy transfer in aggregates and characterised by the chemical dimension.

Considerable attention in theoretical studies has been paid to the so-called weak gels composed of nanoparticles. The formation of loose fractal aggregates in these systems causes gelation even at very low particle concentration (2 vol.% – 3 vol.%). Such systems possess unusual rheological properties. For instance, two regimes of Newtonian flow of dispersions of silica particles at low and high shear stress can differ in viscosity by nine orders of magnitude. At the same time, it is possible to analyse these systems theoretically. The rheological properties of such gels have been the subject of a large number of studies (see, e.g., Refs 138 and 189–195).

At low shear rates, the viscosity of a gel is determined by relaxation processes related to breakdown and nearly complete re-formation of interparticle bonds. As the shear rate increases, stress overshoot occurs. In this case the energy dissipation mechanism changes. The system goes to the state of a dispersion of hydrodynamically interacting fractal aggregates. In fact, the system seemingly goes from the 'solid-like' to the 'liquid-like' state.

Since in this case the interparticle interaction plays the determining role, the rheological characteristics depend not only on the gel structure but also on the parameters of the interparticle

interaction. The most important parameters are the bonding energy, U_c ; the bonding force, F_c ; and the force constant

$$k_{el} = \frac{d^2 U}{dh_s^2} = k_g \frac{F_c}{h_c} \approx k_g \frac{U_c}{h_c^2}, \quad (41)$$

where U is the potential of the interparticle interaction, h_s is the distance between the particle surfaces and h_c is the distance between the particle surfaces at the potential well minimum.

From the equations for the balance of forces and the energy balance one can derive¹⁹⁵ the dependences of the rheological characteristics of weak gels on the volume fraction of particles of the disperse phase.

In the case of oscillating small-amplitude perturbations, the storage modulus is given by

$$G' \propto c_g k_g^{1/2} c_1^{-1} \frac{F_c}{a^2} \varphi^{\gamma_G}, \quad (42)$$

where c_g is a constant of the order of unity,

$$c_1 = \frac{U_c}{kT} \exp\left(-\frac{z_c U_c}{kT}\right)$$

(z_c is the coordination number of the particles in the aggregate) and

$$\gamma_G = \frac{7 + 2d_c - 2d_f}{3 - d_f}.$$

At low shear rates, the dispersion viscosity is

$$\eta \propto c_\eta c_1^{-2} \tau_0 \frac{F_c h_c}{a^3} \varphi^{\gamma_\eta}, \quad (43)$$

where c_η is a constant,

$$\tau_0 = \frac{kT}{6\pi\eta_0 a^3}$$

is the characteristic time of particle diffusion in the disperse medium and η_0 is the viscosity of the disperse medium and

$$\gamma_\eta = \frac{7 + 3d_c - 2d_f}{3 - d_f}.$$

At high shear rates, the effective viscosity is given by

$$\eta = \eta_0 \left(1 - \frac{\varphi_a}{\varphi_m}\right)^{-2.5\varphi_m} + \frac{1}{\gamma} c_\eta \frac{F_c h_c}{a^3} \varphi_a^2 \left(\frac{\varphi}{\varphi_a}\right)^{(5-2d_f-d_c)/(3-d_f)}, \quad (44)$$

where $\varphi_a = \varphi/\varphi_i$ is the volume fraction of aggregates and $\varphi_i \approx (R_g/a)^{d_f-3}$ is the volume fraction of particles in the aggregate. The former parameter depends on the shear rate and aggregate strength and can be determined using the relationship

$$\frac{5\pi}{2} \eta \dot{\gamma} R_g^2 \approx F_c \left(\frac{\varphi}{\varphi_a}\right)^{1/(3-d_f)}, \quad (45)$$

corresponding to the case where the hydrodynamic stress applied to the aggregate equals the ultimate strength of the aggregate. The model correctly reproduces the experimental data. In particular, analysis of Eqn (44) revealed a Newtonian rheology of gel at high shear rates.

The hypothesised gel flow mechanism¹⁹⁵ was confirmed¹⁹⁶ by numerical simulation under constant shear. Gel was shown to have a yield point and three flow regimes corresponding to increasing stress were revealed. At low strain, no stress overshoot occurs and the system is in viscoelastic flow state. An increase in the strain applied causes fragmentation of the system into large

aggregates and transition to the viscoplastic flow state. This favours further fragmentation of aggregates and then the system goes to the pure viscous flow state.¹⁹⁷

The dependences obtained¹⁹⁸ for a two-dimensional system of colloidal particles in a complex potential with inclusion of bending elasticity of the interparticle bonds are similar to relations (42)–(44). The dynamics of gel in shear flow were simulated by the Monte Carlo method. The formation of a fractal gel in the system was followed by applying a shear strain. The temporal evolution of the stress developed in gel and the dependences of the stress on the relative deformation and on the steady-state shear rate were traced. Most dependences showed a power-law behaviour, which is typical of fractal structures. Analogous power-law dependences were obtained from similarity considerations, which also allowed the relations between the exponents and the fractal parameters of gel to be followed. Fragmentation studies of fractal aggregates in shear flow showed that this process is to a great extent determined by the bending elasticity of the interparticle bonds.

IV. Optical properties of fractal aggregates

In Section II, structure-dependent peculiar features of small-angle light scattering were considered assuming single scattering and small sizes of primary particles constituting fractal aggregates compared to the emission wavelength.

A study going beyond the scope of this approximation was reported.¹⁹⁹ To include the multiple scattering effects and the fact that the particle size is comparable with the emission wavelength, the light scattering intensity was calculated in the framework of the Mie theory. Each scattering particle in the aggregate was considered as being in some effective medium characterised by a refractive index corresponding to the average aggregate density. The approach was developed²⁰⁰ with allowance for the fact that the optical characteristics of the effective medium containing the scattering particles vary with the fractal aggregate density. As a result, the form-factor responsible for the scattering by a single particle appeared to be position-dependent, thus affecting the total scattered intensity. The method proposed allows additional information to be extracted (in particular, not only the fractal dimension but also the aggregates sizes were determined).

This approach was experimentally evaluated²⁰¹ taking light scattering by aggregates of 0.8- μm latex particles as an example. Experiments involved variation of the concentration and the extent of aggregation of primary particles. Using the Mie theory for the description of scattering by single particles, a greater body of information was obtained from both small-angle and large-angle light scattering data. This allowed not only the fractal dimension of aggregates but also the aggregate size distribution to be determined.

Interesting results were obtained in studies on the behaviour of electromagnetic radiation in fractal aggregates and on the spectrum of the scattered radiation, especially in the presence of nonlinear effects.

The optical properties of fractal aggregates were first studied by Shalaev and Stockman²⁰² who calculated some optical characteristics in the self-consistent approximation with inclusion of the dipole–dipole interaction between monomers. It was shown that fractal aggregates possess unique optical properties, which differ from the properties of single particles and continuous media. The formation of a fractal causes broadening and splitting of the characteristic lines of the primary particles in the absorption spectrum; however, these lines remain centred near their initial positions, which correspond to the minimum absorption of the fractal. Therefore, the lines can still be treated as resonance ones, which is associated with a fast decrease in the fractal density on going towards its periphery [see Eqn (1)].

Broadening of the lines of the metallic particles forming fractal aggregates was confirmed experimentally (see, *e.g.*, Ref. 203). It is used for monitoring the growth of aggregates in colloidal dis-

persions even under very fast aggregation conditions.^{204,205} The theoretical approach²⁰² was developed by Karpov *et al.*,²⁰⁶ who provided an explanation for all features in the spectra of aggregated colloidal silver particles. In particular, it was found that the second peak in the absorption spectrum of a colloidal dispersion is due to two predominant geometric parameters of aggregates (the size of primary particles and the distance between neighbouring particles) rather than specific resonances in the ensemble of particles. These parameters predetermine the increase in the spectral density of the surface plasmon resonances in a specific wavelength range, which manifests itself in the spectra of sols characterised by rather narrow size distribution of the primary particles (5 to 25 nm).

Yet another important property of fractals is production of surface-enhanced Raman scattering (SERS) by impurity sites.²⁰³ This provides an explanation²⁰⁷ for the experimental observation of the strongest SERS signal from aggregated metallic particles in colloidal solutions.

Studies on the nonlinear optical properties of fractal aggregates of metallic particles showed that aggregation causes a dramatic enhancement of the nonlinear optical response in the region of plasmon resonance characteristic of single metallic particles.^{202, 208–221} When the frequency of incident radiation is off resonance, the decay rate of the absorption of a fractal aggregate is lower compared to single particles while the absorption coefficient per particle increases. The imaginary part of the polarisability of a particle in the cluster is related to the detuning, Δ , by the following power-law dependence²¹⁰

$$\chi''(\Delta) \propto a_p^2(a_p\Delta)^{d_0-1}, \quad (46)$$

where a_p is the distance between primary particles and d_0 is the optical spectral dimension (this parameter lies between 0.3 and 0.6 for different types of fractals). From this relationship it follows that the frequency dependence of the particle's response in the aggregate dramatically differs from the resonance dependence for a single particle. Namely, absorption of the incident wave far from resonance is still high and slowly decreases obeying a power-law dependence as the frequency detuning increases. In some cases, the absorption cross-section increases so greatly that it is more appropriate to describe the situation in terms of the transparency–opacity transition in fractal aggregates.²²²

The results of calculations of the absorption coefficients of fractal and non-fractal aggregates of metallic particles were presented in a comprehensive study²²³ of clusters grown in different aggregation regimes. According to calculations, the absorption spectrum of fractal aggregates must have a complex pattern in contrast to the absorption spectrum of non-fractal aggregates, which exhibits a single sharp maximum. For fractal aggregates, the absorption maximum no longer corresponds to the resonance frequency and there is a system of absorption maxima whose positions and intensities are governed by the aggregate structure and by the number of particles in the aggregate.

Fractal aggregates can also sustain optical (dipolar) eigenmodes,²¹⁰ which can be localised in some range of wavelengths that are shorter than the emission wavelength.^{210,214} This favours concentration of the electromagnetic energy in the domains whose size is smaller than the diffraction limit of conventional optical devices.

The dispersion equation for the eigenmodes of a fractal aggregate has the form

$$\lambda \propto a_p(a_p^3\Delta)^{(d_0-1)/(3-d_f)}, \quad (47)$$

where λ is the emission wavelength.

Near the resonance frequency ($a_p^3\Delta \ll 1$), the dipolar eigenmode is delocalised. As the frequency detuning increases ($a_p^3\Delta \approx 1$), the eigenmode becomes well-localised at the wings of the absorption bands, *i.e.*, $\lambda \approx a_p$. Localisation of optical excitations favours creation of strong local fields, which leads to giant

enhancement of resonant Rayleigh and Raman scattering and nonlinear light scattering^{215–217, 224, 225} observed in colloidal dispersions of some metals. Photomodification of fractal aggregates of silver particles²²⁶ was also explained by localisation of optical excitations.

The results of calculations of dipolar modes localised on fractals are presented in Fig. 1. The local field intensity distributions (shown in Fig. 1 are the isolines corresponding to different electromagnetic field intensities) clearly indicate localisation of the electromagnetic field on the fractal object.

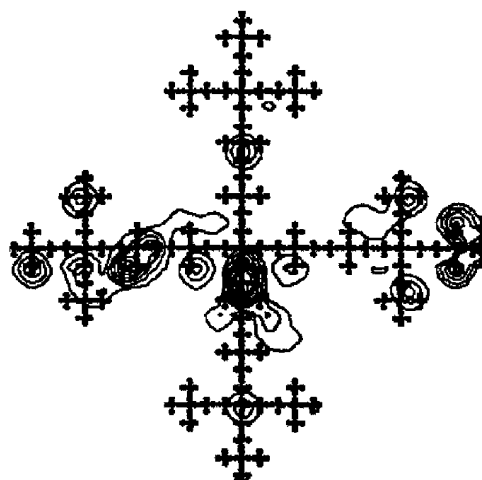


Figure 1. Electromagnetic field intensity distribution on a model fractal aggregate.²²³

The typical size of fractal aggregates composed of nearly 10-nm particles does not exceed the emission wavelength in the optical or IR spectral region. Therefore, such aggregates can be treated as elementary dipoles. Nevertheless, their nonlinear optical characteristics are to a great extent determined by fluctuations of the electromagnetic field inside the aggregates. The corresponding numerical calculations^{214, 227–233} showed that the zones of large fluctuations are localised in different small domains of fractals and their positions vary as the emission wavelength varies.

Estimation of the enhancement factor gave

$$G_e \approx \delta_r \left(1 + \frac{A^2}{\delta_r^2} \right) |\chi''(A)|, \quad (48)$$

where δ_r is the reciprocal Q-factor of resonance, which is determined by resonance amplitude and width. As can be seen, the enhancement factor can be very large at $A \gg \delta_r$.

The calculated dependences of the enhancement factor for different ensembles of particles (regular packs and fractal aggregates of metallic silver particles characterised by a fractal dimension of 1.78) are presented in Fig. 2. As can be seen, the enhancement factor increases to the greatest extent in the case of fractal aggregates. Local enhancement of electromagnetic waves can be explained as follows. In spite of a loose structure, fractal aggregates are characterised by a high probability of finding several particles near a given particle. This is due to the fact that the correlation function of a fractal structure decreases regardless of how the origin of coordinates is chosen.¹ Because of this, neighbouring particles in fractal structures are always strongly coupled. As a result, at any orientation and polarisation of the field there are resonant ensembles of particles, which causes excitation of localised optical modes far from resonance.

Thus, a broad spectrum of localised resonance modes of a fractal aggregate is due to the dipole–dipole interaction between constituent particles. Localisation of modes in different randomly

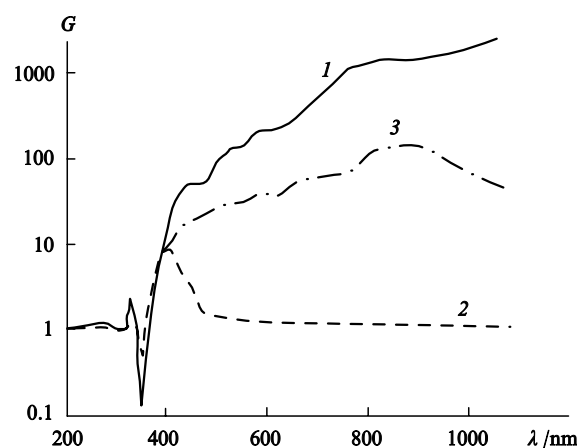


Figure 2. Enhancement factor as a function of the wavelength for fractal aggregates (1), randomly distributed metal particles with the same packing density (2) and close-packed metal particles (3).²²³ The total number of particles in systems is 500. Calculated using the parameters for silver.

located cluster domains causes large local fluctuations of the field and the appearance of ‘strong-field’ and ‘weak-field’ domains. In the case of fractal colloidal aggregates of nearly 10-nm silver particles the localisation length varies with the emission wavelength and equals ≈ 100 nm in the blue spectral region and 20 nm in the near IR region.

Shalaev²²³ reported the results of calculations of the enhancement factors of other nonlinear optical effects in fractal aggregates (four-photon scattering, second optical harmonic generation and Raman scattering). The enhancement mechanism of nonlinear optical effects is analogous to the mechanisms of localisation of optical radiation and enhancement of local fields (see above).

Predictions of giant enhancement of the nonlinear optical properties of single particles^{202, 206–221} aggregated into fractal structures were experimentally tested in the studies of four-photon scattering and nonlinear refraction and absorption.^{234, 235} Aggregation of initially isolated particles into fractal aggregates led to an increase in the conversion factor of four-photon scattering by a factor of 10^6 and to enhancement of nonlinear refraction and absorption by a factor of 10^3 . Localisation and large fluctuations of local fields in fractals were observed using near-field scanning optical microscopy.^{214, 231–233} Experiments²³¹ were carried out with fractal aggregates ($d_f = 1.78$) of 10-nm silver particles. The aggregates were excited by laser radiation at 488 and 514.5 nm. It was established that the field localisation length is 60 to 140 nm, which is in good agreement with the results of calculations.

The list of the nonlinear optical properties of fractal aggregates considered above is far short from being complete. Experimental evidence of nonlinear gyrotropy of fractal silver clusters due to non-local interaction and its enhancement upon aggregation of silver nanoparticles in a colloidal solution was also reported.²³⁶ Using a specially developed procedure, the contributions of the local and non-local effects to gyrotropy were distinguished. Measurements showed that aggregation of particles into fractal aggregates with $d_f = 1.7$ causes a substantial increase (by about two orders of magnitude) in the contribution of nonlinear gyrotropy.

Localisation of dynamic excitations on disordered structures (in particular, fractals) is a universal property and plays a significant role in many physical processes.^{237–241} In addition to localisation of light-induced dipolar excitations, the fractal structure also favours ‘trapping’ of electromagnetic radiation (light).²¹⁷ The light ‘trapping’ mechanism is similar to the mechanism of localisation of electromagnetic field (see above). At the same time, a somewhat different mechanism of light trapping in a fractal aggregate was reported.²⁴² This mechanism ‘works’ in the case of

rather large aggregates and is associated with the predicted²⁴³ strong localisation of light in close-packed granulated media due to the motion of photons along loop trajectories. This light localisation mechanism requires that the aggregate be composed of weakly absorbing particles, the photon wavelength be comparable with the aggregate size and the positions of particles in the cluster be strongly correlated. In this case, at low fractal dimensions of aggregates (a critical d_f value of 2 was obtained²⁴²) this trapping mechanism also leads to high concentration of the electromagnetic field in fractal aggregates, thus providing an explanation for high reactivity of nanoparticles in fractal aggregates.²⁴²

The fractal structure of aggregates is also responsible for enhancement of the Rayleigh resonant scattering of electromagnetic radiation. The corresponding numerical and analytical calculations were reported by Shalaev, Botet and Jullien.²¹⁵ The enhancement factor of the Rayleigh scattering

$$F_R = \frac{\sigma_s}{N\sigma_{s1}}$$

(σ_s is the scattering cross-section for a fractal aggregate composed of N particles and σ_{s1} is the scattering cross-section for a single particle) depends on the fractal dimension and the aggregate size.

For small aggregates one has

$$F_R \propto \frac{N}{a_p^3 \delta_r} (a_p^3 \Delta)^{d_o+1}. \quad (49)$$

For large aggregates

at $d_f < 2$ one has

$$F_R \propto \frac{(a_p/\lambda)^{-d_f}}{a_p^3 \delta_r} (a_p^3 \Delta)^{d_o+1},$$

at $d_f = 2$ one has

$$F_R \propto \frac{(a_p/\lambda)^{-2}}{a_p^3 \delta_r} \ln[(ka_p)^2 N] (a_p^3 \Delta)^{d_o+1},$$

and at $d_f > 2$ one has

$$F_R \propto \frac{(a_p/\lambda)^{-2}}{a_p^3 \delta_r} N^{1-2/d_f} (a_p^3 \Delta)^{d_o+1}, \quad (50)$$

In conclusion, it should be recalled that aggregates of conducting particles in composition materials near the percolation threshold also have a fractal structure. Therefore, percolation systems are also characterised by fluctuations of electromagnetic field and possess nonlinear optical properties.²²³ The nature of the magnetic field fluctuations in and nonlinear optical properties of percolation systems has much in common with the corresponding features of fractal aggregates. Because of this, we leave the percolation systems out of our consideration.[‡]

V. Capillary phenomena in fractal systems

1. Wetting of fractal surfaces

The contact angle on a fractal surface greatly differs from the contact angle on a smooth surface. Theoretically, the contact angle on the fractal surface was determined by Hazlett²⁴⁵ who studied the case where the droplet size exceeded the length scales on which the scaling relations are valid. This situation is typical of macroscopic systems. The expressions derived for the contact angle on the fractal surface were confirmed experimentally.^{246–249} Here, we will present the relationship for the contact angle, which

corresponds to a more general case²⁵⁰ where the droplet size is comparable with the scale range of surface fractality of the substrate. In this case, the contact angle depends on the effective radius, R_d , of the droplet and is given by[§]

$$\cos \theta_f = \cos \theta_0 \left\{ \left[\frac{1 - (\gamma_{02}/\gamma_{01})(d_2/d_1)^{2-d_f}}{1 - (\gamma_{02}/\gamma_{01})} \right] \left(\frac{d_1}{R_d} \right)^{2-d_f} \right\}, \quad (51)$$

where d_1 is the size of the molecules of the liquid; d_2 is the size of the molecules of the gas (or equivalent phase); $\cos \theta_0 = (\gamma_{02} - \gamma_{01})/\gamma_{12}$, θ_0 is the contact angle on the smooth surface and γ_{01} , γ_{02} and γ_{12} are the energies of the liquid/solid, gas/solid and gas/liquid interfaces, respectively. If the droplet size exceeds the longest length scale from the scale range of surface fractality, R_d should be read as denoting the latter parameter.

From relationship (51) it follows that an increase in the droplet size causes the cosine of the contact angle to increase in absolute value. This means that the droplets increasingly better (or worse) wet the surface as the droplet size increases. Deterioration of wetting of fractal surfaces was confirmed experimentally.^{246, 247}

Fractal surfaces possessing very high water- and oil-repellent abilities were reported.²⁴⁸ The results obtained in a large series of experiments on the water- and oil-repellent properties of fractal surfaces were discussed.²⁴⁹ To impart these properties to the surface of anodised aluminium with $d_f = 2.19$, it was treated with perfluoroalkyltrichlorosilanes and perfluorinated monoalkyl phosphates, respectively. The dependences of the contact angle of a water/ethanol mixture on the smooth and fractal surfaces of anodised aluminium treated with various modifiers are shown in Fig. 3. As can be seen, the contact angle on the smooth surface gradually increases as the surface tension increases, while in the case of the fractal surface the regions of slow change in the contact angle are separated by a discontinuity region. Figure 4 presents a correlation between the contact angle on the fractal surface and the contact angle on the smooth surface. The experimental data are well fitted by the equation

$$\cos \theta_f = \cos \theta_0 \left(\frac{d_1}{R_d} \right)^{2-d_f}, \quad (52)$$

which is a particular case of relationship (51).

The fractal nature of the substrate affects not only the contact angle. Investigations of capillary phenomena on fractal surfaces require some relationships to be revised. In particular, the

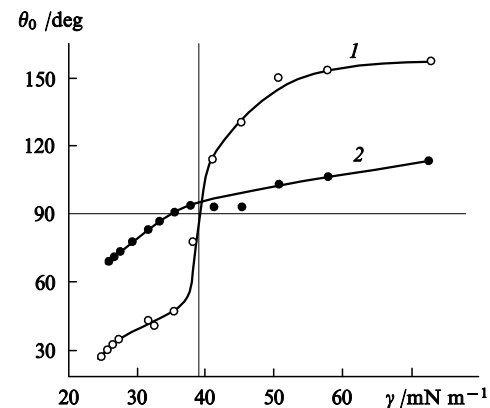


Figure 3. Contact angle of a water/ethanol mixture on a smooth (1) and fractal (2) anodised aluminium surface treated with various modifiers as a function of the surface tension of the mixture.²⁴⁹

[‡] Readers who are interested in this problem are addressed to a review,²⁴⁴ which presents a comprehensive treatment of these effects.

[§] The fractal dimensions of surfaces will be also be denoted as d_f . We believe this should not cause any misunderstanding.

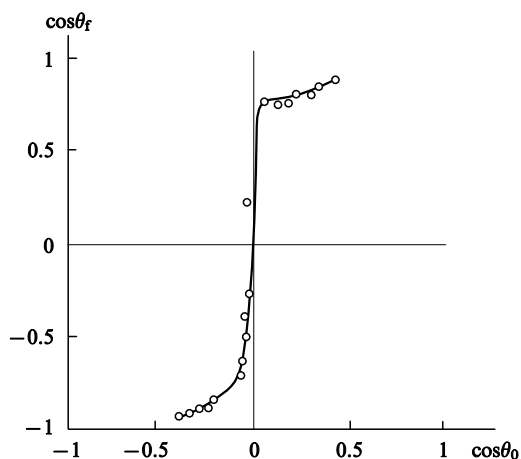


Figure 4. Correlation between the contact angle on the fractal surface and the contact angle on the smooth surface for water/ethanol mixture.²⁴⁹

possibility of significant changes in the kinetics of heterogeneous nucleation on fractal surfaces was pointed out.²⁵⁰ In addition to the classical chemical mechanism of manifestation of the Rebinder effect, yet another mechanism becomes possible^{251, 252} in the case of wetting of a metal surface with an eutectic mixture of metals or with some other liquid metal. It is believed^{251, 252} that high roughness and the fractal structure of the interface can favour creation of a high concentration of photons in the region of metal/metal or metal/eutectic mixture contact. The high photon concentration may cause a mechanical disruption of the surface of solids.

Wetting studies of fractal surfaces are closely related to the problem of determination of the characteristics of porous bodies. To solve this problem, two approaches were developed. One of them is based on capillary condensation on fractal surfaces (wetting of a porous body), while the other is based on a mercury porosimetry technique (intrusion of a nonwetting fluid into a porous medium).

At first, consider the problem of intrusion of a nonwetting fluid into a porous body, because it is somewhat simpler.[†] As mercury intrudes a nonwetting porous body, the first to be filled are those pores whose radius of curvature, r_h , meets the condition

$$r_h \geq \frac{2\gamma_h |\cos \theta_0|}{p}, \quad (53)$$

where p is the pressure of mercury, γ_h is the surface tension of mercury and θ_0 is the contact angle on the smooth surface. This relationship has a simple physical meaning, *viz.*, for a pore to be filled with mercury, the external pressure must exceed the capillary pressure. Here, the radius of curvature determined by the sign of equality in relation (53) acts as the length scale in measuring the fractal surface area. The surface area, Σ , of the mercury/porous body interface is determined from the work W_h done in intruding mercury, which is fully spent for an increase in the interface area,

$$W_h = -\Sigma\gamma_h \cos \theta_0 = - \int_0^V p dV, \quad (54)$$

where V is the volume of mercury intruded in the porous body.

The fractal dimension of the surface of the porous body is determined from experimental data using the equation

$$d_f = 2 - \frac{d \ln \Sigma(r_h)}{d \ln r_h}. \quad (55)$$

This approach was proposed by Neimark.²⁵⁵ A somewhat different method of determination of the fractal dimension of a model porous body was developed earlier,²⁵⁶ but it is applicable to particular cases only. The necessity of refinement of relation (55) was pointed out,²⁵⁷ because a part of the mercury surface does not contact the solid phase. More accurate relationships allowed one to attain agreement between the data on the fractal dimensions of porous bodies obtained using mercury porosimetry and adsorption techniques.

It should be noted that such a refinement is not always necessary. The need for refinement is most probably due to poorly pronounced fractal structures of the porous bodies under study. One should employ a specific procedure (see Ref. 258) for choosing those portions in the $\Sigma(p)$ plot that correspond to the fractal structure. Correct choice of such portions allows the fractal dimensions of various objects (soot, aerogels) determined from mercury porosimetry data²⁵⁸ to be in agreement with the values found using small-angle X-ray scattering and adsorption methods.

A capillary condensation based version of the adsorption technique was also proposed.²⁵⁵ The method assumes that a sufficiently thick adsorption film covers the whole surface of a porous body. The surface area of the film/vapour interface is governed by the vapour pressure; the radius of curvature of the meniscus acts as a 'probe' size and is given by

$$r_1 = \frac{2\gamma_l V_m}{kT \ln(p_s/p_v)}, \quad (56)$$

where γ_l is the surface tension of the liquid, V_m is the volume of the molecule, p_s is the saturated vapour pressure and p_v is the current vapour pressure. The expression for the pressure dependence of the surface area, Σ_1 , of the liquid/vapour interface can be found from the work done in forming the interface and has the form

$$\Sigma_1 = \frac{RT}{\gamma_l} \int_{\Gamma}^{\Gamma_{\max}} \ln\left(\frac{p_s}{p}\right) d\Gamma, \quad (57)$$

where Γ is the adsorption (in moles) and $\Gamma_{\max}$ is the maximum adsorption. The fractal dimension is then determined from Eqn (55) using the radius r_1 instead of r .

A modified capillary condensation method was reported.^{259, 260} However, it cannot be considered rigorously substantiated.

2. Restructuring of aggregates

Capillary phenomena play a significant role in the evolution of fractal aggregates. There are two types of capillary phenomena. The first type includes condensation of liquids on aerosol fractal aggregates. Capillary forces acting at the liquid/vapour interface can cause changes in the aggregate structure provided low strength of fractal aggregates. The second type of capillary phenomena is responsible for the evolution of aggregates due to 'sintering' of particles.

Experiments^{261, 262} revealed changes in the structure of aggregates^{261, 262} exposed to cyclic variation of the relative humidity of the atmosphere. At first, experiments were carried out to obtain qualitative information. Detailed studies²⁶³ involved (i) variation of the composition of aerosol soot particles and of the duration of condensation–evaporation cycles and (ii) measurements of the fractal dimension of aggregates at different instants. Based on the results obtained, it was concluded that capillary forces play the determining role in the evolution of aggregates and a linear correlation between the fractal dimensions of aggregates before and after condensation cycle was established. It was shown that the coefficient of proportionality is to a great extent determined by the degree of particle hygroscopicity. A mechanism of change in

[†]We will not dwell on specific features of the mercury porosimetry technique. Detailed information on the subject can be found in, *e.g.*, Refs 253 and 254.

the structure of aggregates was proposed²⁶⁴ and applied to aggregates of carbon black particles in water and benzene vapours. To change the extent of hydrophobicity, the aggregates were exposed to polyethylene glycol vapours. The extent of particle hydrophobicity was monitored by the adsorption isotherms of water vapours. Experiments showed that the change in the aggregate structure strongly depends on the size of condensate droplets. If the droplets were rather large, densification of the entire aggregate occurred to give a dense globule. At small droplet sizes, densification of a small (mainly central) region of the aggregate occurred. A simple model was also proposed in this study, which qualitatively reproduced the experimental dependences.

As mentioned above, capillary forces also change the structure of aggregates in the absence of condensate. Densification of carbon black aggregates on short-term heating to 300 °C^{265,266} and of silica aggregates on prolonged storage²⁶⁷ was observed. However, in the latter case the mechanism of densification is still to be clarified (formally, the Ostwald ageing and sintering of particles were assumed). The change in the fractal dimension of carbon black particles on heating was also reported.²⁶⁸ A detailed experimental study on the effect of heating on the fractal characteristics of silver particles was carried out.²⁶⁹ Aggregates of particles were heated in an inert gas stream over different periods of time at temperatures between 25 and 520 °C. A good correlation between the heating time, temperature and the fractal dimension of aggregates was established (Fig. 5). Based on the results obtained, the possibility of targeted change in the fractal dimension of aggregates of silver particles by varying the temperature and heating time was suggested. The experimental data were in good agreement with the results of Monte Carlo simulation of the sintering of fractal aggregates.²⁷⁰

It should be noted that sintering of fractal aggregates is not necessarily accompanied by an increase in their fractal dimension. For instance, it was shown²⁷¹ that sintering of rather large fractal aggregates affects the lower and upper cutoff lengths only, whereas the fractal dimension of aggregates remains virtually unchanged. Experiments²⁷² with silica aerogels confirmed these theoretical results. More detailed models for sintering of aerogels, which predict a constant fractal dimension, were also proposed.^{273–275} A detailed study on the laws of changes in the fractal dimension of sintered aggregates was carried out.²⁷⁶ Using numerical experiments, the relation between the aggregate size and the evolution of its fractal dimension was followed. At small sizes, sintering is unavoidably accompanied by an increase in the

fractal dimension. As the aggregate size increases, changes in the fractal dimension become progressively less pronounced in spite of essential changes in the aggregate morphologies.

A thermodynamic analysis²⁷⁷ of sintering of fractal aggregates involved establishment of conditions under which densification of the aggregate structure begins. The possibility of fragmentation of aggregates was also revealed. The calculated temperature dependences of the fractal dimension of gold aggregates coincided with the experimental data.

Numerical simulation of sintering of two-dimensional fractal aggregates due to particle diffusion along the perimeter was carried out²⁷⁸ using the known aggregation procedure²⁷⁹ that allows structures with prescribed fractal dimension to be grown. Fragmentation of fractal aggregates was also simulated. The number of fragments was shown to be proportional to the initial surface area of the aggregate. The coefficient of proportionality was a complex function of the fractal dimension of the aggregate (it is only known that this coefficient decreases as d_f increases).

VI. The fractal surface

Many materials, from classical adsorbents to ore particles, have fractal surfaces.²⁸⁰ In this Section, we will consider the fractal surfaces of porous bodies except for aerogels because of specific morphological features of their surfaces.

The fractal dimension of a surface can be determined using different methods. These are measurements of the surface area using molecules of different size, the micrographs of the cross-sections of porous bodies, the dependence of the surface area of porous particles on their sizes, the time taken to transfer the excitation energy from donor molecules to the adsorbed acceptor molecules, the small-angle X-ray scattering and adsorption measurements, the hydrodynamic permeability of porous bodies, the rates of surface chemical reactions, the kinetics of adsorption, *etc.*^{281–283} Many of these methods are based on the description of the kinetics of processes proceeding on fractal surfaces, which requires introduction of new concepts and dimensions. Because of this, we will restrict ourselves to analysis of the classical methods of determination of the fractal dimension of the surface and point out some new approaches. There are a few studies concerned with the development of various models of porous bodies (see, *e.g.*, Refs 284 and 285) and they have much in common with the models employed for the description of growth of fractal aggregates.

The fractal dimension of porous bodies can be determined in a different manner; however, we will not dwell on all of them. Here, mention may be made that the procedure recommended²⁸⁶ by the IUPAC involves the determination of the fractal dimension of a porous body from the pore size distribution

$$\frac{dV_p}{dr_p} \propto r_p^{2-d_f}, \quad (58)$$

where V_p and r_p are the pore volume and pore size, respectively.

1. Small-angle X-ray scattering

Small-angle X-ray and neutron scattering have long been used for the determination of the structure of porous bodies. These methods are suitable for studies on the length scales from atomic sizes to those observed using conventional optical microscopy. This scale range covers virtually all known porous media, being a prerequisite for a wide use of these experimental techniques. The dependence of the scattered intensity, $I(q)$, on the scattering angle (vector), q , is determined by the structure of the porous body.

X-Ray scattering occurs by collisions with electrons while neutron scattering occurs by collisions with atomic nuclei. The scattering by atomic nuclei is governed by the isotope composition of the nuclei. Using various combinations of isotopes, it is possible to enhance or mask certain properties intrinsic in the structure of

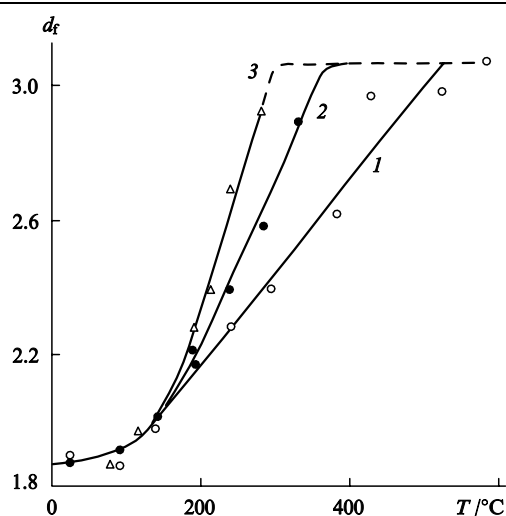


Figure 5. Fractal dimension of silver aggregates plotted vs. heating temperature.²⁶⁹ Heating time/s: 1.6 (1), 3.2 (2) and 4.8 (3).

the porous body. No significant differences between the results obtained by neutron and X-ray scattering were established.

Peculiar features of the atomic structure do not manifest themselves in the case of small-angle scattering. Because of this, the scattering curves are usually analysed using the two-phase model of a porous body, which assumes that the porous body comprises two phases of constant density, a solid and a void. The intensity of scattering by the fractal surface is given by²⁸⁷

$$I(q) = \pi c(\Delta\rho)^2 I_e \Gamma(5 - d_f) \sin \left[\frac{\pi(d_f - 1)}{2} \right]^{- (6 - d_f)}, \quad (59)$$

where c is a constant, $\Delta\rho$ is the electron density difference (or the neutron scattering length difference) between two phases, I_e is the intensity of scattering by single electron (or by one scatterer) and $\Gamma(x)$ is the gamma function.

At small q , the fractal dimension is determined from the slope of logarithm of the scattered intensity plotted vs. logarithm of the scattering angle.

At $d_f = 2$, expression (59) represents the well-known Porod law for X-ray scattering by smooth surfaces,^{288,289} according to which

$$I(q) \propto q^{-4}. \quad (60)$$

This relationship was extended²⁹⁰ to the case for emission wavelengths comparable with the radius of curvature of smooth surfaces and the corresponding corrections to the Porod law were derived. Yet another expression for the scattered intensity with inclusion of the surface curvature corrections has the form²⁹¹

$$I(q) \propto q^{d_f-6} + q^{d_f-8} \frac{(6 - d_f)(5 - d_f)}{12} \times \left[\frac{1}{R_1 R_2} + \frac{3}{8} \left(\frac{1}{R_1} - \frac{1}{R_2} \right)^2 \right], \quad (61)$$

where R_1 and R_2 are the principal radii of curvature averaged over the inner (fractal) surface. This relationship was used to determine the fractal dimension of typical adsorbents and the necessity of allowance for the surface curvature corrections in the case of porous bodies was confirmed.

2. Adsorption technique

On length scales shorter than 1 nm the fractal dimension of a surface can be determined by measuring the adsorption capacities of monolayers of molecules of different size δ , and comparing them with the dependence of the surface area on δ

$$\Sigma(\delta) \propto \left(\frac{1}{\delta} \right)^{d_f-2}. \quad (62)$$

The method of determination of the fractal dimension based on evaluation of the surface area according to Brunauer–Emmett–Teller using molecules of different size is often objectionable.²⁹² This is due to the fact that the surface sites of particular molecules are not known with certainty. As a result, different authors report contradictory data on the fractal dimensions of the same materials, including the values exceeding the limiting d_f value ($d_f = 3$). It should be noted that in some cases one fractal dimension can appear to be insufficient for complete characterisation of the fractal structure of the surface of adsorbents with a complex structure of the pore space. Therefore, one should introduce a hierarchy of fractal dimensions for a given porous body,²⁹³ which can be treated as a particular characteristic of inhomogeneity of the porous body. Introduction of the hierarchy of fractal dimensions corresponds to the so-called multifractal approach (see Section IV in Ref. 1).

On length scales from 1 to 100 nm the fractal dimension is determined from polymolecular adsorption data using two methods. The first is based on the dependence reported by Pfeifer et

al.²⁹⁴ (the number of molecules necessary to cover the free surface of the adsorption layer decreases as the layer thickness increases). In the case of adsorption on fractal surfaces, a modified Frenkel–Halsey–Hill equation is used

$$\ln \left(\frac{p}{p_0} \right) = - \frac{A_F}{k T T^n}, \quad (63)$$

where p is the pressure of the adsorbing gas, p_0 is the saturation pressure, A_F is the parameter determining the adsorbate–adsorbent molecular interaction and T is the number of moles of the adsorbed gas. Ignoring the surface tension effects, one gets

$$n = \frac{3}{3 - d_f}.$$

If the contribution of surface tension predominates,^{295,296} then

$$n = \frac{1}{3 - d_f}.$$

These relationships are valid for self-similar surfaces. In the case of self-affine surfaces, of great importance is the roughness index (α) determining the relation between the surface ‘width,’ w , and the lateral size, L , of the surface

$$w \propto L^\alpha.$$

If the surface tension effects are weak, $n = 3$; if they predominate, $n = 2/\alpha - 1$ at $\alpha > 0.5$ and $n = 3$ at $\alpha < 0.5$ (see Ref. 297).

The Frenkel–Halsey–Hill equation was used by different authors to estimate the fractal dimensions of various porous bodies.^{298–300} Recently, the fractal dimension of the surface of adsorbents has been determined using the Dubinin–Astakhov equation generalised to the case for fractal surfaces.^{301–303} The Neimark method^{304–306} (see above) is also often used to this end.

The fractal dimensions determined using the methods mentioned above were compared in the framework of model calculations.³⁰⁷ The emphasis was placed on the inclusion of the effect of finite scale range of surface fractality. According to calculations, the fractal dimensions determined using different methods are equal to one another if the range of scales covers two orders of magnitude and can differ by more than 10% if it does not exceed an order of magnitude. This conclusion was confirmed³⁰⁸ by measuring the fractal dimensions of titania aerogels prepared under different conditions. It was shown that the monolayer and polymolecular adsorption techniques give similar results, though the corresponding fractal dimensions can differ by nearly 0.1. An analogous conclusion was drawn³⁰⁹ from comparison of the results obtained using different methods in the experiments with silica particles prepared by hydrolysis of tetraethoxysilane in microemulsions. Even the fractal dimensions determined using different methodologies^{255,260} appeared to be similar, though the earlier studies sometimes revealed distinctions between the results obtained by these methods.

Yet another method of determination of the fractal dimensions of porous bodies from the adsorption data was developed by Olivier and co-workers.^{310–312} The approach involves construction of the so-called composite adsorption isotherm assuming independent adsorption in pores of each size. For pores of a particular size, the adsorption isotherm is calculated by employing density functional theory.³¹¹ On these assumptions and on imposing the fractal structure of the surface it is possible to construct a composite isotherm whose shape is determined by the fractal dimension of the surface. Comparison of the experimental and model isotherms allows the fractal dimension of the porous medium to be determined. The fractal dimensions of some objects determined using the composite adsorption isotherm were compared³¹² with the fractal dimensions estimated using the Frenkel–Halsey–Hill and Neimark equations. It was shown that the fractal dimensions determined using different methods are related by a linear dependences with different slopes (they are determined

by the pore size scales on which the surface exhibits fractal properties).

Yet another reason for significantly different results obtained for different adsorbents using different methods is that porous bodies are characterised by some hierarchy of fractal dimensions rather than a single fractal dimension value (see above). The distribution of fractal dimensions can be rather broad and usually covers the values determined in single experiments.³⁰³

Two important features should be pointed out. The lower limit of the scale range of surface fractality can be found³⁰⁴ by comparing the adsorption isotherm for a given sample and the standard adsorption isotherm for the smooth surface. (Strictly speaking, Neimark and Unger³⁰⁴ reported the upper limit of the scale range of surface fractality.) At the same time, the method proposed provides no possibility for the surface fractality to be established unambiguously and requires additional studies.

The fractal structure of the surface governs the shape of the adsorption isotherms. This is due to the fact that the fractal nature of the substrate affects the properties of the adsorption layer.^{313, 314} In particular, it was shown³¹⁵ that the inclusion of adsorbent surface fractality allows the Temkin adsorption isotherm to be obtained in the case of non-interacting adsorbate molecules. It was also assumed that wide use of the Temkin isotherm can be explained by frequent occurrence of adsorbents with fractal surfaces.

3. Surface profiles

The adsorption technique is usually employed in studies of the closed fractal surfaces. The fractal dimension of an open surface can be determined by measuring the surface profiles (a single profile for isotropic surface). In the case of anisotropic surfaces, one cross-section is insufficient. There are several methods of processing the surface profile. In particular, it is possible to obtain the height (h_f) correlation function using the relationship

$$R_s(y) = \langle h_f(x)h_f(x+y) \rangle, \quad (64)$$

or to determine the structure function

$$S_s(y) = \langle [h_f(x) - h_f(x+y)]^2 \rangle, \quad (65)$$

where x and $x+y$ are the coordinates in the xy plane.

For fractal surfaces, both the height correlation function and the structural function are related to y by a power-law dependence

$$S_s(y) \propto R_s(y) \propto y^{6-2d_f}.$$

The possibilities of determining the dimensions of the open fractal surfaces using scanning probe microscopy data and surface profile measurements were analysed in detail.³¹⁶ It was shown that the shape of the correlation or structural function permits not only the fractal dimension to be determined but also the characteristic length scale of surface fractality to be revealed in the case of self-affine surfaces.

Going to longer length scales exceeding the upper limit of surface fractality does not mean³¹⁷ a constant surface area measured by probes of different size. Even on long length scales, the surface area measured depends on the probe size because it becomes rough due to fluctuations. In this case, the surface area measured decreases obeying a power law as the probe size increases,³¹⁷ the exponent being dependent on the fractal dimension in a much more complex manner compared to relation (62).

Peculiarities of the behaviour of the structure and correlation functions as well as problems that arise in determining the fractal dimension of anisotropic surfaces were considered in detail by Wu.^{318, 319} In particular, it was shown that the fractal dimensions of model surfaces can depend on the type of the function (S_s or R_s) employed in the computational procedure. The fractal dimension can also be a function of other physicochemical parameters of solids.³²⁰

4. Other methods

An original method³²¹ of determination of the fractal dimension of metallic surfaces involves scattering studies of surface plasmon polaritons (SPP) by rough surfaces. In the case of well-developed fractal surface, localisation of the SPP is possible. The scheme of calculations of the fractal dimension using the laws of SPP scattering was evaluated taking films grown by evaporation – condensation in different regimes suitable for preparation of smooth and rough surfaces. The fractal dimensions determined are in good agreement with those found using the film surface profiles.

The fractal dimensions of the surfaces of conducting solids can be determined using electrochemical methods. Comparison of the fractal dimensions determined using atomic force microscopy and cyclic voltammograms appeared to be similar.³²²

The method proposed³²³ for semiconductor films involves measurements of the photocurrent from their surface. It was assumed that the photocurrent (I_f) is proportional to the absorbed energy and, correspondingly, to the surface area of the specimen. In this case

$$I_f \sim L^{d_f}, \quad (66)$$

where L is the linear dimension of the specimen.

Experiments³²³ carried out using films of different linear size gave the fractal dimensions which coincided with those determined for the same films using atomic force microscopy.

Yet another method of determination of the fractal dimensions of the open surfaces was proposed in a study³²⁴ on the laws of scattering of helium atoms by silver submonolayers of different structure on Pt (111). According to calculations, the scattered intensity is related to the difference between the tangential components of the wave vectors of the incident and scattered atomic beams (Δk)

$$I_a(\Delta k) \sim (\Delta k)^{d_f-4}. \quad (67)$$

This relation was confirmed experimentally. The technique seems to be promising because experimental methods of studies on scattering of atoms and molecules by solid surfaces are well developed.

VII. Aerogels

Aerogels are used as heat insulators, catalyst supports,³²⁵ reservoirs for flammable fluids and elements of acoustical and optical devices,³²⁶ in Cherenkov counters³²⁷ and solar cells,³²⁸ for the growth of photoluminescent silicon crystals³²⁹ (in this case, aerogels themselves can possess photoluminescent properties³³⁰). Aerogels are highly porous, low density materials characterised by small pore sizes. They are produced by drying hydrogels prepared by a sol–gel process under supercritical conditions. In particular, the most widely used silica aerogels are prepared by hydrolysis of tetraethoxysilane or tetramethoxysilane in aqueous alcoholic solutions. Aerogels of other metal oxides are prepared from corresponding alkoxides.³²⁶

The sol–gel process involves hydrolysis of precursors followed by polycondensation of hydrolysis products. Particles formed during polycondensation (sol) aggregate and then form a continuous network (gel). Preparation of gel is followed by its drying. Depending on the drying regime, a glass, ceramic or aerogel can be obtained. The density of aerogels can be varied within two orders of magnitude from several hundredth to 1 g cm^{-3} .

Studies of aerogels face some difficulties³³¹ because of strong perturbations introduced into the structure of aerogels when using conventional methods such as mercury porosimetry, thermoporosimetry and adsorption technique. Therefore, these objects are often studied using contact-free methods, *viz.*, small-angle neutron, light and X-ray scattering as well as optical, acoustical and thermomechanical methods.

It has long been established using small-angle X-ray^{332, 333} and neutron^{334, 335} scattering that aerogels have a fractal structure on the length scales from several to 1000 Å and that their mass fractal dimensions lie between 2.1 and 2.4. The pore surface of aerogels is also fractal; the parameter d_f can approach the limiting value (≈ 3).

The longest length scale, ξ , of aerogel fractality is usually called the correlation length (by analogy with the correlation length in percolation theory). The size of fractal domains is, as a rule, from several tens to a hundred of nanometres. The density of aerogels equals that of the gel-forming fractal clusters and is determined by the correlation length

$$\rho(\xi) = \rho_0 \left(\frac{\xi}{a} \right)^{d_f-3}, \quad (68)$$

where ρ_0 is the density of the substance the primary particles of radius a are made of. The pore size distribution for aerogels also obeys a power-law dependence.³³⁶

Consider the results of several recent investigations on the structure of aerogels. Reidy *et al.*³³⁷ reported a small-angle neutron scattering study of the structures of three aerogels prepared by hydrolysis of tetraethoxysilane (TEOS), triethoxysilane (TES) and trimethoxysilane (TMS). Three gel models were employed, the interference, fractal and maximum entropy ones. The first model assumes that aerogel is composed of homogeneous spheroidal granules with a prescribed aspect ratio and lognormal size distribution.³³⁸ According to the second model, gel comprises fractal fragments of size ξ . The third model treats gel as a system of homogeneous particles and derives a particle size distribution consistent with the maximum configuration entropy.³³⁹ Analysis of scattering patterns showed that the TEOS aerogels were best described by the maximum entropy model, while the TES and TMS aerogels were best described by the fractal model (a version with fractal primary particles for TES aerogels and with fractal surface of the pore space for TMS aerogels).

The structures of aerogels can be modified in a different manner. The most efficient way is to introduce an aerosil into the disperse medium. This can result in aerogels which either have no fractal structure³⁴⁰ or have a binary fractal structure.³⁴¹ When aerogels were prepared from sodium silicate solutions, the gel structure was strongly dependent³⁴² on the pH value of the medium, which can be attributed to the change in the surface charge of the primary particles, which governs the rate of coagulation and the fractal dimension of aggregates. The addition of hydrogen peroxide to aerogels prepared by hydrolysis of methyl silicate led to somewhat unexpected results.³⁴³ Namely, the fractal dimension of certain systems remained unchanged and even increased as their density decreased.

The mechanical properties of aerogels are of great practical value and therefore attract particular attention. The power-law dependence of the Young's modulus, E , of aerogels on their density ρ (ρ_0 is the density of the framework-forming material)

$$E = E_0 \left(\frac{\rho}{\rho_0} \right)^m \quad (69)$$

was confirmed in numerous studies. The exponent m is not a universal scaling factor; even for the silica-based gels it varies from 2.5 to 3.8 depending on the substances used for the preparation of aerogels and on the regimes of subsequent drying and heat treatment. Apparently, this exponent is related to the fractal dimension of aerogel; however, this was not rigorously substantiated. A possible relation is as follows:³⁴⁴

$$m = \frac{5 - d_f}{3 - d_f}. \quad (70)$$

The mechanical properties of aerogels are often described using the bulk modulus K_b , which relates the change, Δp , in the

pressure applied to a sample to the relative change in the sample volume

$$\Delta p = -K_b \left(\frac{\Delta V}{V} \right). \quad (71)$$

The moduli E and K_b are related by

$$K_b = \frac{E}{3(1 - 2\nu)},$$

where ν is the Poisson ratio.

The modulus K_b is also related to the density by a power-law dependence

$$K_b = \rho^{\kappa_b}, \quad (72)$$

where the exponent κ_b for silica aerogel varies from 3.08 to 3.38 (the mean values are ≈ 3.2 and 3.6 in the regions of plastic and elastic deformation, respectively).³⁴⁵ Analysis of a large array of experimental data on the elastic moduli of aerogels revealed³⁴⁶ an unambiguous relation between the parameter κ_b and the pore size distribution and a hierarchy of pore size distributions over a broad range of length scales provided that relationship (72) is valid.

At temperatures below 1 K, the specific heat of aerogels obeys the law

$$C_p \sim T^{\alpha_c},$$

where the exponent α_c ($\alpha_c \approx 1.4$) is virtually independent of the density of ultralight aerogels ($\rho < 0.4$).³⁴⁷ The thermal conductivity of aerogels is a constant at low temperatures and increases in proportion to T^{α_t} ($\alpha_t \approx 1.2$) at higher temperatures. At low temperatures, the specific heat of aerogels is determined by the phonon density of states. Brillouin scattering studies revealed that the frequency dependence, $N_v(\omega)$, of the density of phonon states at the wavelengths comparable with the length scales of domains of the fractal structure of aerogels deviates from the dependence typical of the phonon spectrum. Namely, this dependence still obeys a power law but the exponent changes from $(d-1)$ to $(d_{fr}-1)$

$$N_v(\omega) \sim \omega^{d_{fr}-1}.$$

The new exponent is called a fracton or the spectral dimension. For silica aerogels, $d_{fr} \approx 1.3$. The fracton dimension characterises specific features of the oscillations of those aerogel fragments which have a fractal structure. Peculiarities of the vibrational spectra of fractal structures and aerogels have been analysed in detail (see Refs 189 and 348, respectively); therefore, we will not dwell on them. Mention may be made that the fracton concept was first proposed by Alexander and Orbach.²³⁷

Fractons are natural oscillations of a fractal. If aerogel is treated as a set of fractal clusters, fractons characterise peculiar features of their vibrational dynamics. Strictly speaking, the fracton dimension of clusters 'grown' in numerical experiments can be determined only in analogous numerical simulation (see, e.g., Ref. 349). According to calculations, the fracton dimension weakly depends on the fractal dimension. At the same time, an analytical relation between these dimensions was derived in the framework of a certain model. A simple equation was proposed,³⁵⁰

$$d_{fr} = \frac{d_f}{1 + b(3 - d_f)}, \quad (73)$$

in which the parameter b determines the dependence of the velocity of sound, v_s , on the aerogel density

$$v_s(\rho) \propto \rho^b.$$

Relation (73) was reported³⁵¹ as a particular case of general relations derived for elastic and thermal characteristics of hierarchic structures. Some other relationships are as follows:

$$b = \frac{m-1}{2}, \quad (74)$$

$$\alpha_t = d_{fr} + \frac{1-2d_{fr}}{d_f},$$

$$\alpha_c = d_{fr}.$$

In addition to Brillouin scattering, the Raman light scattering also plays a significant role in studies of aerogels. It was shown³⁵² that the response of the Raman scattering by aerogels depends on the frequency of electromagnetic radiation (ω) and is described by a universal law

$$\chi_R(\omega) \sim \omega^{-\phi}, \quad (75)$$

where the exponent ϕ is determined by three dimensions, viz., the mass fractal dimension, d_f ; the fracton dimension, d_{fr} , which characterises the density of vibrational states; and the dimension d_σ characterising the deformation of particles by fractons. The dependence of the exponent ϕ on these dimensions is determined by the mechanism of Raman scattering. If the mechanism involves the interaction between permanent and induced dipoles, then

$$\phi_{dd} = 2 \left[\frac{d_{fr}}{d_f} (d_f - 3 - d_\sigma) \right] + 1. \quad (76)$$

If the mechanism involves modulation of the polarisability by atomic oscillations, one has

$$\phi_p = 2 \left(1 - \frac{d_{fr} d_\sigma}{d_f} \right). \quad (77)$$

Relationships (75)–(77) were verified taking silica aerogels of different density as examples.³⁵³ Gels were heat treated and exposed to hydrostatic load and uniaxial compression. Experiments with all samples showed that the parameter ϕ is independent of the density of gel and remains unchanged during heat treatment of aerogels resulting in their densification. However, mechanical deformation favoured a decrease in ϕ due to a change in the fracton dimension of the loaded samples.

Changes in other mechanical and fractal characteristics of aerogels due to their densification were also studied.^{354–356} Structural changes were mainly detected using small-angle X-ray scattering. Densification of aerogels caused the correlation length to decrease, while the fractal dimension slightly increased (Fig. 6). As a rule, the corresponding parameters of the densified aerogels and of the initially more dense aerogels coincided. In some cases the fractal dimension of the mechanically compressed aerogels remained unchanged.³⁵⁶

More significant were the changes in the fractal dimension upon densification by sintering.^{357–359} Analysis showed^{271, 274, 360, 361} that, in spite of an increase in the fractal dimension of aerogels on sintering, a great body of information on the initial structure is retained. The difference between mechanical compression and sintering consists in that sintering causes densification of the network of bonds while mechanical compression causes restructuring of aggregates without formation of new bonds. Noteworthy is that the changes in the structure of aerogels on compression or sintering implicitly affect their physicochemical properties. For instance, it was shown both theoretically³⁶² and experimentally³⁶³ that the gas permeability of aerogels depends solely on their density which can vary over a wide range.

Aerogels have a fractal pore surface.^{308, 330, 364–370} The fractal dimension can be determined by various methods and usually lies between 2.5 and 2.8, though in some cases can reach the limiting values 2.92–2.98 (see Refs 308 and 364). The fractal dimension of

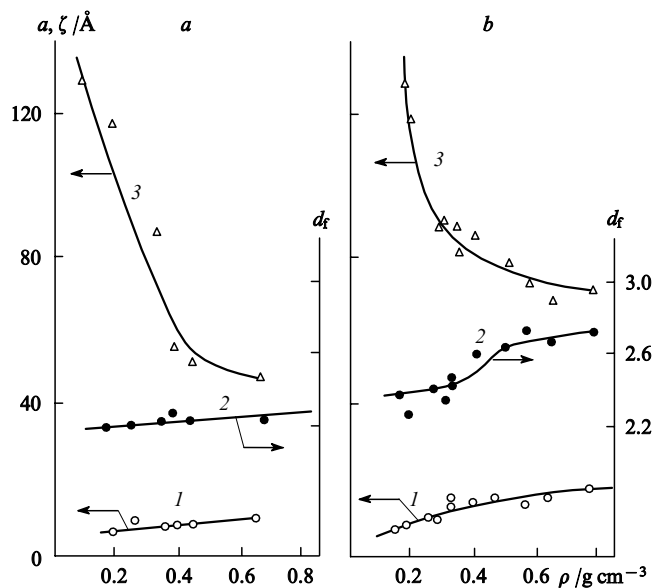


Figure 6. The size of primary particles (1), the fractal dimension (2) and the correlation length (3) plotted vs. the bulk density for mechanical densification (a) and sintering (b) of aerogels.³⁵⁶

the surface of aerogels strongly depends on the procedure employed for the preparation of gel (more exactly, on the regimes of drying,^{365–368} ageing³⁶⁹ and mechanical treatment.³⁷⁰) Heat treatment of aerogels usually causes the fractal dimensions of their surfaces to decrease, while mechanical treatment can cause both a decrease and an increase in d_f .³⁷⁰

No rigorous correlation between the bulk fractal dimension of aerogels and the fractal dimension of their surfaces was established as yet. Even an increase in the bulk fractal dimension was observed³⁶⁹ in the experiments on ageing of aerogels accompanied by a dramatic decrease in the fractal dimension of the surface from 2.75 down to a value of 2, which is typical of a non-fractal surface.

VIII. Conclusion

The methods of fractal geometry are widely used in natural science. As shown by the material presented in this review and in Ref. 1, intensive research on the fractal structures is being carried out. Because of the extensive literature on the subject, many aspects of physical chemistry of the surface phenomena and colloidal systems are left out of consideration. We can only give a short list of the most important research avenues. The fractal approach is employed in the studies on the properties of foams^{371, 372} and on the kinetics of binding of bioactive molecules with surface-immobilised receptors.^{373–378} The fractal analysis is used to describe replacement of nucleotides in DNA molecules³⁷⁹ and to analyse spontaneous aggregation of multilayered lipid vesicles.³⁸⁰ Recently, considerable attention has been paid to fractal aggregates growing in sea water.^{381, 382} Sedimentary rocks also have fractal surfaces.^{383–385} The fractal structure of cracks developing in brittle materials and polymers^{386–388} is described using not only the conventional fractal approach but also multifractal methodology.^{389, 390} The behaviour of grain boundaries in polycrystalline materials³⁹¹ and their transformations on exposure to various external factors³⁹² is considered in the framework of fractal formalism. Reversal of the magnetisation of thin polycrystalline layers is treated³⁹³ as a development of fractal clusters composed of magnetic domains. Fractal concepts are used in studies on capillary electrophoresis³⁹⁴ and simulation of growth of gallstones.³⁹⁵ This list of research avenues that successfully employ the concepts of growth of fractal structures is far short from being complete.

In spite of extensive literature concerning the fractal structures in various colloidal systems, many problems are still to be solved. The totality of experience accumulated during the last two decades shows that often solving new applied problems requires revision of the foundations of theory of fractal objects. Therefore, the development of fractal concepts is inevitable.

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Thermolysis of organic peroxides in solution

V L Antonovskii (deceased), S L Khursan

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Abstract. The results of investigations on the kinetics and mechanisms of thermolysis of the main classes of organic peroxides in solution are generalised. The relationship between the kinetics and mechanism of thermolysis and the peroxide structure is analysed. The main attention is given to the decomposition reactions of peroxides that are not confined to mere homolysis of the O–O bond and the factors responsible for the abnormalities in the thermolysis mechanism. The thermolysis mechanisms of trioxides, dioxiranes and peroxides are considered in detail. The bibliography includes 210 references.

I. Introduction

Organic peroxides are the main sources of free radicals in chemical practice. They are widely used for initiating radical (including chain) processes and crosslinking of polymers.^{1,2}

The low thermal stability of peroxides due to the presence of a weak O–O bond and the strong dependence of the decomposition time on their structures allow their wide use as initiators in a broad range of temperatures, from ~ 40 to ~ 200 °C. Redox systems of the type 'hydroperoxide–metal ion' and 'diacyl peroxide–amine' enable initiation even at 0 °C.

The present review is the first attempt to generalise the published data on the thermolysis of virtually all classes of organic peroxides in solution. Some previous publications were intentionally included in the review in order to present the problem in a complete and comprehensive way.

Thermal decomposition of peroxides in solution follows both homolytic (with cleavage of one or two bonds simultaneously) and

non-radical routes. The kinetics and mechanism of thermolysis depend on the structures of peroxides and the modes of their interactions with the solvent. The latter is especially important for hydroperoxides, which easily form hydrogen bonds.

The kinetics and mechanisms of reactions occurring in solutions were discussed in several monographs and reviews.^{1–3} Special attention was given to motion and collisions of the reacting species in liquid media and effects of their direct interactions with solvent molecules. As a result of such interactions, the original species and the transition states become surrounded by a structured shell consisting of solvent molecules, which changes their electronic structures and, as a consequence, their reactivities.

There are few papers devoted to the analysis of a relationship between the structure of peroxides and the mechanism of their thermolysis in the gas phase (see Ref. 4 and references cited therein), whereas thermolysis in solution has been studied for virtually all synthesised organic peroxides. This circumstance permits one to compare structural features of these compounds and to establish differences between them.

It is noteworthy that the mechanism of homolysis is not always sensitive to specific characteristics of the medium, since this process is not accompanied by any significant redistribution of charges in the molecules of the starting peroxides. However, if there is a competition between ordinary homolysis and other thermolysis routes, including non-radical rearrangements and, especially, heterolytic transformations, changes in solvent properties may have a crucial effect on the mechanism of the thermolysis.

Intermolecular contacts and reactions occurring in the solvent cage affect essentially the kinetics, mechanism and, as a consequence, composition of reaction products.^{1,2} Thermal decomposition of organic peroxides has previously been considered in several monographs.^{5–10} The effect of pressure on the kinetics and mechanisms of thermolysis (including $\Delta V^\ddagger$) depends on the mode of the interaction of the reactants with the solvent, the viscosity of the solvent and the processes occurring in the solvent cage.¹¹

The idea of N N Semenov on the competition between bimolecular homolytic reactions and monomolecular reactions simultaneously generating a highly stable product was confirmed by the calculations of Denisov^{12,13} based on the use of a semi-empirical parabolic model. Such a decomposition route also takes place in the thermolysis of peroxides.

V L Antonovskii N N Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 119991 Moscow, Russian Federation. Fax (7-095) 938 21 60

S L Khursan Bashkirian State University, ul. Frunze 32, 450054 Ufa, Russian Federation. Fax (7-347) 233 16 71. Tel. (7-347) 223 67 27. E-mail: KhursanSL@ufacom.ru

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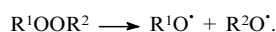
In the limiting step, thermolysis of peroxides usually involves initial cleavage of the weakest O—O bond. However, depending on the structures of the reactants and the reaction conditions, there may be some deviations from the 'simple' mechanism. The main attention in this review is given to the abnormalities of the mechanisms of thermal decomposition of peroxides, particularly of non-trivial mechanisms with complex rearrangement of the bonds.

II. Alkyl and aralkyl peroxides

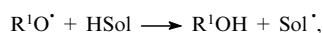
As a rule, the passage from gas-phase decomposition to thermolysis in solution does not result in any changes in the reaction mechanism. Thus rate constants for high-pressure decomposition of di-*tert*-butyl peroxide in cyclopropane¹⁴ in vapour (124–160 °C) and in the liquid phase (100–124 °C) represent a common straight line with a preexponential parameter $\log A = 15.52 \pm 0.23$ (s⁻¹) and $E = 156.9 \pm 0.4$ kJ mol⁻¹ in the $\log k_1 - 1/T$ coordinates. The values around the critical point of cyclopropane phase transition also fall on this straight line.

The decomposition kinetics of a series of alkyl and aralkyl peroxides in the gas phase and in hydrocarbon solvents were compared.¹⁵ The correlation dependence for these compounds [$\log A = 1.883E - 1.0$ (A in s⁻¹, E in kJ mol⁻¹)] was shown to correspond to the isokinetic temperature of 483 K. The activation energies for the decomposition of the symmetrical peroxides ROOR increase in the following order: Et < PhMe₂C < Me ≈ Prⁿ < Bu^t ≈ EtMe₂C.

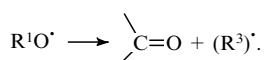
The main decomposition route for the peroxides R¹OOR² includes homolysis of the O—O bond:



The oxy radicals thus formed undergo either further recombination in the solvent cage with subsequent regeneration of the original peroxide, or reaction with the surrounding solvent molecules (HSol):



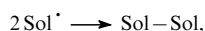
or monomolecular decomposition to form a ketone and a radical of lower molecular mass (β -decomposition):



The radicals thus generated are eventually replaced by the radicals derived from the solvent



which are then recombined into dimers

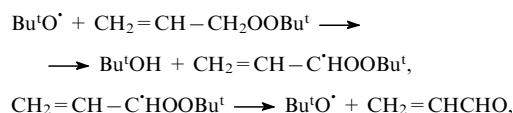


or undergo disproportionation to give an alkene and a stable saturated molecule.

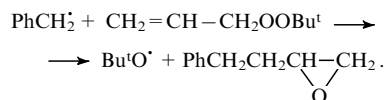
As a rule, electronic effects of substituents only slightly affect the rate of thermal decomposition of alkyl peroxides. Thus the coefficient ρ^* in the Taft equation for the electron-withdrawing groups of tertiary peroxides is -0.13 (150 °C, chlorobenzene),¹⁶ whereas that for *tert*-butyl peroxybenzoates is 0.38 (120 °C, CCl₄).¹⁷ A very strong effect of electron-donor groups ($\rho^* = -11.0$) and a small effect of electron-withdrawing groups ($\rho^* = -0.13$) were observed in the decomposition of dialkyl peroxides.^{18,19} However, such a discrepancy in the ρ^* values can be attributed to the fact that steric effects have not been taken into consideration.²⁰

The thermolysis of allyl *tert*-butyl peroxide in toluene,²¹ in addition to ordinary homolysis of the O—O bond, is accompanied by two types of induced decomposition:

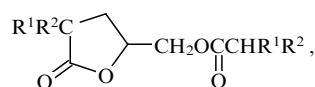
(1) abstraction of H[•]



(2) addition

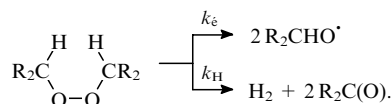


The presence of an allyl group in a peroxide offers diverse possibilities for their synthetic use in the thermolysis in solution. Thus the thermolysis of allyl *tert*-butyl peroxide in the presence of carboxylic acids (R¹R²CHCOOH) gives rise to lactones (yield 20%–50%)



which represent recyclisation products of the expected epoxy acids.²²

The presence of α -C—H bonds in peroxides brings about a competition between homolysis of the O—O bond and concerted cyclic formation of molecular hydrogen:



These reactions were studied in detail;^{21,23,24} the yields of H₂ for different peroxides are listed in Table 1.

Table 1. The formation of H₂ in the thermolysis of the peroxides ROOR in solution.

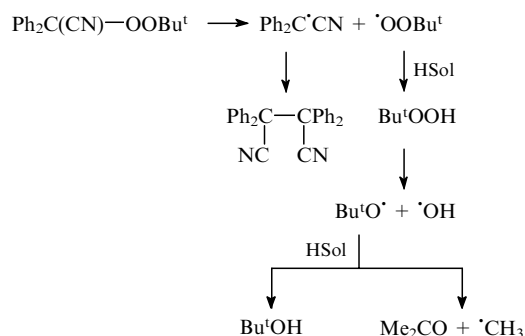
R	Solvent	Yield of H ₂ (%) ^a	10 ⁵ k_H /s ⁻¹ (see b)	E_H /kJ mol ⁻¹
Temperature 130 °C				
EtMeCH	toluene	22	1.35	134
Ph ₂ CH	"	95	19.3	117
Temperature 140 °C				
Me ₂ CH	toluene	7.5	5.0 (62.6)	134
	propan-2-ol	8.4	28.5 (310.5)	—
	methanol	30.5	67.2 (152.6)	72
	water	41.5	296.0 (419.0)	—

^a Upon complete decomposition of the peroxide; ^b the rate constant for the homolysis is given in parentheses (10⁵ k_r /s⁻¹).

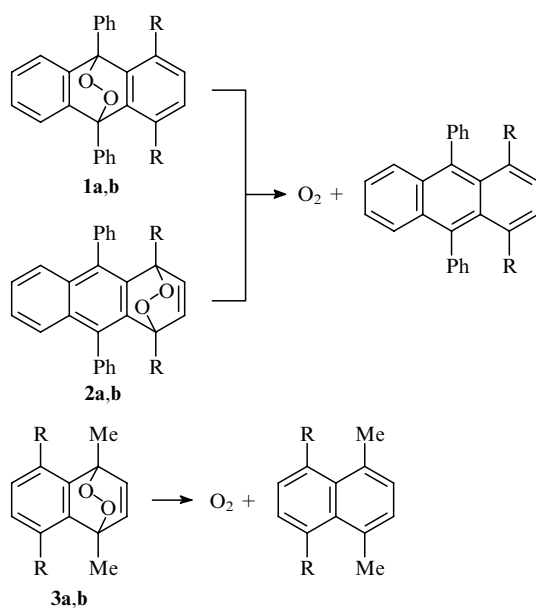
With an increase in the solvent polarity, the rate constant for hydrogen formation increases much faster than the homolysis rate constant. The yield of H₂ in the pyrolysis of diisopropyl peroxide in the gas phase is insignificant, which confirms the polarity of the transition state of the concerted cyclic reaction.

The presence of a double bond and other substituents favouring stabilisation of a carbon-centred radical formed in the α -position with respect to the peroxy group favours decomposition of peroxides at the C—O bond instead of the O—O bond.

tert-Butyl diphenylcyanomethyl peroxide undergoes decomposition in boiling cumene²⁵ to give acetone and *tert*-butyl alcohol in low yields (5% and 16%, respectively); tetraphenylsuccinonitrile is formed as the main product.



Endoperoxides of anthracene and its derivatives are readily decomposed into the original aromatic compounds and oxygen. Thus the thermolysis of 9,10- (**1**) and 1,4-anthracene endoperoxides (**2**) and 1,4-naphthalene endoperoxides **3** affords the original arenes and oxygen in yields exceeding 95%.^{26, 27}

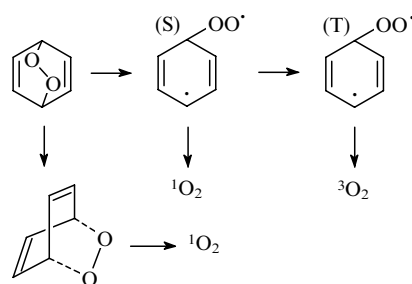


Part of the oxygen is formed in the singlet state (¹O₂) (Table 2). As can be seen, the yield of ¹O₂ decreases with an increase in the preexponential factor *A* (positive activation entropy Δ*S*[‡]); for low values of *A*, the yield of ¹O₂ is virtually quantitative. It is of note that the biradical mechanism of oxygen formation provides low yields of ¹O₂ due to S,T conversion, whereas the concerted mechanism with simultaneous bond cleavage ensures a quantitative yield of ¹O₂:

Table 2. Activation parameters and the yield of ¹O₂ in the thermolysis of endoperoxides.

Peroxide	<i>T</i> / °C	10 ⁶ <i>k</i> / s ^{−1}	<i>E</i> _a / kJ mol ^{−1}	log <i>A</i>	Yield of ¹ O ₂ (%)
1a	60.2 ^a	0.45	138	15.4	32
	66.2 ^b	1.70	133	14.9	35
1b	60.2 ^a	0.44	135	14.9	52
	66.2 ^b	1.74	126	13.7	73
2a	73.2 ^a	0.43	127	13.0	92
	15.1 ^b	2.09	103	13.0	95
3a	12 ^b	5.30	103	13.7	76
3b	24.8 ^b	2.10	110	13.8	69

^a In 1,4-dioxane; ^b in chlorobenzene.



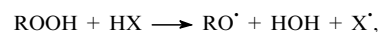
The high exothermicity of O₂ formation and the drop in ¹O₂ yields with an increase in temperature point to the predominance of the biradical mechanism. The enrichment of triplet oxygen generated from endoperoxide **1a** with the isotope ¹⁷O was observed in a strong magnetic field,²⁷ which is the result of ultrafine interactions within the biradical and provides additional evidence in favour of the biradical mechanism.

Studies of the thermolysis of β-hydroxyperoxides^{28–30} characterised by relatively high solubility in water revealed that their decomposition, similar to the decomposition of other peroxides R¹OOR², begins with the cleavage of the O—O bond. In the case of acyl derivatives and in the presence of water, thermolysis is accompanied by simultaneous hydrolysis of the ester bond.

III. Hydroperoxides

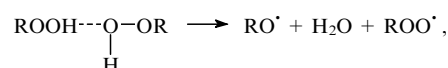
Thermolysis of hydroperoxides, which form homo- and hetero-associates in solution, is more complex than in the gas phase.^{31, 32}

According to Denisov,³¹ bimolecular decomposition of the type



occurs much faster than monomolecular decomposition, since the stability of the newly formed H—OH bond (483 kJ mol^{−1}) usually exceeds that of the H—X bond cleaved. The role of HX can be played by saturated hydrocarbons, alkenes, amines, alcohols and other compounds.³³

In the case of thermolysis involving association of two hydroperoxides



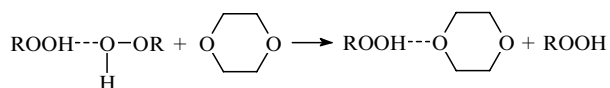
the activation energies of their decomposition in the complexes formed are the lower the higher is the enthalpy of the hydrogen bond.

According to X-ray diffraction data,³⁴ the hydroperoxide homoassociates R—O⁽¹⁾—O⁽²⁾—H can have different structures depending on the structure of the radical R. Thus *tert*-butyl hydroperoxide molecules form a hydrogen bond including the O⁽¹⁾ atom, whereas 1,1-diphenyl hydroperoxides form a hydrogen bond including the O⁽²⁾ atom. Because of steric hindrance, triphenylmethyl hydroperoxide forms a hydrogen bond with the π-electrons of the benzene ring of the second hydroperoxide molecule rather than with oxygen atoms. Obviously, the difference in the structures of the associates determines the mechanism of their thermolysis.

The dependence of specific rates of the decomposition of 1-methylcyclohexyl hydroperoxide and the consumption of the inhibitor on the initial concentration of the starting compound³⁵ suggests that homoassociation of hydroperoxides increases their reactivities up to a certain threshold level. Further aggregation of the hydroperoxide into a polymolecular associate does not lead to any further decrease in its thermal stability.

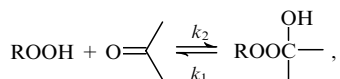
The addition of compounds that form stable associates with hydroperoxides results in dissociation of homoassociates with subsequent monomolecular decomposition (with respect to the hydroperoxide). Thus the addition of dioxane decreases the rate of

initiation of hydroperoxide decomposition in comparison with the initial solution.³⁶

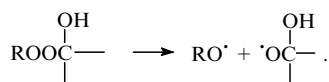


The formation of hydroperoxide associates with electrophiles in solution favours the homolysis of the O—O bond: the stronger the electron shift in this bond, the more intense the homolysis.

At low concentrations of hydroperoxides in solution, their decomposition occurs predominantly by a monomolecular mechanism; with an increase in the hydroperoxide concentration, the bimolecular mechanism becomes predominant. The effect of addition of alcohols on the rate of hydroperoxide thermolysis is concentration-dependent. For example, the addition of cyclohexanol to a solution of cyclohexyl hydroperoxide in chlorobenzene^{5,37} results in the increase in the reaction rate to a maximum at a definite concentration of the alcohol and then to its decrease. The inhibition observed at higher concentrations of the alcohol is attributed to the formation of ternary complexes $\text{ROOH} \cdot 2 \text{ROH}$ which dissociate into radicals more slowly. The presence of carbonyl compounds along with associates in the reaction mixture results in the formation of 1-hydroperoxides

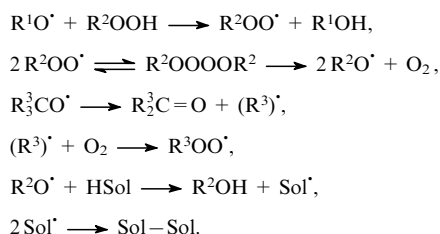


which are less thermostable than the original hydroperoxides³⁸ and undergo decomposition by the reaction:



The kinetic and thermodynamic parameters of reactions of cycloalkyl hydroperoxides with cyclohexanone in cyclohexane (the initial concentrations of the hydroperoxide and the ketone are equal to 0.02–0.05 mol litre⁻¹) (see Ref. 39) are listed in Table 3. Special mention should be made of the inertness of higher cyclic ketones in this reaction. Similar inactivity of higher cyclic ketones due to steric hindrance in the transition from the planar sp²-configuration to the sp³-configuration is observed in the addition of HCN to the corresponding ketones. The reversible formation of 1-hydroxyperoxides is catalysed by carboxylic acids. The data listed in Table 4 point to an increase in the rates of thermal decomposition of hydroperoxides upon addition of a ketone.

Of special note are reactions of hydroperoxides with the radicals formed upon thermolysis; these are accompanied by induced decomposition of hydroperoxides and their chain decomposition. This occurs in parallel with a series of secondary reactions:



The reaction of secondary hydroperoxides with the radicals $\text{ROO}^\bullet$ is accompanied by further destruction of hydroperoxides:

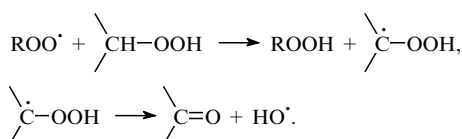


Table 3. Kinetic parameters of the reactions of hydroperoxides ROOH with cyclohexanone at 25 °C.

R	$10^3 k_2$ /litre mol ⁻¹ s ⁻¹	$K = k_2/k_1$ /litre mol ⁻¹	E_a /kJ mol ⁻¹	$Q = E_1 - E_2$ /kJ mol ⁻¹
Cyclohexyl ^a	1.0	8.0	21.2	39.4
Cyclooctyl	1.0	7.0	25.5	41.9

^a The reaction with cyclooctanone and cyclododecanone does not take place.

Table 4. Increase in the rate of the thermal decomposition of octyl hydroperoxide at 110 °C upon addition of cyclohexanone.

Reaction time /h	Decomposition (%)	
	without additives	with cyclohexanone
2	1.5	14.2
4	5.9	30.0
6	11.1	40.1

Note. For octyl hydroperoxide, $c_0 = 0.06$ mol litre⁻¹, for cyclohexanone $c_0 = 0.33$ mol litre⁻¹

The introduction of free radical scavengers suppresses induced decomposition of peroxides and permits one to estimate the contribution of the peroxide thermolysis proper (see also Refs 5 and 31). The kinetic characteristics of the reactions of the radicals $\text{RO}^\bullet$ and $\text{ROO}^\bullet$ with hydroperoxides are listed in Table 5 (data from Refs 40–47).

In biological objects, hydroperoxides exist in an aqueous medium. It is noteworthy that the transition from a hydrocarbon to an aqueous medium is accompanied by a significant decrease in the activation energy and an increase in the rate of hydroperoxide thermolysis. The corresponding parameters for *tert*-butyl hydroperoxide are as follows:⁶

Solvent	Initial concentration /mol litre ⁻¹	Decomposition rate constant /s ⁻¹ (T /°C)	E_a /kJ mol ⁻¹
n-Hydrocarbon	0.17	0.9×10^{-5} (150)	163
Water	0.05	0.14×10^{-5} (130)	126

The effect of pH on the decomposition kinetics of this hydroperoxide in water was studied.⁴⁸

Hydroperoxides are formed upon free-radical oxidation of DNA, which plays a crucial role in mutagenesis induced by ionising radiation. Thus the oxidation of 2'-deoxythymidine yields eight diastereomers of 5(6)-hydroxy-6(5)-hydroperoxy-5,6-dihydro-2'-deoxythymidine (**4a–d**, **5a–d**) and 5-(hydroperoxymethyl)-2'-deoxyuridine (**6**). The thermolysis of thymidine hydroperoxides in aqueous solutions was studied by Wagner *et al.*⁴⁹

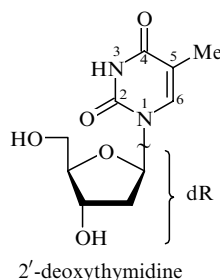
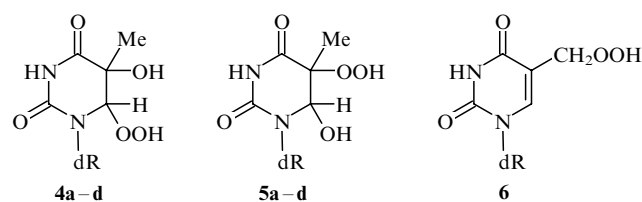
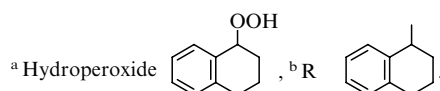


Table 5. Kinetic parameters ($\log k$) of the reactions of peroxy and alkoxy radicals $\text{ROO}^\bullet$ and $\text{RO}^\bullet$ with hydroperoxides.

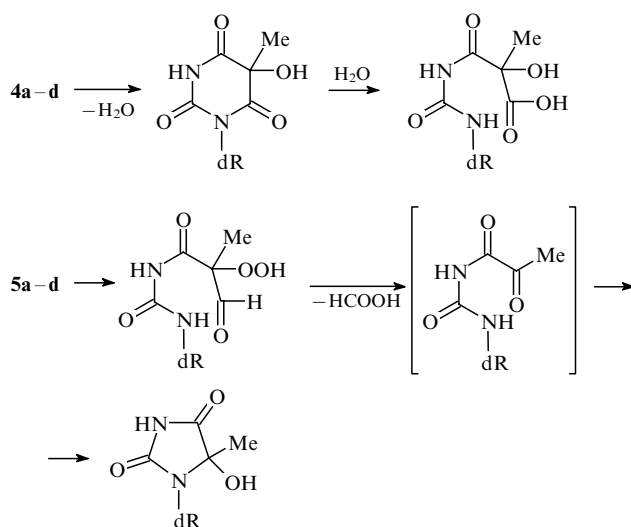
R in $\text{ROO}^\bullet$	Hydroperoxide	$T/^\circ\text{C}$	$\log k$	R in $\text{ROO}^\bullet$	Hydroperoxide	$T/^\circ\text{C}$	$\log k$
cyclo- C_6H_{11}	cyclo- $\text{C}_6\text{H}_{11}\text{OOH}$	75	1.25	PhMe_2C	PhMe_2COOH	30	7.95
		21	0.20	EtMe_2C	EtMe_2COOH	30	7.95
cyclo- C_6H_{11}	cyclo- $\text{C}_6\text{H}_{11}\text{OOH}$	75	1.08	1-Me-cyclo- C_6H_{10}	1-Me-cyclo- $\text{C}_6\text{H}_{10}\text{OOH}$	30	7.60
$\text{Bu}^\dagger$	Et(Me)CHOOH	21	2.68	$\text{Bu}^\dagger$	cyclo- $\text{C}_6\text{H}_{11}\text{OOH}$	30	8.45
$\text{Bu}^\dagger$	see ^a	30	2.75	$\text{Bu}^\dagger$	1-Me-cyclo- $\text{C}_6\text{H}_{10}\text{OOH}$	30	8.18
		75	3.17	$\text{Bu}^\dagger$	$\text{Bu}^\dagger\text{OOH}$	30	8.40
PhMe_2C	see ^a	30	2.78	$\text{Pr}^\dagger$	$\text{Pr}^\dagger\text{OOH}$	30	7.70
See ^b	PhMe_2COOH	30	3.40				

Note. The reactions of cyclo- $\text{C}_6\text{H}_{11}\text{OO}^\bullet$ with hydroperoxides are related to the $\text{S}_{\text{N}}2(\text{C}-\text{H})$ type; the reactions of other radicals are of the type $\text{S}_{\text{N}}2(\text{OO}-\text{H})$.



trans-(5*R*,6*R*) (**a**), *trans*-(5*S*,6*S*) (**b**), *cis*-(5*S*,6*R*) (**c**), *cis*-(5*R*,6*S*) (**d**).

The thermolysis of thymidine hydroperoxides in highly purified water occurs in accordance with the following schemes (see Table 6):

**Table 6.** Kinetic parameters of the thermal decomposition of thymidine hydroperoxides in aqueous solutions.

Hydroperoxide	$10^5 k_1/\text{s}^{-1}$ (37 °C)	$\Delta H^\ddagger$ /kJ mol ⁻¹	$\Delta S^\ddagger$ /J mol ⁻¹ K ⁻¹
4a	19	103	9.6
4b	12	105	15.4
4c	1.9	96	-31
4d	1.9	96	-31
5a	2.3	121	52
5b	2.0	125	64
5c	1.2	119	41
5d	0.56	147	125

As can be seen, the decomposition of the hydroperoxides **4a-d** involves dehydration of secondary hydroperoxide groups and subsequent hydrolysis, whereas the thermolysis of compounds **5a-d** involves tautomeric conversion of the hydroperoxide into an aldehyde and recyclisation.

IV. Dioxiranes

A series of novel oxidants, *viz.*, dioxiranes, possessing a unique combination of properties (high regio- and stereoselectivity of oxidation, high reactivity and mild reaction conditions) have been introduced into laboratory practice since the mid-1980's. The majority of investigations into the chemical properties of dioxiranes were carried out with dimethyldioxirane (**7b**, DMDO) and methyl(trifluoromethyl)dioxirane (**7c**) as examples.



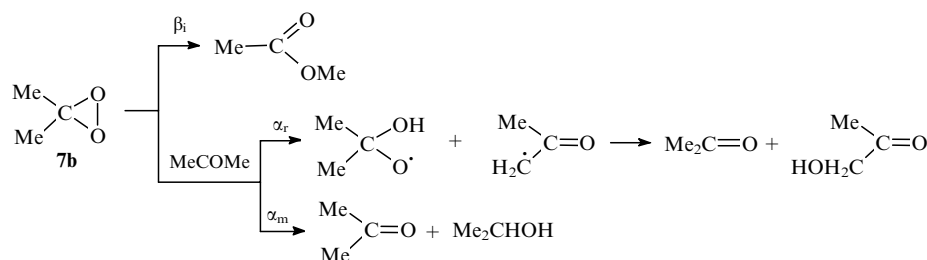
$\text{R}^1 = \text{R}^2 = \text{H}$ (**a**), Me (**b**); $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{CF}_3$ (**c**).

Thermal stability studies have shown that highly reactive dioxiranes react simultaneously by several routes. This accounts for discrepancies in results obtained by different authors. According to some authors,^{50, 51} the half-life ($\tau_{1/2}$) of dioxirane **7b** at room temperature is 7 h or 26 days, respectively. According to other authors,^{50, 52, 53} the decomposition of dioxiranes **7b** and **7c** cannot be described by first- or second-order kinetic equations, since the corresponding kinetic curves display a distinct induction period. However, at low concentrations of the dioxirane **7b** ($< 3 \times 10^{-2}$ mol litre⁻¹, see Refs 51 and 53) the rate of its thermolysis obeys the first-order kinetic law. Oxygen, which suppresses the decomposition of DMDO, has a pronounced effect on the composition of the reaction products.⁵³

The thermolysis of the dioxirane **7b** in acetone^{54, 55} occurs by three main routes, *viz.*, isomerisation (i), radical (r) and molecular (m) routes (Scheme 1).

The composition of the thermolysis products of DMDO depends on the presence of oxygen in the solution as well as on the presence and number of C-H bonds in the solvent molecule. The ratio of the main reaction products also depends on temperature (Table 7). If the decomposition is carried out in the presence of oxygen at 10 °C, methyl acetate is virtually the only reaction product. Its proportion in the total yield of the reaction products diminishes to 59%, if the reaction is carried out at 50 °C. Under these conditions, acetol (1-hydroxypropan-2-one) (39%) and acetic acid (2%) are formed in addition to methyl acetate. Quite a different situation is observed in the decomposition of DMDO in the absence of oxygen (the latter is removed by purging the

Scheme 1

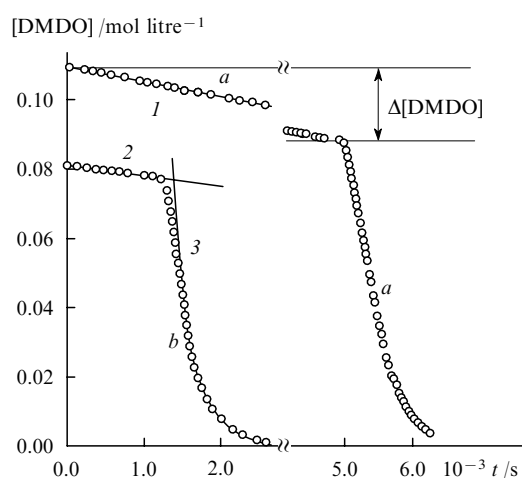
**Table 7.** Yields of the thermal decomposition products of dimethyldioxirane.

Atmo- sphere	$T/^{\circ}\text{C}$	MeCOMe 	MeCCH_2OH 	$\text{MeCOCH}_2\text{CMe}$ 	MeCOH
O_2	10	0.98	0.02	—	—
O_2	50	0.59	0.39	—	0.02
O_2^a	50	1.00	—	—	—
Ar	41	traces	traces	1	traces

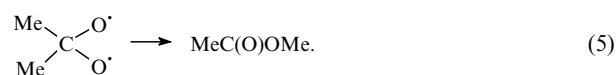
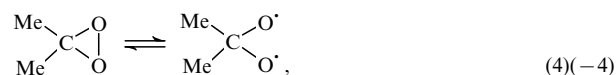
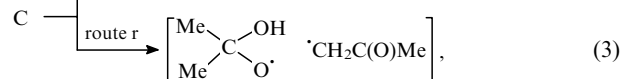
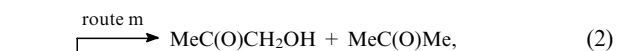
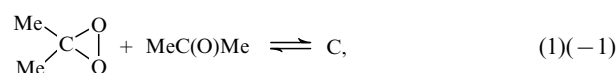
^a CCl_4 was used as a solvent; in other cases, acetone was used.

solution of DMDO with argon). Acetol acetate $\text{MeC(O)OCH}_2\text{C(O)Me}$ is the main thermolysis product at 41°C ; methyl acetate and acetol were found in insignificant amounts. The decomposition rate of dimethyldioxirane decreases in CCl_4 . The reason is the absence of C—H bonds in the solvent molecule; therefore, the isomerisation of DMDO into methyl acetate is the main pathway of its consumption.

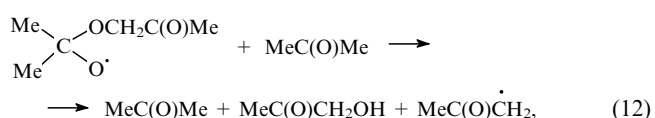
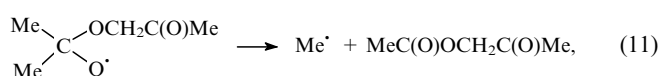
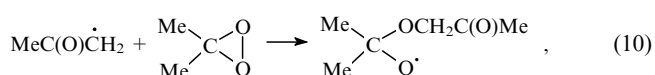
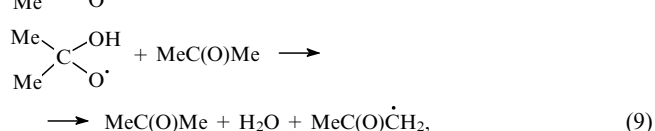
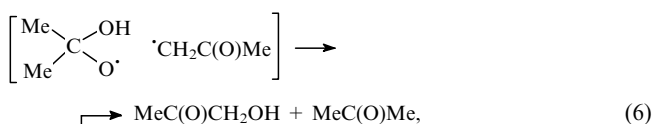
The presence of dissolved oxygen is critical for the stability of dioxirane solutions. When oxygen is present in the solution, the rate of DMDO thermolysis is relatively small and obeys the first-order kinetic law with respect to dioxirane (Fig. 1). Removal of oxygen by purging the solution with argon or by chemical binding sharply increases the rate of DMDO consumption (see Fig. 1, curve 3); the reaction order is intermediate between the first and the second with respect to dioxirane. The reason for the sharp increase in the reaction rate is intense radical-chain induced

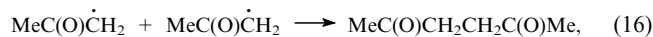
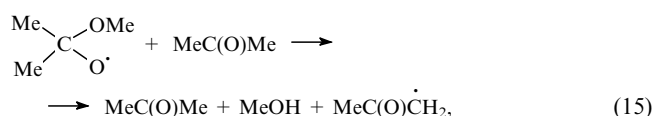
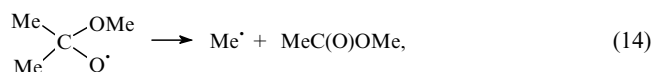
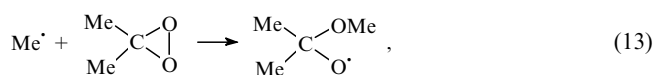
**Figure 1.** Typical kinetic curves for the consumption of dimethyldioxirane. Conditions: acetone, 50°C , preliminary purging of the solution with oxygen (a) or argon (b). The solid lines designate the results of treatment of the kinetic curves using a first-order (curves 1 and 2) or a mixed (first + second)-order equation (curve 3).

decomposition of the peroxide in the absence of O_2 . The thermolysis of DMDO proceeds in accordance with the following scheme (C is a complex):^{54,55}

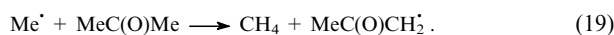


Further transformations of radical intermediates are apparent: the alkyl radicals react with oxygen and induce the decomposition of dioxirane **7b** in the absence of oxygen [reactions (10)–(13)] and undergo decay in the recombination [reactions (16)–(18)]. Oxygen-centred radicals undergo β -cleavage [reactions (8), (11), (14)] or abstract the hydrogen atom from the acetone molecule [reactions (9), (12), (15)].





The induced decomposition of dioxirane under the action of the methyl radical [reaction (13), $k_{13} \approx 10^5 - 10^6 \text{ litre mol}^{-1} \text{ s}^{-1}$] ⁵⁶⁻⁵⁸ competes with the abstraction of hydrogen from the acetone molecule with the rate constant of $2.7 \times 10^3 \text{ litre mol}^{-1} \text{ s}^{-1}$ (see Ref. 59)



In the absence of oxygen, the chain decomposition of dioxirane **7b** occurs with the involvement of $\text{Me}\cdot$ and $\text{MeC(O)CH}_2\cdot$ radicals. In the presence of oxygen, the induced decomposition of compound **7b** is suppressed, while the chain termination involves the peroxy radicals.



Under these conditions, the thermolysis of DMDO is described by equations (1)–(9), (20), (21). A kinetic analysis of the decomposition reaction gave the following expression for the reaction rate:

$$W_{7b} = \{(\alpha_m + \alpha_r)k_1[\text{MeC(O)Me}] + \beta_i k_4\} [7b] = k_{\text{eff}}[7b], \quad (22)$$

where α_m and α_r are the contributions of the molecular and radical routes during the conversion of the complex C: $\alpha_m = k_2/A$, $\alpha_r = k_3/A$, where $A = k_{-1} + k_2 + k_3$; $\beta_i = k_5/(k_{-4} + k_5)$. Indeed, thermal decomposition of DMDO in acetone solutions saturated with oxygen obeys the kinetic law for first-order reactions with respect to dioxirane. The effective thermal decomposition rate constant, k_{eff} , does not depend on the concentration of dioxirane. At 50 °C:

$$k_{\text{eff}} = 1.8 \times 10^{-5} + 1.5 \times 10^{-6} [\text{MeC(O)Me}] \text{ s}^{-1}.$$

The activation parameters, *i.e.*, the preexponential factor $\log A$ and the energy of activation E_a , for the overall decomposition of DMDO in acetone are described by the expression:

$$\log k_{\text{eff}} = (10.2 \pm 0.6) - \frac{(90.4 \pm 3.8)}{\theta},$$

where $\theta = 2.3 RT \text{ kJ mol}^{-1}$. As mentioned above, the thermolysis of DMDO in carbon tetrachloride occurs at a slower rate, since in this case the thermal decomposition occurs by only one route, *viz.*, isomerisation of dioxirane into methyl acetate. The temperature dependence of the rate constant $k_i = \beta_i k_4$ in CCl_4 appears as:

$$\log k_{\text{eff}} = \log k_i = (7.1 \pm 0.3) - \frac{(75.3 \pm 2.1)}{\theta}.$$

The activation parameters of the isomerisation of the dioxirane **7b** into methyl acetate are consistent with the results of quantum-chemical calculations of a high basis set.⁶⁰ The energy diagram for the isomerisation of DMDO and the simplest dioxirane **7a** on a standard enthalpy of formation scale is shown

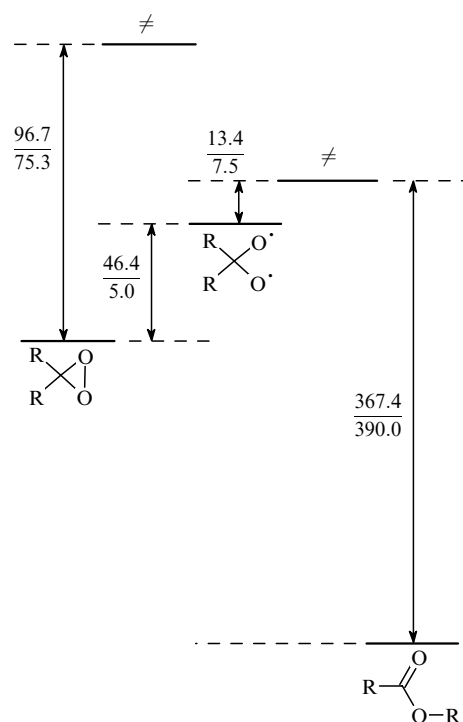


Figure 2. The energy diagram of isomerisation of dioxirane **7a** ($R = \text{H}$, $\Delta H_f^\circ = -1.3 \text{ kJ mol}^{-1}$) and dimethyldioxirane **7b** ($R = \text{Me}$, $\Delta H_f^\circ = -105.9 \text{ kJ mol}^{-1}$) into formic acid and methyl acetate, respectively. (The corresponding values for compounds **7b** and **7a** (in kJ mol^{-1}) are given in the numerator and the denominator, respectively). The sign $\neq$ designates the transition state.

in Fig. 2. The difference between experimental and calculated values of E_a seems to be related to the effect of the solvent. The limiting step of isomerisation, *viz.*, the formation of a biradical, requires the opening of the dioxirane ring in order to minimise the repulsion of lone electron pairs coplanar with the ring. The opening of the ring associated with the reduction of the bond angle between the substituents at the carbon atom is more difficult for substituents with larger size, which explains the increase in E_a in the homolysis of the dioxirane **7b** in comparison with compound **7a**. Indeed, the dioxirane **7a** is thermally much less stable than **7b**. Contrariwise, sterically hindered bis(mesityl)dioxirane forms stable crystals even at room temperature.⁶¹

The O–O bond homolysis product (biradical) decomposes through migration of H or Me resulting in the formation of the corresponding acid or its ester. This process is characterised by low activation energy, *e.g.*, for the biradical $\cdot\text{OCMe}_2\text{O}\cdot$ it is 13.4 kJ mol^{-1} . The decomposition of the biradical (or DMDO) into CO_2 and ethane requires much energy; therefore, this reaction cannot compete with the rearrangement into an ester.⁶⁰ Indeed, vacuum flash-pyrolysis of the dioxirane **7c** gives quantitative yields of methyl trifluoroacetate ($> 98\%$).⁶² The photolysis and thermolysis of dioxiranes in solutions are complicated by the decomposition of the peroxide induced by free radicals.

While analysing the ratio of the radical (r) and molecular (m) routes of dioxirane decomposition, one should bear in mind that dioxiranes react with many organic compounds at a very fast rate ($k_m \gg k_r$). In this case, we deal with a manifestation of a high oxidative activity of dioxirane with respect to the other reactant rather than with its thermolysis. The problems related to the products, kinetics and mechanisms of oxidation of various organic compounds by dioxiranes are documented.⁶³⁻⁶⁸ In the presence of compounds with non-activated C–H bonds, the radical route of dioxirane oxidation becomes more pronounced.

As mentioned above, complete removal (purging or chemical binding) of O_2 shifts the reaction towards radical-chain decom-

position of DMDO. This includes chain initiation [reactions (1)–(9)], propagation [reactions (10)–(15), (19)] and termination [reactions (16)–(18)]. It was found⁵⁵ that cross recombination is the most plausible step in the chain termination (17). In this case, the kinetic analysis of DMDO decomposition gives the following expression for the rate of consumption of the dioxirane **7b**:

$$W_{7b} = k^{(1)}[7b] + k^{(2)}[7b]^2, \quad (23)$$

where $k^{(1)}$ and $k^{(2)}$ are complex combinations of kinetic constants and acetone concentration. The first component of Eqn (23) reflects the consumption of compound **7b** in the reaction with the acetonoyl radical, while the second one describes the contribution of reaction (13) to the total rate of DMDO decomposition. This differential equation is readily transformed into an analytical expression which appears as:^{57, 66}

$$\ln \frac{(k^{(1)} + k^{(2)}[7b])[7b]_0}{(k^{(1)} + k^{(2)}[7b])} = k^{(1)}t. \quad (24)$$

Equation (24) effectively describes the kinetic curves of consumption of the dioxirane **7b** under conditions of induced decomposition.

Thus the role of oxygen in the thermolysis of DMDO consists of the inhibition of free-radical induced decomposition of the peroxide by route r. The calculation of the ratio of the amount of dissolved oxygen to the dioxirane **7b** decomposed in the induction step can be used for determining the contribution of the radical route of thermal decomposition of DMDO to the overall process. The ratio of decomposition reactions by routes r and m was studied⁵⁵ in the reactions of DMDO with acetone and some aliphatic hydrocarbons (Table 8). These data suggest that the reaction of DMDO with aliphatic hydrocarbons is indeed a radical reaction; it is not excluded that it proceeds exclusively by a homolytic mechanism ($k_3 \gg k_2$), whereas the efficiency of initiation is decreased due to intracage recombination [reaction (6)].

The known contribution of the radical route of the reaction of dioxirane **7b** containing a C–H bond and the kinetic parameters of the overall reaction allow one to determine the rate constants k_r and k_m as well as the corresponding activation parameters. The data for the reactions of DMDO with acetone and 2,2,4-trimethylpentane are given below.

Reagent	Reaction route	
	radical	molecular
Acetone	$\log k_r = 11.9 - 112.1/\theta$	$\log k_m = 9.5 - 96.2/\theta$
2,2,4-Trimethylpentane	$\log k_r = 11.1 - 91.2/\theta$	$\log k_m = 4.0 - 51.5/\theta$

The preexponential factors of the rate constants for the radical reaction of the dioxirane **7b** with acetone and 2,2,4-trimethylpentane are similar (with allowance for the statistic correction for six C–H bonds of acetone). The difference in the activation energies for these reactions (21 kJ mol^{−1}) reflects the difference in the strengths of the C–H bonds of acetone and 2,2,4-trimethylpentane subjected to the attack.

The values of partial rate constants for the reaction of DMDO with RH were calculated from the effective rate constant for the consumption of dioxirane in the oxidation of hydrocarbons (RH) and acetone:^{55, 57, 58, 69}

$$k^H = \frac{k_{\text{eff}}}{n[\text{RH}]} = \frac{(\alpha_r + \alpha_m)k_1}{n},$$

where n is the number of equivalent C–H bonds attacked by dioxirane. The results of calculations of k^H are listed in Table 9. Although the ratio of reaction routes for the reaction **7b** + RH changes in the series of compounds under study, the calculated

Table 8. Ratio of the molecular and radical routes in the reactions of dimethyldioxirane with organic compounds.

Substrate	[RH] ₀ /mol litre ^{−1}	[7b] ₀ /mol litre ^{−1}	T /°C	[O ₂]/Δ[7b]
Acetone	13.6	0.108	50	0.20
	13.6	0.096	56	0.23
	0.61	0.061	41	0.68
	0.83	0.083	41	0.76
	0.99	0.079	41	0.73
	1.1	0.078	41	0.76
2,2,4-Tri-methyl-pentane	1.2	0.075	41	0.71
	1.7	0.070	25	0.57
	0.84	0.077	41	0.51
	1.2	0.071	41	0.53
	1.7	0.078	41	0.66
n-Octane	0.52–4.6	0.019–0.071	25	0.50
Cyclohexane	1.7	0.078	41	0.66
2-Methyl-butane	0.52–4.6	0.019–0.071	25	0.50

Table 9. Partial rate constants for the reaction of dimethyldioxirane with organic compounds (RH) at 25 °C.

RH	[RH] /mol litre ^{−1}	log k_{eff} (s ^{−1})	k_{eff} /s ^{−1}	k^H /litre mol ^{−1} s ^{−1}
Acetone	13.7	10.2 – 90.4/θ	2.3×10^{-6}	2.8×10^{-8}
2-Methyl-butane	1.0	—	2.1×10^{-4}	2.1×10^{-4}
Adamant-ane ^a	—	7.94 – 59.4/θ	3.4×10^{-3}	8.4×10^{-4}
Cumene	4.0	6.4 – 52.3/θ	1.7×10^{-3}	4.2×10^{-4}

^a Temperature dependence of a bimolecular rate constant.

values of partial rate constants can be used to determine the relative reactivities of the substrates RH. The changes in k^H demonstrate the following regularities (Table 9):

1. Dioxirane is a pronounced regioselective oxidant. The primary C–H bond is attacked 10⁴ times less actively than the tertiary bond. Probably, the true value of the $k_{\text{tert}}/k_{\text{pri}}$ ratio is somewhat smaller, since the reactivity of acetone is decreased due to deactivation of the α-C–H bonds by the carbonyl group.

2. The activity of tertiary C–H bonds changes in the following order: aliphatic (1.0) < 'aromatic' (H–CAlk₂Ar) (2.0) < cage (4.0). Weakening of the C–H bond strength and retention of the radical reaction mechanism result in an increase in k^H on going from 2-methylbutane to cumene. The presence of carbocation-stabilising fragments in the molecule RH increases the contribution of the molecular route and the reactivity of the C–H bond (2-methylbutane and adamantane).

The ratio of radical and molecular routes is quantitatively characterised by the [O₂]/Δ[7b] ratio. The conditions influencing the ratio of these two routes are as follows:

— the contribution of the radical mechanism increases with temperature (see Table 8);

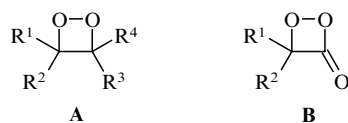
— the energy of homolytic dissociation of the C–H bond depends on the nature of the substrate to be oxidised: an increase in energy diminishes the contribution of the radical route. The energy of homolytic dissociation of tertiary C–H bonds is lower than that of secondary bonds.

The ratio of molecular and radical routes of reactions of peroxide oxidants with substrates to be oxidised has been repeatedly discussed in the literature. It is well known that the more pronounced the electrophilic properties of the peroxide (the affinity of the oxidant for the electron can be used as a measure of activity) and the electron-donor properties of the compound to be oxidised, the lower the temperature and the more polar the

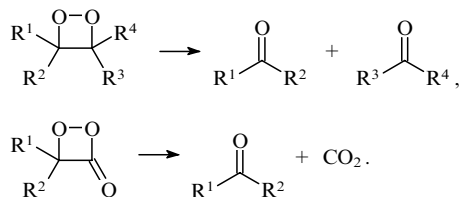
solvent, the higher the probability of the molecular route of the oxidation. A similar situation is observed in the chemistry of dioxiranes. From a synthetic point of view, it is more reasonable to select conditions favouring the nonradical mechanism, *viz.*, low temperature, the use of dioxiranes possessing stronger oxidising properties (*e.g.*, **7c**) and compounds to be oxidised with activated C–H bonds that can effectively stabilise the positive charge on the C atom generated upon partial transfer of the electron density to dioxirane.

V. 1,2-Dioxetanes

Luminescence appearing upon formation of an electron-excited product is the main characteristic feature of the thermolysis of 1,2-dioxetanes (**A**) and their keto derivatives (α -peroxy lactones, **B**) (see Refs 70–74 and the references cited therein).



The excitation of the product is due to the fact that the difference between the enthalpy of activation $\Delta H^\ddagger$ of thermolysis and the standard enthalpy of the same reaction ΔH° exceeds the energy of the electron-excited state E^* , *i.e.*, $\Delta H^\ddagger - \Delta H^\circ \geq E^*$. The main routes of the thermolysis of 1,2-dioxetanes (**A**) and α -peroxy lactones (**B**) are as follows:



The schemes illustrating the ratios of energies in the individual steps of the thermolysis of some typical representatives of dioxetanes and α -peroxy lactones are shown in Fig. 3.⁷²

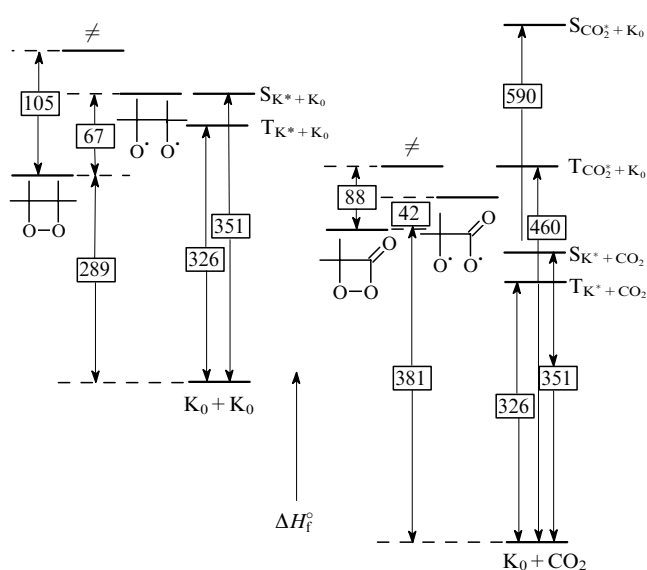


Figure 3. Diagram of the enthalpies of formation of reaction products (ΔH_f° /kJ mol^{−1}) in the thermolysis of tetramethyl-1,2-dioxetane and dimethyl-1,2-dioxetanone.

Product states: singlet S_K , triplet T_K , excited K^* and ground K_0 . The figures designate the energy of the transition from one state to another.

The values of ΔH° for different compounds lie in the range from -250 to -380 kJ mol^{−1}, while $\Delta H^\ddagger$ varies from 85 to 140 kJ mol^{−1}, which enables the occupation of triplet ($E_T^* = 250-330$ kJ mol^{−1}) and singlet [$E_S^* = E_T^* + (20-63)$ kJ mol^{−1}] states. A comparison of 1,2-dioxetanes and α -peroxy lactones has shown that the decomposition of the latter is much more exothermic. This is not surprising, however, since the incorporation of an sp^2 -hybridised carbon atom into a strained four-membered 1,2-dioxetane ring increases the exothermic character of the ring opening. The decomposition of α -peroxy lactones yields electron-excited CO_2 molecules; the energies of their excited triplet and singlet states are very high. The kinetic characteristics of the

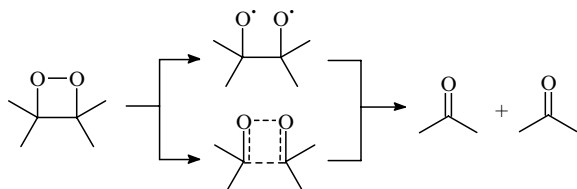
Table 10. Kinetic parameters and yields of the excited states (T^* , triplet; S^* , singlet) in the thermolysis of dioxetanes in solution.

Compound	R ¹	R ²	R ³	R ⁴	Solvent	E_a /kJ mol ^{−1}	$\Delta H^\ddagger$ /kJ mol ^{−1}	$\Delta S^\ddagger$ /J mol ^{−1} K ^{−1}	Yield (%)	
									T^*	S^*
	Me	Me	Me	Me	toluene	116	104	−11.7	35	0.25
	Me	Me	Me	Me	<i>o</i> -xylene	115	—	—	—	—
	Me	Me	Me	Me	benzene (liquid)	117	—	—	—	—
	Me	Me	Me	Me	benzene (solid)	116	—	—	—	—
	Me	Me	Me	H	toluene	109	98	−19.7	25	0.1
	Me	H	H	Me	"	103	94	−21.3	7.8	0.018
	Me	Me	H	H	"	104	90	−31.8	12	0.018
	Me	H	Me	H	"	101	90	−30.9	13	0.019
	Me	H	H	H	"	95	90	−23.4	4.3	0.003
	H	H	H	H	"	95	79	−52.7	0.24	0.0003
					acetonitrile	151	145	20.1	17.3	1.8
					xylene	166	141	12.1	15	2
						139	136	−0.84	3.8	0.43
						153	148	−2.1	1.1	0.07

thermolysis of some dioxetanes in solution are listed in Table 10.^{75–78}

The kinetic parameters of the thermolysis of tetramethyldioxetane in various solvents are very similar. The conservation of the activation energy in the decomposition of tetramethyldioxetane in benzene solutions and solid benzene templates at low temperatures is of note.⁷⁵ The activation energy of the thermolysis of unsubstituted dioxetane in the gas phase is equal to $91 \pm 5 \text{ kJ mol}^{-1}$, *i.e.*, it is 4 kJ mol^{-1} less than that for toluene. Thus, the energy of molecular thermolysis does not virtually depend on the phase state of the medium in the absence of a direct interaction with the solvent molecules. The stability of dioxetanes of the diadamantylidene series with respect to decomposition is especially high: E_a reaches 153 kJ mol^{-1} . The data listed in Table 10 and other published data suggest that the yields of excited singlet states are many times smaller than those of triplet states, *i.e.*, spin-forbidden processes occur much more intensely than spin-allowed ones. The yields of excited triplets usually increase with an increase in the stability of the starting peroxide.

Two main mechanisms for the thermal decomposition of dioxetanes have been proposed: formation of a biradical and concerted redistribution of the bonds.

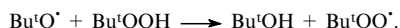


The effect of substituents on the chemical kinetics of thermolysis and thermochemical and quantum-chemical calculations confirm the biradical mechanism of thermolysis.^{73, 74, 77} The enthalpies of formation, the geometry of the central fragment, the torsion angle $\text{O}-\text{C}-\text{C}-\text{O}$ and the strain energies in the ring were calculated for a large series of substituted dioxetanes and intermediate biradicals on the basis of a biradical model using the molecular mechanics method (MM2).⁷⁹ Together with the thermochemical calculations the use of the Benson additive group contribution method has made it possible to obtain efficient correlation equations relating the Arrhenius and free activation energies with the values of angle strain energies in the starting dioxetane and in the biradical. A relatively high predictive capacity of these correlation equations provides additional evidence in favour of the biradical mechanism.

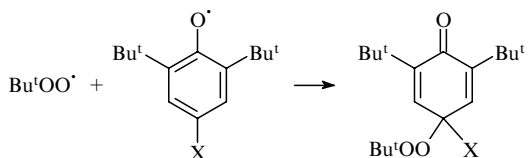
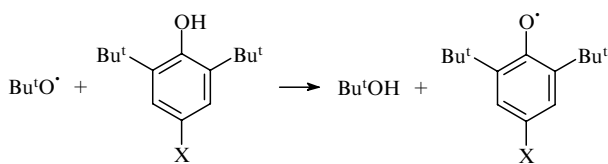
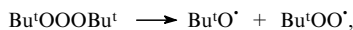
VI. Trioxides

Compounds containing three or more neighbouring oxygen atoms are considerably less thermostable than peroxides ($\text{RO}-\text{OR}$).⁸⁰

Thermal decomposition, which proceeds exclusively by a homolytic mechanism, is the most typical reaction of dialkyl trioxides. Their decomposition yields alkoxy ($\text{RO}^\bullet$) and peroxy ($\text{ROO}^\bullet$) radicals which determine all subsequent reactions and reaction products. Direct evidence for the formation of peroxy radicals in the decomposition of di-*tert*-butyl trioxide was obtained by ESR (see, *e.g.*, Ref. 81). The *tert*-butoxy radical was identified from the signal of its adduct with a spin trap (2-methyl-2-nitrosopropane).⁸² Indirect evidence for the generation of $\text{Bu}^\bullet\text{O}^\bullet$ radicals also follows from a significant increase in the concentration of the radical $\text{Bu}^\bullet\text{OO}^\bullet$ after addition of *tert*-butyl hydroperoxide to a solution of $\text{Bu}^\bullet\text{OOOBu}^\bullet$ in CH_2Cl_2 :

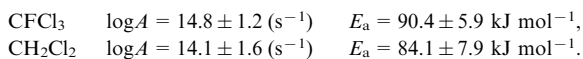


The decomposition of $\text{Bu}^\bullet\text{OOOBu}^\bullet$ in the presence of free radical scavengers (sterically hindered phenols) occurs without evolution of oxygen, but is accompanied by yellow colouration of the solution due to the formation of quinolide peroxide.^{81, 83}



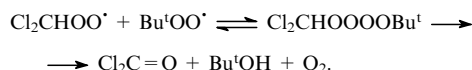
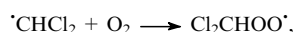
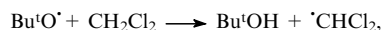
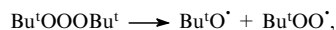
$\text{X} = \text{Me}, \text{Bu}^\bullet.$

The kinetics of radical decomposition of di-*tert*-butyl trioxide in CFCl_3 and CH_2Cl_2 (-20 to 7°C) was followed⁸⁴ by monitoring ionol (2,6-di-*tert*-butyl-4-methylphenol) consumption. The following activation parameters were established:



The probability (e) of the exit of radicals into the solution in the decomposition of di-*tert*-butyl trioxide does not virtually depend on temperature and constitutes $(90 \pm 10)\%$.⁸⁴

Under certain conditions, the decomposition of ROOOR is accompanied by chemiluminescence (CL) in the visible (350–650 nm) and IR (1000–1300 nm) regions of the spectrum.⁸⁵ Excited carbonyl compounds (*e.g.*, singlet-excited phosphene in the case of CH_2Cl_2) emit in the visible region, while singlet oxygen $^1\Delta_g\text{O}_2$ emits in the IR region. CL emitters are formed upon recombination of peroxy radicals generated in the decomposition of di-*tert*-butyl trioxide with subsequent involvement of the solvent in the radical-chain reaction.⁸⁶



The energy of the last reaction ($\sim 375 \text{ kJ mol}^{-1}$) is sufficient to generate phosphene or oxygen in the excited states (the excitation energies are equal to ~ 290 and 94 kJ mol^{-1} , respectively).⁸⁷ The chemiluminescence method was used to determine the excitation yields of singlet oxygen upon decomposition of di-*tert*-butyl trioxide in CH_2Cl_2 .⁸⁷ At -5.5°C , this yield is 22% (as calculated per original trioxide) and diminishes slightly with an increase in temperature (18% at 5.0°C). The termination of the kinetic chains in the decomposition of di-*tert*-butyl trioxide in CH_2Cl_2 occurs predominantly as cross recombination of peroxy radicals.⁸⁶

The quenching of the chemiluminescence in both visible and IR regions of the spectrum obeys first-order kinetics and is characterised by similar rate constants. The activation parameters of the thermal decomposition of dialkyl trioxides obtained in the temperature range from -20 to 18°C using the CL method are listed in Table 11.

The rate constants for the decomposition of di-*tert*-butyl trioxide (at 0°C) in carbon tetrachloride ($\epsilon = 2.23$) and nitromethane ($\epsilon = 38.6$) are 0.6×10^{-3} and $9.7 \times 10^{-3} \text{ s}^{-1}$, respectively (see Ref. 88), *i.e.*, they increase with the medium polarity. The same is true of di-*tert*-butyl peroxide; however, in the latter case this effect is less pronounced. For example, at 125°C the

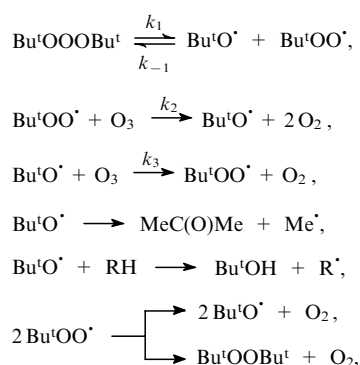
Table 11. Activation parameters of the decomposition of dialkyl trioxides ROOOR in CH₂Cl₂ inferred from the chemiluminescence data.

R	Method ^a	log <i>A</i> (s ⁻¹)	<i>E</i> _a /kJ mol ⁻¹	Ref.
Bu ^t	IR	14.5 ± 2.2	87.0 ± 2.5	85
	Vis	14.5 ± 0.7	85.4 ± 3.8	86
EtMe ₂ C	IR	13.2 ± 1.0	80.3 ± 5.4	87
	Vis	16.3 ± 1.8	94.1 ± 9.6	87
PhMe ₂ C	IR	15.5 ± 0.9	92.0 ± 4.6	87
	Vis	15.0 ± 1.6	89.5 ± 8.2	87

^a Designations: IR, infrared spectroscopy; Vis, spectroscopy in the visible region of the spectrum.

decomposition rate constants of Bu^tOOBu^t in cumene ($\epsilon = 2.37$) and acetonitrile ($\epsilon = 37.5$) are equal to 16.0×10^{-6} and 34.7×10^{-6} s⁻¹, respectively. A symmetrical transition state of the peroxide RO...OR is stabilised by the solvent to a lesser degree than the non-symmetrical transition state of the trioxide RO...OOR. Therefore, the dependence of the activation energy on the medium polarity is expressed to a greater degree for the latter.

Di-*tert*-butyl trioxide is an effective initiator of the chain decomposition of ozone in CFCl₃ (−23 °C).⁸⁹ The consumption of O₃ occurs in accordance with the first-order kinetic law; the value of the effective rate constant k_{eff} depends linearly on [Bu^tOOOBu^t]^{1/2}. This process is described by the following scheme:



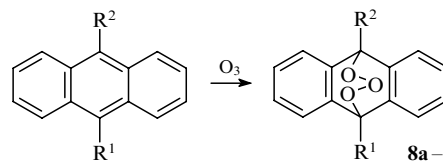
where RH = Bu^tOOOBu^t and its decomposition products.

The termination of the kinetic chains takes place as a result of cross-recombination of the radicals Bu^tO[•] and Bu^tOO[•] into the original trioxide; the contributions of irreversible consumption of the *tert*-butoxyl radical and the quadratic decay of the peroxy radicals are negligibly small. For this reason, the concentration of the trioxide does not change throughout the experiment ($\sim 10^4$ s), which simplifies the reaction scheme and yields the following expression for the effective rate constant for this reaction:

$$k_{\text{eff}} = 2(Kk_2k_3[\text{Bu}^t\text{OOOBu}^t])^{1/2},$$

where $K = k_1/k_{-1}$. The product of the rate constants for the reactions of O₃ with alkoxy and peroxy radicals was calculated from the linear dependence of k_{eff} on [Bu^tOOOBu^t]^{1/2}; k_3 was found to be equal to $\sim 1.7 \times 10^7$ litre mol⁻¹ s⁻¹ at −23 °C.

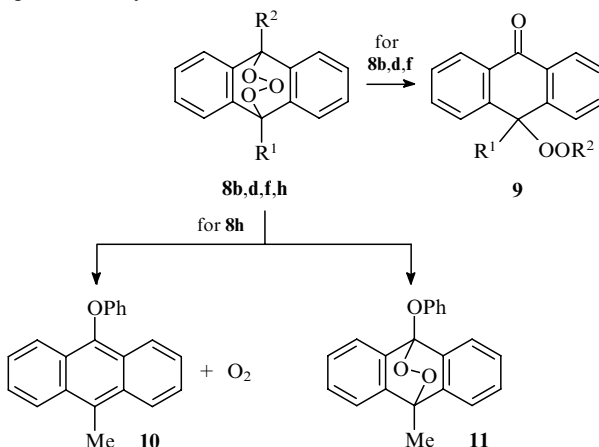
Transannular ozonides (cyclic analogues of dialkyl trioxides) are formed upon addition of ozone to anthracene and its 9,10-substituted derivative.^{90–94}



R¹ = H: R² = H (**a**), Me (**b**), Bu^t (**c**); R¹ = Me: R² = Me (**d**), Et (**e**), Bu^t (**f**), OMe (**g**), Ph (**h**), CH₂Ph (**i**); R¹ = R² = OMe (**j**).

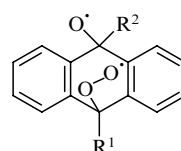
The stability of transannular ozonides strongly depends on the nature of the substituents R¹ and R². The preparation of 9-(*tert*-butyl)-10-methylantracene ozonide (**8f**) stable at room temperature has been described.⁹³ The latter was isolated in a crystalline state and studied by X-ray diffraction analysis. The decomposition of the ozonide **8f** obeys the first-order kinetic law and is characterised by the following activation parameters: log *A* = 14.6 ± 0.3 (s⁻¹); *E*_a = 119.7 ± 2.1 kJ mol⁻¹. The activation energy of the decomposition of this compound exceeds those of the ozonides **8b** (*E*_a = 105 kJ mol⁻¹)⁹² and **8c** (*E*_a = 100 kJ mol⁻¹),⁹⁵ which points to stabilisation of transannular ozonides by bulky alkyl substituents. Interestingly, in the case of *cis*-1,2,3-trioxolanes their structures are destabilised by bulky substituents.

Heating of the ozonides **8b**, **8d** and **8f** results in their isomerisation into 10-methyl-10-(alkylperoxy)-9-anthrone (**9**) in nearly quantitative yields.^{90, 91, 93}



The decomposition of the ozonide **8h** is accompanied by evolution of molecular oxygen and a shift of the phenyl substituent to the oxygen atom; this affords 9-methyl-10-phenoxyanthracene (**10**). Endoperoxide **11** is formed in a small amount upon decomposition of the ozonide **8h**.

The radical decomposition of transannular ozonides was confirmed in the studies carried out in the presence of the free radical scavenger 2,4,6-tri-*tert*-butylphenol.⁹⁴ Selective homolysis of one of the O–O bonds is the first step in the decomposition of transannular ozonides and dialkyl trioxides.



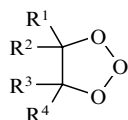
Attempts to detect the formation of singlet oxygen in the decomposition of the ozonide **8g** in the presence of the ¹O₂ scavengers cyclohexene and 1,2-dimethylcyclohexene were unsuccessful.⁹⁴

Table 12. Activation parameters of the thermal decomposition of 1,2,3-trioxolanes.

Ozonide	$\log A$ (s ⁻¹)	E_a /kJ mol ⁻¹	Ref.
<i>trans</i> - 12a	5.3	28.9	96
<i>trans</i> - 12b	8.4	39.7	96
<i>trans</i> - 12c	11	59.8	96
<i>cis</i> - 12b	—	< 13.8	96
<i>cis</i> - 12d (see ^a)	—	—	97
12e (see ^b)	14	37.7	97
12f	—	< 13.8	96
	—	33.5	96
	9	29.3	98

^a $\tau_{1/2}$ = 0.06 s at -92 °C; ^b $\tau_{1/2}$ = 0.74 s at -92 °C.

Data on the kinetic regularities of the thermolysis of 1,2,3-trioxolanes (**12**) (primary ozonides) are relatively scarce (Table 12).

**12a–f**

$R^1 = R^3 = H$; $R^2 = R^4 = Et$ (**a**), Pr^i (**b**), Bu^t (**c**), Me (**d**);

$R^1 = R^2 = R^3 = R^4 = Me$ (**e**); $R^1 = Bu^n$, $R^2 = R^3 = R^4 = H$ (**f**).

Their decomposition was studied by IR⁹⁶ and ¹H NMR spectroscopy⁹⁷ by following the changes in the ozonide concentration and the accumulation of the ozonide transformation products.⁹⁸ In all cases studied, the thermolysis of 1,2,3-trioxolanes obeyed the first-order kinetic law.^{96–98}

The decomposition of primary ozonides yields a carbonyl compound $R^1R^2C=O$ and a carbonyl oxide R^3R^4COO ; the existence of the latter in the liquid phase was confirmed by spectroscopic data.⁹⁹ The final decomposition products (1,2,4-trioxolanes, peroxides and polymeric peroxides) are formed in subsequent reactions of carbonyl oxide molecules with one another, with carbonyl compounds and with the solvent or special additives.

The homolytic cleavage of the O–O bond is the most typical reaction of all trioxides under consideration. Thermal stability of

peroxides is the main feature which makes them different from trioxides. For example, the same rates of decomposition of di-*tert*-butyl trioxide and di-*tert*-butyl peroxide ($k = 1 \times 10^{-5}$ s⁻¹) are observed at -40 and 120 °C, respectively.

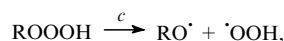
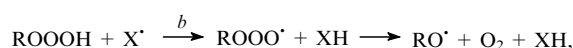
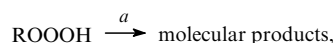
VII. Hydrotrioxides

Thermolysis of hydrotrioxides ROOOH was considered in detail in a recently published review;¹⁰⁰ therefore, here we shall confine ourselves to the description of the main characteristic features of this process.

The decomposition of ROOOH occurs in accordance with the first-order kinetic law.^{101–110} The activation parameters for the decomposition of some hydrotrioxides are listed in Table 13. High proneness of hydrotrioxides to homoassociation and complexation with a solvent determines a broad range of activation energies and preexponential factors which are interrelated in a compensation law. The thermal decomposition rate constant of ROOOH increases with the enhancement of the electron-withdrawing properties^{101–104} and polarity¹⁰⁵ of the substituent R.

In the thermal decomposition of hydrotrioxides, part of O₂ is evolved in a singlet excited state. In addition, the decomposition of some hydrotrioxides is accompanied by chemiluminescence in the visible region of the spectrum, which suggests the formation of free radicals during the thermolysis.

The thermal decomposition of hydrotrioxides may occur by different pathways:



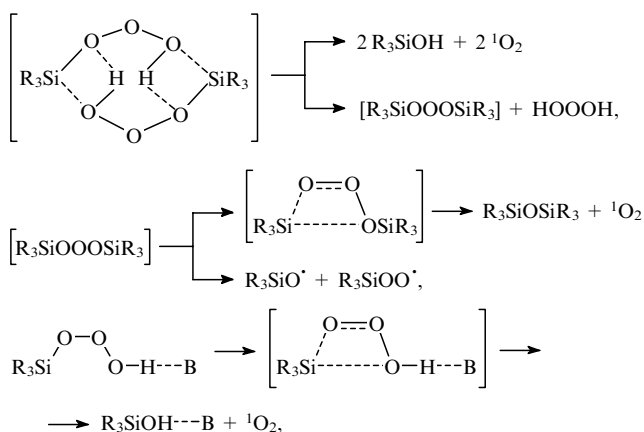
where X[·] is any radical leaving the solvent cage and inducing the decomposition of ROOOH.

The first reaction (route *a*) takes place in the case of silyl hydrotrioxides. The decomposition mechanism of these compounds was studied in detail in the example of dimethylphenylsilyl hydrotrioxide.¹⁰⁴ The kinetic and activation parameters of this decomposition (high negative values of entropy of activation), considerable effects of substituents, dependence of the decomposition rate on the solvent polarity and the absence of the effect of the radical inhibitor (ionol) on the decomposition kinetics correlate with the predominantly molecular (> 90%) decomposition mechanism of silyl hydrotrioxides.

Table 13. Kinetic parameters of the thermal decomposition of hydrotrioxides.

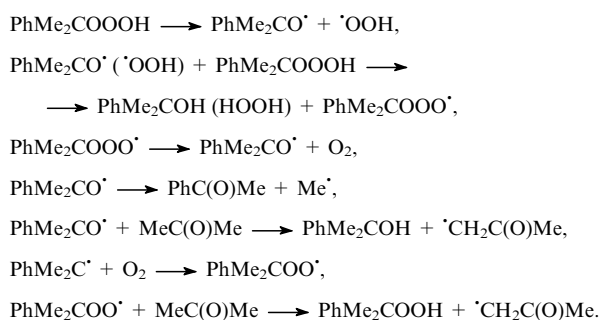
Hydrotrioxide	Solvent	T /°C	$\log A$ (s ⁻¹)	E_a /kJ mol ⁻¹	Ref.
Me ₂ C(OMe)OOOH	RH	-38 to -9	11.5	69.5	106
PhMeC(OMe)OOOH	Me ₂ CO	-30 to -10	16.0	83.3	103
Me ₂ C(OPr ⁱ)OOOH	RH	-50 to 30	11.0	67.8	101
MeC(OMe) ₂ OOOH	RH	-20 to -10	15.6	86.6	102
MeC(OEt) ₂ OOOH	RH	-50 to -10	18.2	95.4	107
MeCH(OH)OOOH	RH	-70 to -30	3.08	29.3	108
Me ₂ C(OH)OOOH	RH	-30 to 8	7.93	56.1	105
PhMeC(OH)OOOH	Me ₂ CO	-35 to -15	13.4	70.7	103
Ph ₃ COOH	CH ₂ Cl ₂	-2 to 20	9.0	55.6	54
EtMe ₂ COOOH	CH ₂ Cl ₂	7 to 27	11.5	77.8	54
PhMe ₂ SiOOOH	(CD ₃) ₂ CO	-60 to -20	5.5	39.7	104
Bu ₃ SiOOOH	RH	-70 to -50	6.84	25.1	109
HOOOH	(CD ₃) ₂ CO	-50 to 10	6.1	46.0	110

Note. RH is a starting compound used for the preparation of the corresponding hydrotrioxide.

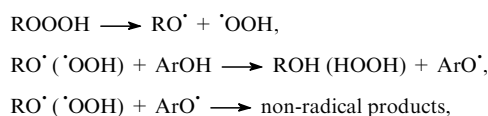


B is a base.

The decomposition of ROOOH induced by free radicals (route *b*) is especially well pronounced in the case of cumyl hydrotrioxide.^{111,112} The thermal decomposition of this compound in acetone ($E_a = 66.9 \pm 0.4 \text{ kJ mol}^{-1}$; $\log A = 10.4 \pm 0.1$) is significantly retarded in the presence of ionol. The activation parameters of the reaction ($E_a = 100.0 \pm 0.4 \text{ kJ mol}^{-1}$; $\log A = 16.4 \pm 0.1$) change under these conditions. In the absence of the inhibitor, the reaction products are dimethylphenylmethanol (the main product), acetophenone and isopropylphenyl hydroperoxide. The decomposition occurs in accordance with the following scheme:

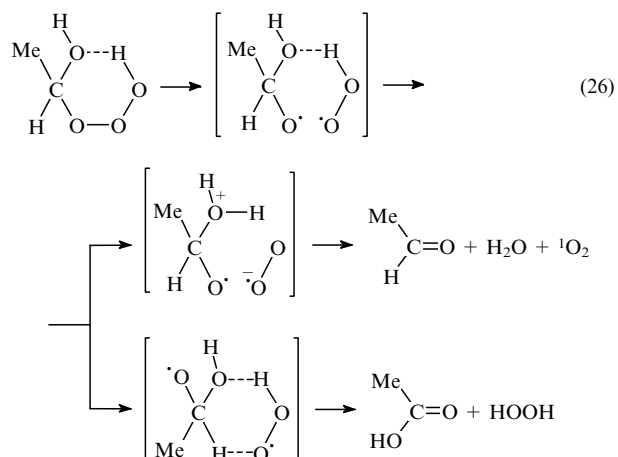
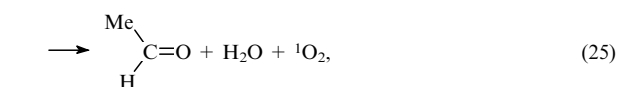
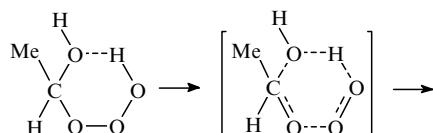


In the presence of ionol (ArOH), the induced decomposition is suppressed and dimethylphenylmethanol is formed as the only organic reaction product.^{111,112}



R = PhMe₂C.

Intramolecular hydrogen bonds can be formed in hydrotrioxides that are derivatives of alcohols, esters and acetals containing an additional oxygen atom at the α -C atom. For these compounds, the molecular mechanism for the decomposition [reaction (25)] is feasible.¹¹³ However, the experimental data altogether are more consistent with the radical mechanism of ROOOH decomposition; its first step includes the homolysis of the RO—OOH bond [reaction (26)] (the cleavage of ROOOH was demonstrated for α -hydrotrioxyethanol).



Self-association of ROOOH and the formation of intermolecular hydrogen bonds are responsible for the low exit of the radicals from the solvent cage.^{114,115} The main factors determining the direction of decomposition of ROOOH are as follows:¹⁰⁰

1. The nature of the atom bound to the hydrotrioxide group. The polarity of the X—O bond in the hydrotrioxide R¹R²R³XOOOH is the higher, the greater is the difference between the electronegativities of X and O atoms. It may therefore be expected that in the case of silyl hydrotrioxides (X = Si) the contribution of the molecular route will be greater than in the case of C-hydrotrioxides.

2. Temperature. Hydrotrioxides are typical peroxide compounds. An increase in temperature determines the relative increase in the proportion of radical processes characterised by higher values of activation energies and preexponential factors. At low temperatures, polar rearrangements without formation of radical intermediates are more probable.

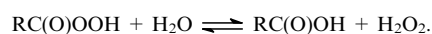
3. Solvent. Polar solvents accelerate molecular decomposition of ROOOH, whereas the homolysis of the O—O bond is less dependent on the nature of the solvent.

4. Presence of an oxygen atom in the α -position with respect to the hydrotrioxide group. Such hydrotrioxides are characterised by the formation of an intramolecular hydrogen bond. Their decomposition occurs by a non-chain radical route.

VIII. Acyl peroxides

1. Peroxy acids

Peroxy carboxylic acids RC(O)OOH possess high oxidative properties and low thermal stabilities.^{6,116} Diverse reactions involving peroxy acids occur in solution and thus complicate the thermolysis itself. For example, hydrolysis in aqueous solutions is catalysed by mineral acids:

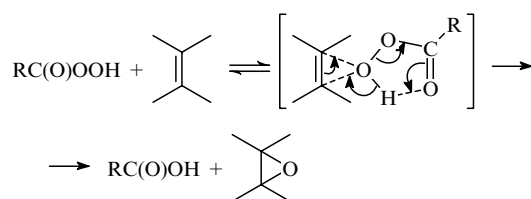


The non-catalytic decomposition of aliphatic and aromatic peroxy acids in aqueous solutions is second order with respect to the peroxy acid:^{117,118}

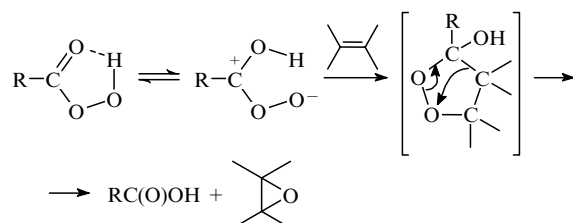
$$\frac{d[\text{RC(O)OOH}]}{dt} = k_{\text{eff}}[\text{RC(O)OOH}]^2.$$

The dependence of k_{eff} on the pH of the medium is described by a curve with a maximum at $\text{pH} \approx \text{pK}_a$ of the peroxy acid.⁶

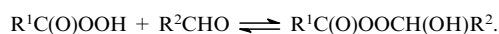
Reactions of alkenes with peroxy acids yield epoxides.^{119,120}



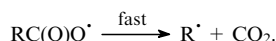
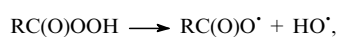
In addition to the cyclic concerted epoxidation mechanism, the following scheme for the 1,3-dipolar cycloaddition has been proposed:¹²¹



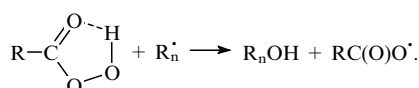
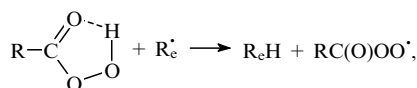
The reversible reaction of peroxy acids with aldehydes yields 1-hydroxyperoxides:



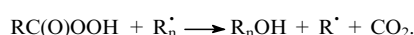
The kinetic regularities of the thermolysis of peroxy acids depend on the reaction conditions. According to the published data,^{122, 123} the thermolysis of peroxy acids in solutions occurs by a radical mechanism:



A significant contribution to the thermolysis of peroxy acids is made by induced decomposition steps:



Oxygen-containing electrophilic radicals $\text{R}_e^\bullet$ attack the hydrogen atom, but do not react with the O—O bond. This reaction yields acylperoxy radicals. Nucleophilic radicals $\text{R}_n^\bullet$ (mainly, alkyl radicals) attack the peroxide group to give alcohols R_nOH . The presence or the absence of oxygen in the solution is the crucial factor which determines the route of radical decomposition of peroxy acids. In the presence of O_2 , nucleophilic radicals $\text{R}_n^\bullet$ are converted into electrophilic radicals $\text{R}_n\text{OO}^\bullet$. In the absence of oxygen, nucleophilic radicals $\text{R}_n^\bullet$ react with the solvent (provided that the latter acts as a donor of hydrogen atoms) to give radicals $\text{Sol}^\bullet$ or with a peroxy acid to give an alcohol R_nOH :



Radicals $\text{Sol}^\bullet$ react in a similar way.

Table 14. Thermolysis of the aliphatic peroxy acids RC(O)OOH in methanol at 25 °C.¹²⁴

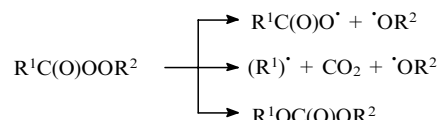
R	$10^5 k_1 / \text{s}^{-1}$	R	$10^5 k_1 / \text{s}^{-1}$
n-C ₇ H ₁₅	1.75	n-C ₁₁ H ₂₃	2.35
n-C ₈ H ₁₇	2.23	n-C ₁₂ H ₂₅	1.75
n-C ₉ H ₁₉	2.93	n-C ₁₃ H ₂₇	1.75
n-C ₁₀ H ₂₁	1.60		

The thermal stabilities of peroxy acids also depend on the nature of the acid. The data illustrating the dependence of decomposition rate constants of peroxy acids on the length of the aliphatic chain are listed in Table 14.¹²⁴

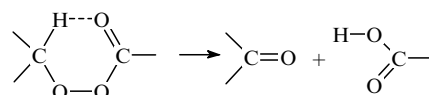
2. Peroxy esters and peroxy carbonates

Thermolysis of peroxy esters has been discussed in several reviews.^{125–130} The main peculiarities of their decomposition mechanisms are related to asymmetry and the presence of an acyl group, which favour competition between the homolytic and heterolytic decomposition routes and their rearrangements.

Depending on the structure of peroxy esters, their thermolysis involves the homolysis of one or two bonds simultaneously. Peroxy esters can also undergo rearrangements.



The presence of α -hydrogen atoms favours the formation of a ketone and a carboxylic acid as a result of cyclic redistribution of the bonds.



Bartlett¹³⁰ proposed the classification of the peroxy esters $\text{R}^1\text{C(O)OOR}^2$ into two groups according to the mechanism of their thermal decomposition. In peroxy esters of the first group, the radical R^1 cannot exist in the form of a relatively stable free radical, whereas in peroxy esters of the second group the radicals R^1 can be stabilised due to delocalisation of the unpaired electron.

To the first type one may assign such peroxy esters as *tert*-butyl peroxyacetate and peroxybenzoate. The second group includes, in particular, *tert*-butyl peroxyphenyl acetate and its derivatives along with fairly unstable peroxy esters with $\text{R}^1 = \text{Ph}_3\text{C}$. Peroxy esters of the second group decompose much faster than their first-group analogues; their thermolysis is usually accompanied by simultaneous cleavage of two bonds, *viz.*, O—O and R—C. The decomposition rate of peroxy esters is usually the lower, the stronger is the starting carboxylic acid.

Denisov^{131, 132} and Pokidova¹³³ used the semi-empirical parabolic model of a bimolecular reaction modified for the calculation of kinetic and thermodynamic parameters of decomposition of molecules into radicals with simultaneous cleavage of several bonds for the determination of the corresponding parameters for a series of peroxy esters that dissociate presumably with simultaneous cleavage of R—C and O—O bonds. It was found also that with regard to the structure of the reaction centre, concerted decomposition is similar to addition reactions of carbon-centred radicals to the carbonyl group and of oxygen-centred radicals to alkenes.

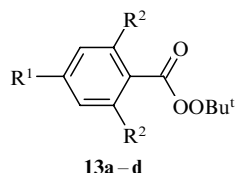
A comparison of decomposition rates of dialkyl peroxides, peroxy esters and diacyl peroxides revealed that the presence of a carbonyl group at the α -carbon atom favours the cleavage of the O—O bond due to the conjugation of the free valence formed with the C=O group. On the whole, the effects of the substituents in the starting peroxide are rather diverse. The introduction of vinyl, phenyl and alkyl groups into the acyl fragment sharply increases the decomposition rate. Besides the inductive effect of substituents, this entails changes in the decomposition mechanism: fragmentation with simultaneous cleavage of two bonds caused by the weakening of the R—C(O) bond even in the transition state and stabilisation of the radical R^1 due to mesomeric and hyperconjugation effects of the substituents takes place instead of the cleavage of one O—O bond. The dependence of the homolytic decomposition of the peroxy esters $\text{R}^1\text{R}^2\text{R}^3\text{CC(O)OOBu}^1$ on the size of the alkyl substituents can be illustrated by the data

Table 15. Kinetic parameters of the thermolysis of $R^1R^2R^3CC(O)OObu^t$ in ethylbenzene at 60 °C.¹³⁴

R^1	R^2	R^3	k_1 (relative)
Me	Me	Me	1.0
Me	Me	Et	1.29
Me	Me	n-C ₈ H ₁₇	1.73
Me	Me	Bu ⁱ	2.30
Et	Et	Et	3.19
Et	Et	Pr ⁱ	6.50
Me	Me	Bu ^t	3.40
Me	Me	Bu ^t CH ₂	2.60
Pr ⁱ	Pr ⁱ	Pr ⁱ	32

presented in Table 15.¹³⁴ Here, both the steric strain created in a peroxy ester by the substituents R^1 – R^3 and the inductive effects must be taken into consideration.

The introduction of *ortho*-substituents into the phenyl group of peroxybenzoates **13** leads to destabilisation of the ground state due to rotation of the carboxy group and its exit from the conjugation with the aromatic ring. As a result, the decomposition rates of peroxides **13c,d** are increased dramatically (Table 16).¹³⁵

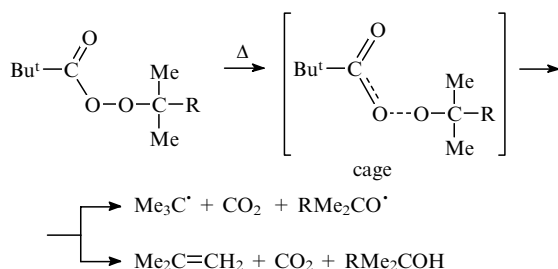


$R^1 = R^2 = H$ (a); $R^1 = Me$; $R^2 = H$ (b), Me (c); $R^1 = R^2 = Bu^t$ (d).

Table 16. Kinetic and thermodynamic parameters of the thermal decomposition of peroxybenzoates **13a–d**.¹³⁵

Peroxy 13	R^1	R^2	k_1/s^{-1} (at 100 °C in cumene)	$\Delta H^\ddagger$ /kJ mol ⁻¹
a	H	H	9.7×10^{-6}	142.3
b	Me	H	1.2×10^{-5}	134.7
c	Me	Me	1.1×10^{-4}	133.5
d	Bu ^t	Bu ^t	2.8×10^{-4}	137.7

It is of note that the decomposition of peroxyacetate occurs several times more slowly than that of peroxybenzoates. The thermolysis of *tert*-alkyl peroxy-pivalates in the solvent cage^{136–138} affords equimolar amounts of *tert*-butyl and *tert*-alkoxyl radicals as a result of concerted cleavage of two bonds.



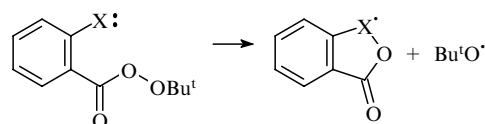
$R = Me, Et, Pr, Pr^i, Bu^i, PhCH_2$.

The reaction products correspond to nearly quantitative β -dissociation into alkyl and alkoxy radicals and CO₂.

The transition from the simple cleavage of the O–O bond to the decomposition with simultaneous cleavage of the O–O bond and decarboxylation results in a simultaneous decrease in the enthalpy and entropy of activation.

In the case of thermolysis of peroxy esters containing an ¹⁸O-labelled carbonyl group, the reverse recombination of the RC(O)O· radical in the solvent cage leads to the averaging of the distribution of the label between the carbonyl and peroxide oxygen atoms. An increase in the solvent viscosity favours reverse recombination and increases the degree of averaging of the label content. The secondary isotope effect (k^H/k^D) observed in the thermal decomposition of *tert*-butyl peroxyacetate is equal to unity,¹³⁹ which points to a non-synchronous cleavage of the bonds in its decomposition. At the same time, the magnitude of the isotope effect for *tert*-butyl *p*-methylphenylperoxyacetate and its derivatives markedly exceeds unity [1.03–1.06 per one H(D) atom], which unequivocally testifies to a synchronous mechanism of their decomposition.^{139–142}

The effects of substituents able to interact directly with the peroxide group and thus accelerate the homolysis of the peroxide bond are presented in Table 17.¹⁴³ As can be seen from these data, the presence of an unshared electron pair in the groups X in the *ortho*-position of the benzene rings of *tert*-butyl peroxybenzoates favours the formation of relatively stable radicals due to the cleavage of the O–O bond.



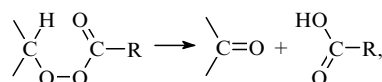
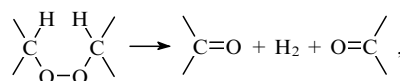
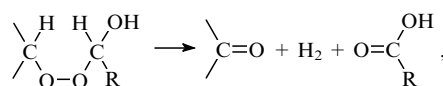
This effect of the substituent was termed by Martin¹⁴³ as ‘anchimeric acceleration’. Presumably, such substituents have a similar effect on the decomposition of diacyl peroxides.

Table 17. Kinetic and thermodynamic parameters of the decomposition of *tert*-butyl *o*-X-peroxybenzoates in chlorobenzene.¹⁴³

X	k (relative) at 60 °C	$\Delta H^\ddagger$ /kJ mol ⁻¹	$\Delta S^\ddagger$ /J mol ⁻¹ K ⁻¹
PhS	2.8×10^4	96.2	–14.2
MeS	1.8×10^4	94.6	–23.0
PhS(O)	73	12.3	18.8
Ph ₂ C=CH	67	110	–20.9
I	54	117	–2.9
Bu ^t	3.8	143.1	52.3
MeS(O) ₂	0.4 ^a	159	39.7
PhC≡C	1.8	148.1	62.8
H	1.0	142.7	41.8

^a With respect to H at 120 °C.

The presence of a C–H bond at the α -carbon atom enables the decomposition of peroxy esters according to a scheme acceptable for various classes of peroxides.¹⁴⁴



$R = H, Alk, Ar$.

In solution, the decomposition of peroxy esters by this concerted mechanism yields carboxylic acids and aldehydes or ketones.

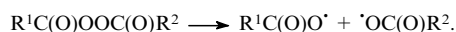
The thermolysis of dicyclohexyl peroxydicarbonate in a pressure range from 0.1 to 500 MPa^{147, 148} revealed that its first step includes the cleavage of the O—O bond and the formation of oxycarboxy radicals. The volume effects of activation in benzene, toluene and acetonitrile are equally high ($11 \pm 0.5 \text{ cm}^3 \text{ mol}^{-1}$), which is attributed to the changes in the ratios of diffusion and recombination reactions occurring in the solvent cage and is regarded as evidence in favour of the cleavage of one O—O bond in the first decomposition step.

For a detailed description of peroxycarbonate thermolysis see Refs 10 and 149.

3. Diacyl peroxides

Decomposition of diacyl peroxides upon heating in solution was the subject of extensive studies which allowed identification of reaction products and elucidation of mechanisms and kinetic regularities of this process. The thermolysis of such peroxides occurs by two main competing routes with radical and non-radical mechanisms.

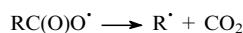
The homolytic decomposition begins with the cleavage of the O—O bond:



The solvent cage retains the radicals in the form of a radical pair and thus favours their recombination. Therefore, in the case of incomplete decomposition of a peroxide containing an isotopically labelled carbonyl oxygen the distribution of the latter will be averaged as a result of intraradical exchange:



This is followed by decarboxylation



and further reactions of the radicals with themselves and the solvent.

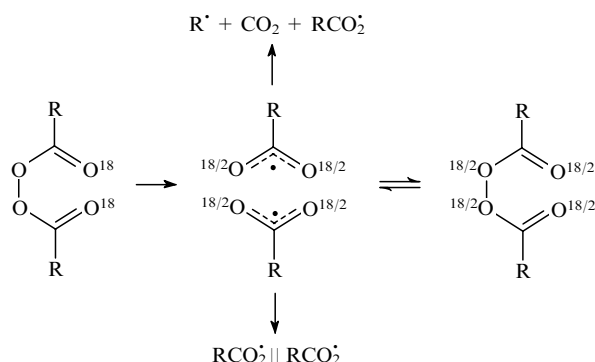
The averaging of the ^{18}O label over the carbonyl oxygen atom of the starting diacyl peroxide upon its partial thermolysis provides direct evidence for the initial formation of a contact radical pair. This is confirmed by the following facts:^{150, 151}

1. The thermolysis rate of cyclopropanecarbonyl peroxide decreases with an increase in the solvent viscosity, whereas the averaging rate of ^{18}O diminishes to a much lesser degree.

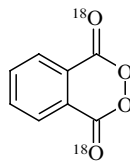
2. The enthalpy of activation of the decomposition of this peroxide exceeds the enthalpy of activation of the averaging of the ^{18}O content in CCl_4 by 8.4–11.7 kJ mol⁻¹. The entropy of activation of the averaging of ^{18}O is characterised by a small, although positive value in contrast to high negative values of entropies of activation of ordinary concerted sigmatropic rearrangements.

3. Substitution of the phenyl group for the cyclopropyl group leads to a decrease in the averaging rate of the label.

Hence, the mechanism of averaging of the isotopic label fits into the following scheme:



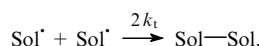
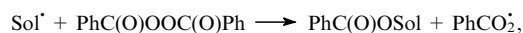
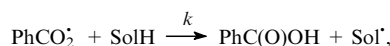
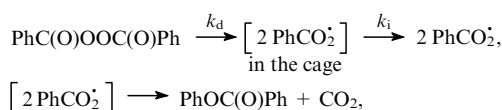
It is interesting to note that in the cyclic phthaloyl peroxide



the averaging of the isotopic label in solution at 80 °C occurs 40 times faster than its decomposition.¹⁵¹

Quantum-chemical studies (B3LYP calculations) of formyl peroxide¹⁵² confirmed the averaging mechanism involving the formation of a σ -acyloxy radical pair.

A high contribution of induced decomposition of acyl peroxides to the overall rate of their thermolysis in solution is yet another characteristic feature.^{153–155} For example, induced decomposition of benzoyl peroxide includes the following steps:



The corresponding expression for the reaction rate appears as:

$$W = k_d[\text{PhC}(\text{O})\text{OOC}(\text{O})\text{Ph}] + k_{\text{ind}}[\text{PhC}(\text{O})\text{OOC}(\text{O})\text{Ph}]^{3/2},$$

where $k_{\text{ind}} = k k_i^{1/2} (2k_t)^{-1/2}$ and $k_i = 2ek_d$, e is the proportion of radicals that exit the cage into the bulk.

The kinetic parameters of reactions of the radicals $\text{Me}^\bullet$, $(\text{Bu}^\bullet)$ and $\text{PhCH}_2^\bullet$ with various peroxides were calculated¹⁵⁴ using a parabolic model for bimolecular reactions (Table 20).

The rate of chain decomposition of benzoyl peroxide in the alcohols $\text{R}^1\text{R}^2\text{CHOH}$ is increased by an order of magnitude due to the reaction of the radicals $\text{R}^1\text{R}^2\text{C}^\bullet\text{OH}$ with the peroxide. This reaction was also studied using the aforementioned model.^{155, 156}

The ester $\text{RC}(\text{O})\text{OR}$ is formed from acetyl and benzoyl peroxides as a result of recombination of $\text{R}^\bullet$ and $\text{RC}(\text{O})\text{O}^\bullet$.

The volume of activation $\Delta V^\ddagger$, i.e., the change in the volume of a molecule upon the formation of an activated complex, in the cleavage of one bond approximates to 10 cm³ mol⁻¹, whereas that in the concerted cleavage of two bonds is 2–5 cm³ mol⁻¹ (see Ref. 11). The $\Delta V^\ddagger$ values for the thermolysis of diacyl peroxides without rearrangement vary from 2 to 5 cm³ mol⁻¹. The volumes of activation for the thermolysis of the following compounds are listed in the table below:^{157, 158}

Peroxide	$\Delta V^\ddagger / \text{cm}^3 \text{ mol}^{-1}$
Bis(3,5,5-trimethylhexanoyl) peroxide	2–3
Diocanoyl peroxide	2–3
Dibenzoyl peroxide	1–2

Asymmetric structures of diacyl peroxides and the use of polar solvents favour their decomposition into esters by non-radical routes involving both ionic and concerted mechanisms.

The formation of an ester $\text{ArC}(\text{O})\text{OC}(\text{O})\text{OAlk}$ in the thermolysis of $\text{ArC}(\text{O})\text{OOC}(\text{O})\text{Alk}$ as a result of a concerted rearrangement concomitant with a carboxy inversion was first reported by Leffler.^{159, 160} Here, the alkyl group migrates to the electron-deficient oxygen atom resulting in a nearly complete inversion of the configuration of the migrating group.

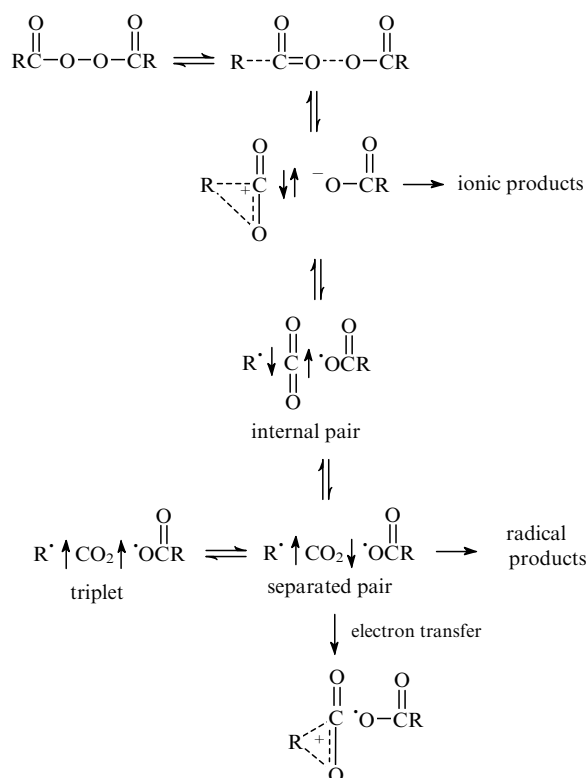
Table 20. Kinetic parameters of the bimolecular reactions of the radicals $\text{Me}^\bullet$, $(\text{Bu}^\text{t})^\bullet$ and $\text{PhCH}_2^\bullet$ with some peroxides at 80 °C.

Peroxide	$E_a/\text{kJ mol}^{-1}$			$k_1/\text{litre mol}^{-1} \text{s}^{-1}$		
	$\text{Me}^\bullet$	$(\text{Bu}^\text{t})^\bullet$	$\text{PhCH}_2^\bullet$	$\text{Me}^\bullet$	$(\text{Bu}^\text{t})^\bullet$	$\text{PhCH}_2^\bullet$
H_2O_2	36.7	33.6	48.6	1.51×10^4	1.31×10^4	3.14×10^2
$\text{Bu}^\text{t}\text{OOH}$	27.5	24.8	37.9	7.76×10^4	1.96×10^5	2.17×10^3
$[\text{MeC}(\text{O})\text{O}]_2$	37.3	39.8	48.0	5.40×10^3	2.40×10^3	1.40×10^2
$[\text{PhC}(\text{O})\text{O}]_2$	38.7	41.1	49.6	3.30×10^3	1.50×10^3	78.0
$\text{Bu}^\text{t}\text{OOBu}^\text{t}$	50	56	—	68	8.6	—

In this case, the redistribution of the ^{18}O label between the carbonyl and the peroxide oxygen atoms is either insignificant or altogether absent.^{161–170} The carboxy inversion is enhanced in the presence of Brønsted and Lewis acids.

Carboxy inversion is characterised by higher negative volume of activation and lower energy and entropy of activation than an ordinary radical decay.¹⁶⁷ The ionic type of this reaction was confirmed by a strong dependence of the decomposition rate on the changes in the electron-donor or electron-withdrawing properties of the aryl and alkyl groups.

The formation of compound RSol in the reaction of the radicals with the solvent and the formation of the recombination and disproportionation products ArR , RH and $\text{ArC}(\text{O})\text{OR}$ is yet another characteristic feature of the decomposition route of diacyl peroxides. An analysis of kinetics and compositions of decomposition products led Walling to suggest^{165–167} that both the radical and ionic pathways are realised through the same rate-limiting step in accordance with the following scheme:



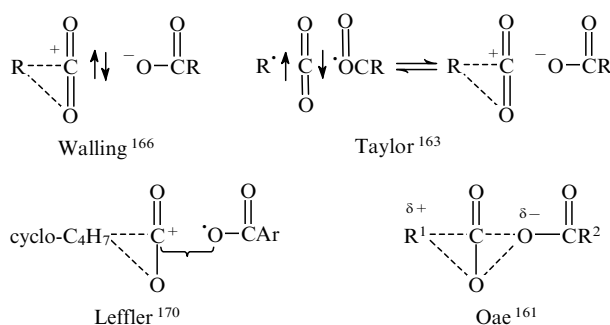
This scheme includes the interaction and disproportionation of radicals. Supporting evidence for this mechanism was obtained in the studies of chemically induced dynamic nuclear polarisation (CIDNP) in the rearrangement products formed upon decomposition of *tert*-butylacetyl-*m*-chlorobenzoyl peroxide.

The formation of an ester from diacyl peroxide ($\text{PhMe}_2\text{CCH}_2\cdot\text{COO}$)₂ as a result of rearrangement on silica gel was also attributed to the electron transfer in the neophylcarbonyloxy radical pair $\{\text{PhMe}_2\text{CCH}_2\text{C}(\text{O})\text{O}^\bullet \cdot^\bullet\text{OC}(\text{O})\text{CH}_2\text{CMe}_2\text{Ph}\}$.¹⁷¹ If

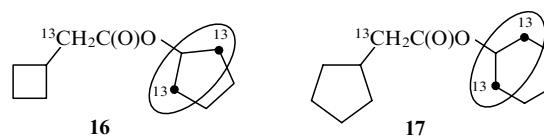
the reaction is carried out on silica gel, the reaction rate increases considerably in comparison with the reaction carried out in solution. The decomposition products of $(\text{PhMe}_2\text{CCH}_2\text{COO})_2$ obtained in solution and on the surface of silica gel are also different. In the latter case, alkanes are not formed.

According to Taylor,¹⁶³ the electron transfer mechanism cannot be used for interpreting the results of thermal decomposition of cyclopropylacetyl cyclobutanecarbonyl peroxide and 4-pentanoyl *m*-chlorobenzoyl peroxide. Evidence in favour of the formation of an ion pair-like intermediate in the decomposition of a peroxide containing an R group able to form a stable cation was obtained.¹⁶⁴ An argument against the formation of a radical pair is the low value of CIDNP or its complete absence from the systems under study. However, some authors¹⁶² made reference to the difficulty in detecting polarised signals in complex samples and the strong dependence of experimental values of CIDNP on the relative rate of the reaction and on spin relaxation.

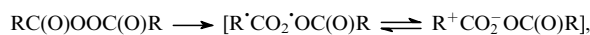
The following structures have been proposed for the intermediate species formed in the first step by different groups of investigators:



Special mention should be made of the studies^{172–174} of chemical polarisation of nuclei in the decomposition products formed in the thermolysis of cycloalkanoyl and cycloalkylacetyl peroxides in benzene and a benzene- CHBr_3 mixture; the data obtained testify to a radical mechanism of their formation. However, chemical polarisation of nuclei takes place only in those cases where relatively long-living radicals (methyl, cyclopropyl) or radicals stabilised by the π -bond are formed. No CIDNP was observed in other peroxy esters, which points either to a non-radical decomposition mechanism or the exclusive formation of short-living (less than 10^{-10} s) radicals in the solvent cage. The thermolysis of cyclobutyl and cyclopentylacetyl peroxides yields esters **16** and **17**, respectively. ^{13}C labelling studies have shown that in this case we deal with a skeletal rearrangement in the absence of hydride transitions.



The absence of hydride transitions points to the formation of an ion-radical pair in the transition state where the carbocation-like species undergo skeletal rearrangement:

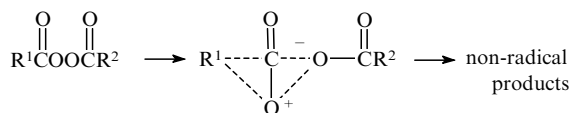


R = cyclo-C₄H₇CH₂, cyclo-C₅H₉CH₂.

However, the energies and lifetimes of these species are not high enough for hydride transitions to occur.

Studies of a series of asymmetrical diacyl peroxides^{175–177} have shown that in the case of electron-donor and/or polar substituents thermolysis in nonpolar solvents proceeds by a radical route and yields acyl alkyl carbonates, alkenes, carboxylic acids and/or esters.

The proportion of heterolytic processes increases with stabilisation of the negative charge formed in the transition state.



The contribution of the homolytic process to the thermal decomposition of diacyl peroxides shows a good correlation with the energy of dissociation of the R–H bond, which characterises the stability of the radical R.

Studies on chemical polarisation of nuclei ¹H and ¹³C in the thermolysis products of these peroxides in CCl₄ revealed¹⁷⁸ that the contribution of secondary processes occurring outside the solvent cage diminishes with an increase in temperature.

IX. Sulfonyl peroxides

1. Alkanesulfonylperoxy acids

The thermal decomposition of the decanesulfonylperoxy acid C₁₀H₂₁SO₂OOH (R¹SO₂OOH) in *n*-decane (R²H) in an atmosphere of argon results in quantitative yields of C₁₀H₂₁SO₂OH (R¹SO₂OH) and a relatively high yield of the alcohols C₁₀H₂₁OH (R²OH) (ketones and H₂O are formed in trace amounts).¹⁷⁹

According to data from gas chromatography/mass spectrometry, the decomposition of decanesulfonylperoxy acid yields a mixture of primary and secondary alcohols. *n*-Decanol is not formed in noticeable amounts, whereas the ratio of decan-2-, -3-, -4- and -5-ols formed is close to the statistical value (1.2 : 1.0 : 1.2 : 1.15). With an increase in the initial concentration (*c*₀) of the peroxy acid, the total yield of *sec*-decanols with respect to the peroxy acid decreases (Table 21). The yield of the alcohols does not virtually depend on the nature of the bubbling gas (O₂ or Ar). This suggests that sulfonylperoxy acids are effective reagents for oxidative functionalisation of even non-activated C–H bonds of organic compounds.¹⁸⁰

Table 21. Yields of the secondary alcohols in the decomposition of decanesulfonylperoxy acid in oxygen-saturated *n*-decane at 50 °C.

10 ² <i>c</i> ₀ /mol litre ^{−1}	10 ² Δ <i>c</i> /mol litre ^{−1}	10 ² [sec-C ₁₀ H ₂₁ OH] /mol litre ^{−1}	[sec-C ₁₀ H ₂₁ OH]/Δ <i>c</i> (%)
0.82	0.77	0.58	75
2.6	2.6	1.5	57
6.5	6.5	2.3	35
7.6	7.5	2.0	27
11.0	11.0	2.4	22

Ketones are accumulated in much smaller amounts in comparison with alcohols (~0.6%–0.7% of the alcohol yield) owing to their ability to react fast with the peroxy acid. For example, the effective rate constant for the reaction of decanesulfonylperoxy acid with ethyl methyl ketone in *n*-decane at 50 °C is 0.5 litre mol^{−1} s^{−1} (see Ref. 181). Indeed, decanesulfonylperoxy

acid is an extremely potent oxidant of ketones in the Baeyer–Villiger reaction.^{182–184}

The thermolysis of decanesulfonylperoxy acid is complicated by its reaction with the solvent and homoassociation. As a consequence, the rate of this thermal decomposition depends on reaction conditions, in the first place, on the concentration of the sulfonylperoxy acid used. For this very reason, the kinetics of thermal decomposition of the sulfonylperoxy acid was formally characterised by an effective first-order rate constant.¹⁷⁹ The value of *k*_{eff} increases with an increase in the temperature and initial concentration of the peroxy acid (*c*₀).

Substitution of CCl₄ for *n*-decane leads to a significant decrease in the decomposition rate. Thus at 70 °C and *c*₀ = 0.07 mol litre^{−1} the half-lives of decanesulfonylperoxy acid in *n*-decane and CCl₄ are 4 and 33 min, respectively.

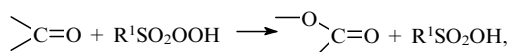
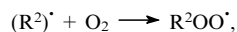
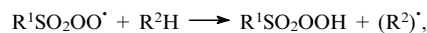
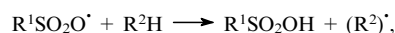
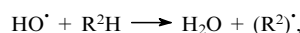
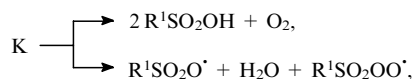
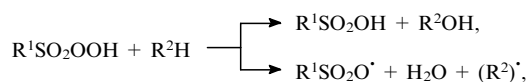
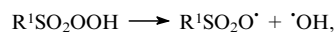
Some experimental results suggest the formation of free radicals in the thermolysis of sulfonylperoxy acids.

1. The thermal decomposition of an R¹SO₂OOH–R²H–O₂ system is accompanied by consumption of oxygen.

2. The decomposition of R¹SO₂OOH in an atmosphere of argon proceeds much faster than that in the presence of oxygen. For example, at *c*₀ = 9 × 10^{−3} mol litre^{−1} the initial decomposition rates of sulfonylperoxy acid in an atmosphere of O₂ and Ar are 1.3 × 10^{−5} and 4 × 10^{−6} s^{−1}, respectively. In an atmosphere of argon, the reaction rate decreases with time; for the 60% conversion of R¹SO₂OOH in Ar and O₂, the decomposition rates are levelled off.

3. The decomposition rate of peroxy acid in an R¹SO₂OOH–R²H–Ar system in the presence of the free radical scavenger 2,2,6,6-tetramethyl-4-hydroxypiperidin-*N*-oxyl is essentially the same as that in the R¹SO₂OOH–R²H–O₂ system.

Based on the data obtained, the following mechanism has been proposed for the thermal decomposition of the alkanesulfonylperoxy acids R¹SO₂OOH in R²H in an atmosphere of O₂:^{179, 181}



where C is a complex comprising two sulfonylperoxy acid molecules.

With regard to their oxidative capacities, alkanesulfonylperoxy acids are in no way inferior to such a potent oxidant as trifluoroperoxyacetic acid, but even surpass it in many aspects.

2. Acetyl cyclohexylsulfonyl peroxide

Of prime interest among other representatives of sulfonylperoxy acid derivatives is acetyl cyclohexylsulfonyl peroxide [cyclo-C₆H₁₁SO₂OOC(O)Me (ACSP)] which has found wide industrial application.

A significant contribution of radical processes to the thermolysis of ACSP can be illustrated by the chemiluminescence (CL)

observed during its decomposition.¹⁸⁵ However, whereas in the presence of O₂ the spectral pattern of CL (*i.e.*, the maxima at 400–440 and 500–540 nm) indicates the formation of excited triplet carbonyl groups as CL emitters, in an inert atmosphere the situation is less apparent. The intensity of CL decreases with ACSP consumption. In addition to a distinct maximum at 580–600 nm, the CL spectrum contains two signals of lower intensities with maxima around 650 and 690 nm. The intensity of CL decreases after addition of alkyl radical traps to ACSP. Presumably, the radiation emitter is formed in reactions involving alkyl radicals.

The kinetics of thermal decomposition of ACSP in an atmosphere of O₂ obeys the first-order kinetic law.¹⁸⁶ The activation parameters of the thermal decomposition of ACSP in various solvents are listed in Table 22.

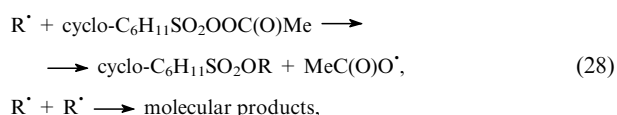
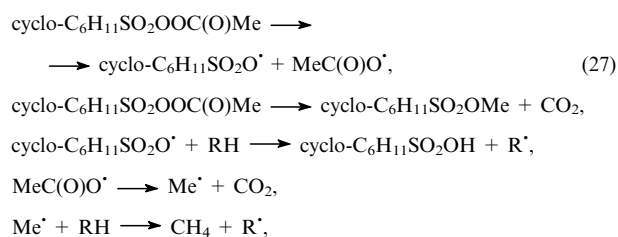
Table 22. Effect of the solvent on the activation parameters of the decomposition of acetyl cyclohexylsulfonyl peroxide.¹⁸⁶

Solvent	log <i>A</i> (s ⁻¹)	<i>E_a</i> /kJ mol ⁻¹
n-C ₁₀ H ₂₂	16.2	123
cyclo-C ₆ H ₁₂	14.0	101
CCl ₄	16.5	127
PhH	14.5	114
PhMe	13.8	108
PhEt	13.1	104
PhPr ⁱ	14.7	115
MeCN	15.8	126
EtOH	12.5	103
Pr ⁱ OH	14.0	113

In argon, the kinetics of ACSP thermolysis is different. The kinetic order of this reaction with respect to peroxide increases to 1.5. Thus in n-decane:

$$\log k_{\text{ind}} = (13.2 \pm 0.5) - (93 \pm 3)/2.3 RT \text{ (litre}^{1/2} \text{ mol}^{-1/2} \text{ s}^{-1}\text{)}.$$

An analysis of the whole body of experimental data has made it possible to propose the following mechanism for ACSP decomposition:¹⁸⁷

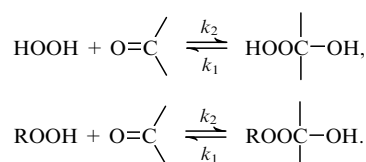


where RH is n-decane.

Reaction (28) is the limiting step in the chain process. Oxygen inhibits induced chain decomposition of ACSP due to rapid oxidation of alkyl radicals to ROO[•]. Peroxy radicals are inactive with respect to ACSP and undergo recombination resulting in chain termination. The following expression was proposed for the rate constant of induced decomposition of ACSP in n-decane [reaction (28)]: $\log k = 10.8 - 36/2.3 RT$ (litre mol⁻¹ s⁻¹). For the rate constant for the monomolecular decomposition of ACSP in C₆H₄Cl₂ [reaction (27)], $\log k = 14.5 - 115.4/2.3 RT$ s⁻¹ (the activation energy is expressed in kJ mol⁻¹).

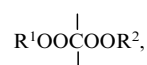
X. Peroxide derivatives of carbonyl compounds

Upon heating in neutral media, hydroxyperoxides formed in the reaction of hydrogen peroxide and hydroperoxides with carbonyl compounds easily dissociate into the original compounds.¹⁸⁸



The rate constants for the forward (*k*₂) and reverse (*k*₁) reactions are listed in Tables 23 and 24 (see Refs 39 and 188).

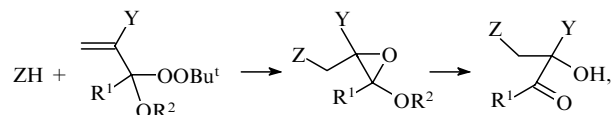
Different peroxy acetals and peroxy ketals including



and cyclic polyperoxides are formed in acidic media as a result of condensation of aldehydes or ketones with 1-hydroxyperoxides.^{188, 189}

The thermolysis of monoperoxy ketals¹⁹⁰ is characterised by the parameters listed in Table 25. Despite the large distance between the peroxide group and the substituent, the structure of the latter has a strong effect on the kinetic parameters of the thermolysis. In particular, non-valent interactions of the oxygen atoms of the substituent with the peroxide group are possible.

In the presence of an allyl substituent, the thermolysis of monoperoxy ketal occurs in accordance with the following scheme:¹⁹¹



Z = cyclo-C₆H₁₁; Y = H, Me, Ph; R¹ = H, Me; R² = Me, Et,

Table 23. Kinetic parameters of the decomposition of 1-hydroxyperoxides and their formation from hydroperoxides and aldehydes at 20 °C.

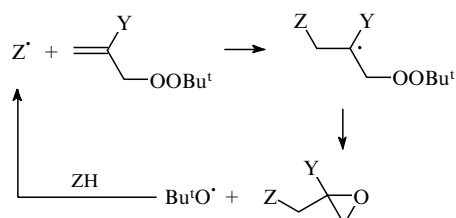
Aldehyde	Hydroperoxide	Solvent	10 ² <i>k</i> ₂ /litre mol ⁻¹ min ⁻¹	10 ² <i>k</i> ₁ /min ⁻¹	10 ² <i>K</i> /mol litre ⁻¹	<i>E_a</i> /kJ mol ⁻¹	
						<i>E</i> ₂	<i>E</i> ₁
Acetaldehyde	<i>tert</i> -butyl	CCl ₄	7	1.3	1.8	13	42
	tetralyl	CCl ₄	11	0.9	0.8	13	38
	cumyl	CCl ₄	6	1.3	2.2	17	38
	diphenylethyl	CCl ₄	3.5	1.5	4.3	17	42
	<i>tert</i> -butyl	Pr ⁿ ₂ O	0.9	0.4	4.8	25	42
	<i>tert</i> -butyl	CHCl ₃	1.7	0.8	4.7	21	46
Butyraldehyde	<i>tert</i> -butyl	CCl ₄	6	1.1	1.9	17	38
Crotonic aldehyde	<i>tert</i> -butyl	CCl ₄	0.08	5.0	6.0	—	—

Table 24. Kinetic parameters of the formation of 1-hydroxyperoxides (from tetralyl hydroperoxide and ketones) and their dissociation.

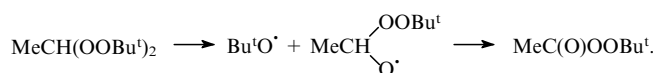
Ketone	$10k_2/\text{litre mol}^{-1} \text{ min}^{-1}$	$10^2 k_1/\text{min}^{-1}$	$10^2 K/\text{mol litre}^{-1}$	$E_a/\text{kJ mol}^{-1}$	
				E_2	E_1
Cyclohexanone	18	6	0.33	33	40
4-Methylcyclohexanone	17	7	0.41	33	40
3-Methylcyclohexanone	14	8	0.57	33	38
2-Methylcyclohexanone	3.1	11	3.5	—	—
Acetone	3.7	7	1.9	—	—
Ethyl methyl ketone	3.5	9	2.6	—	—
Isopentyl methyl ketone	2.1	9	4.3	—	—
Acetophenone		no reaction			
Benzyl ethyl ketone		no reaction			

Note. Concentrations: tetralyl hydroperoxide, 0.18 mol litre⁻¹; ketone, 0.02 mol litre⁻¹; solvent, CCl₄–tetralin (1 : 1), 20 °C.

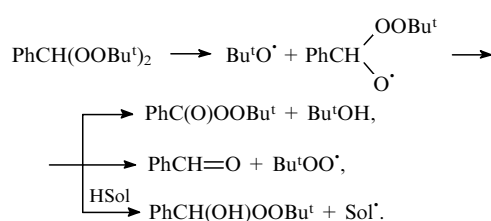
which includes the well-established reactions of induced decomposition of allyl peroxides:



The decomposition of diperoxyacetals is accompanied by the transient formation of peroxy esters¹⁹²



The decomposition of aromatic peroxy acetals occurs in accordance with the same scheme, *i.e.*, with the formation of peroxybenzoates as intermediates:¹⁹³



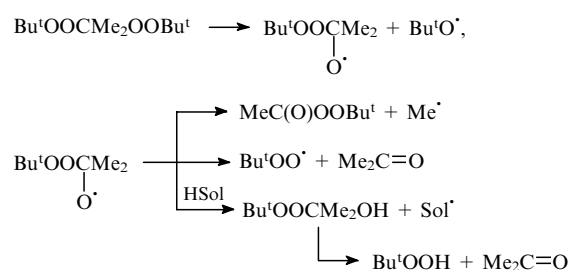
Under these conditions, the contribution of other parallel conversions of the initially formed radical increases.

The thermolysis of 2,2-bis(*tert*-butylperoxy)alkanes^{194–197} proceeds through selective cleavage of the O–O bonds rather than by a concerted mechanism. This confirms the similarity of the activation parameters of 2,2-bis(*tert*-butylperoxy)propane ($\Delta H^\ddagger = 145.6 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = 47.3 \text{ J mol}^{-1} \text{ K}^{-1}$) and di-

Table 25. Thermolysis of monoperoxy ketals $\text{RMeC}(\text{OMe})\text{OOBu}^t$ in alkylaromatic hydrocarbons.

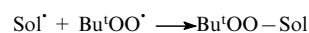
R	$-\ln k (\text{s}^{-1})$ at 20 °C	$E_a/\text{kJ mol}^{-1}$
Me	9.21	138.3
Et	8.27	128.7
Pr	8.27	131.7
Bu	8.23	135.8
Bu ⁱ	7.90	127.5
Pr ⁱ	7.07	127.1
MeOCH ₂	4.77	113.7
EtOC(O)CH ₂	9.58	143.8

tert-butyl peroxide ($\Delta H^\ddagger = 153.6 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = 48.1 \text{ J mol}^{-1} \text{ K}^{-1}$) at 90–120 °C in the absence of induced decomposition (in cumene). The products formed are consistent with the following decomposition scheme:



A high volume of activation ($\Delta V^\ddagger = 22.3 \text{ ml mol}^{-1}$ at 200 °C)¹⁹⁸ is an argument in favour of a concerted decomposition mechanism. However, at relatively high temperatures this mechanism can be different.

A method for the introduction of Bu^tOO groups into organic molecules by the thermolysis of 2,2-bis(*tert*-butylperoxy)propane has been proposed.¹⁹⁷ Diperoxy ketals that simultaneously generate the radical Bu^tO·, causing the abstraction of the active hydrogen atom from the substrate, and the radical Bu^tOO·, which undergoes recombination with the radical Sol·,



were used as sources of Bu^tOO· radicals.

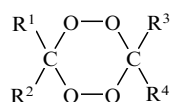
The thermolysis of 1,1-bis(*tert*-butylperoxy)cycloalkanes^{18, 199–201} in solution occurs with homolytic cleavage of one O–O bond which occurs at a much faster rate than the thermolysis of the corresponding alkyl *tert*-butyl peroxides

Table 26. Rate constants (at 110 °C) and activation parameters of the thermolysis of peroxides in cumene.²⁰¹

Peroxide	$10^5 k/\text{s}^{-1}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$	$\Delta S^\ddagger/\text{J mol}^{-1} \text{ K}^{-1}$
(CH ₂) ₄ C(OOBu ^t) ₂	21.7	33.3	11.0
(CH ₂) ₅ C(OOBu ^t) ₂	16.2	33.8	12.0
(CH ₂) ₇ C(OOBu ^t) ₂	13.6	33.8	14.4
(CH ₂) ₁₁ C(OOBu ^t) ₂	9.9	34.6	13.2
Me ₂ C(OOBu ^t) ₂	2.97	34.9	11.3
EtMeC(OOBu ^t) ₂	3.89	34.9	11.7
Bu ^t MeC(OOBu ^t) ₂	13.8	33.8	11.6
Bu ^t OOBu ^t	0.25	36.9	11.5
EtMe ₂ COOBu ^t	0.39	36.8	12.3
Pr ⁱ Me ₂ COOBu ^t	0.71	36.8	12.3

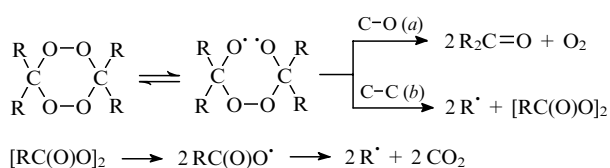
(Table 26). For cycloalkanes, the decomposition rate decreases in the following order: cyclopentane > 3,3,5-trimethylcyclohexane > cyclohexane > cyclooctane > cyclodecane. The dependence of the decomposition rate on the ring size suggests that stabilisation of the transition state due to the electron-donor effect of the cycloalkyl substituent and repulsion of free electron pairs of the oxygen atoms of the O—O group is a critical factor which determines the decomposition kinetics of geminal diperoxides.

The decomposition of cyclic diperoxides of the type



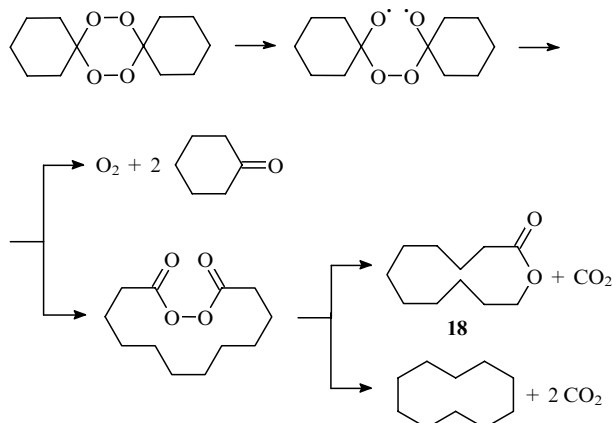
$\text{R}^{1-4} = \text{Alk, Ar}$

occurs with primary homolysis of one O—O bond with subsequent destruction of the biradical and cleavage of a C—O or a C—C bond.^{199, 202–206}



The choice of a decomposition route (*a* is the formation of ketones, *b* is the formation of hydrocarbon radicals) depends on the structure of the substituents: for $\text{R} = \text{Ar}$, the yields of ketones are 90%, whereas for $\text{R} = \text{Alk}$ they are as low as 10%–20% (in benzene) and even smaller. The higher the stability of the radical $\text{R}^\bullet$ the higher the yield of the ketone.

Cyclic diperoxides prepared from cyclohexanone undergo decomposition to give cyclohexanone and O_2 , lactone **18** and CO_2 , or cyclodecane and CO_2 .²⁰⁷



On the whole, cyclic diperoxides are more stable than their non-cyclic analogues.^{199, 207}

The generation of a biradical in the first step of the thermolysis of a cyclic diperoxide prepared from an indene derivative was confirmed by analysis of polarisation of nuclei in the decomposition products (the thermolysis of acyl peroxides, peroxy carbonates and other peroxy derivatives (see above) was studied using a similar approach).²⁰⁸

The thermolysis of cyclic triperoxides, like the thermolysis of cyclic diperoxides, begins with the formation of a radical pair which undergoes further destructive rearrangements. As a result, the kinetics of decomposition of cyclic triperoxides characterised by high degrees of conversion is first order. The kinetic data on the thermolysis of cyclic di- and triperoxides in solution are generalised in Table 27.²⁰⁹ The contribution of induced decomposition is insignificant, thus the activation parameters listed in the Table refer exclusively to the monomolecular decomposition.

Table 27. Kinetic parameters of the thermolysis of cyclic di- and triperoxides.

Peroxide	Solvent	$\Delta H^\ddagger / \text{kJ mol}^{-1}$	$\Delta S^\ddagger / \text{J mol}^{-1} \text{K}^{-1}$	$10^5 k / \text{s}^{-1} (145^\circ \text{C})$
	toluene	174.5	77.4	0.49
	acetone	174.5	76.6	0.37
	toluene	203.8	169.5	6.6
	"	193.7	142.7	14.3
	acetone	191.6	142.3	29.3
	toluene	120.9	−57.3	0.28
	"	167.4	70.7	5.5

XI. Conclusion

Depending on the structure of the compounds undergoing decomposition and the nature of the solvent, the thermolysis of organic peroxides in solution proceeds by both a homolytic mechanism with the cleavage of the O—O or OO—X bond and non-radical routes, through concerted rearrangement, in particular. Radical and non-radical decomposition reactions of peroxides normally occur in parallel. The formation of complexes and associates can increase the rates of both thermolysis routes.

Induced decomposition and recombination of radicals in the solvent cage diminish the proportion of radicals (*e*) released into the solvent. Kinetic estimates²¹⁰ show that the values of *e* for the peroxides R¹OOOR² are the closest to unity. In the case of symmetrical diacyl peroxides, *e* does not usually exceed 0.3–0.6 (*cf.* 0.3–0.7 for diaryl peroxides; 0.2–0.4 for dialkylperoxy ketals; and 0.5–0.9 for aromatic acids of *tert*-butyl peroxyesters).

This multivariant mechanism of thermolysis must be taken into consideration in those cases where organic peroxides are used as radical initiators of chemical reactions.

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Catalyst systems based on immobilised porphyrins and metalloporphyrins

A B Solovieva, S F Timashev

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Abstract. The key approaches to the preparation of catalysts based on porphyrins and porphyrin metal complexes immobilised on polymeric supports are analysed. The factors determining the catalytic activity of porphyrin-containing polymer systems are outlined. Processes catalysed by such systems are considered. The bibliography includes 99 references.

I. Introduction

The design of metal complex systems immobilised on various supports has been vigorously progressing in recent decades. The main principles of immobilisation of metal complexes (MC) have now been formulated and routes for the development of this line of research have been outlined.¹ It should be noted that the reactions of transition metal compounds with the support restrict their mobility, which affects the rates and, in some cases, also the mechanisms of catalysed reactions. This should be taken into account when preparing supported metal complex catalysts.

The design of immobilised catalysts with active sites having a known structure and environment contributes to better understanding of the mechanisms of catalytic transformations and allows theoretically substantiated choice of the catalysts and prediction of the catalytic effect. The immobilised catalysts should be stable and show reproducibility of functional properties; it is also required that they be readily separable from the reaction products.²

When homogeneous metal complexes are used as catalysts, the catalytic transformation occurs in the coordination sphere of the transition metal under 'steric participation' of ligands in electron density redistribution and formation of intermediate active com-

plexes. It is generally considered that in this case, all metal complexes are identical and equally accessible to reactants. Meanwhile, the MC immobilised on supports (inorganic, polymeric, *etc.*) possess, generally speaking, different activities and some of the complexes can be inactive or even catalyse side reactions.^{1,2} However, immobilised systems have obvious advantages because they are more easily separated from products and recycled, which is especially important when dealing with fairly expensive metal porphyrins.

The problem of separation of catalysts from the reaction mixture is so acute that chemical processes based on homogeneous catalysts are seldom implemented in industry. Exceptions include the Ziegler–Natta catalysts (olefin polymerisation) and catalysts of the Wacker (ethylene oxidation to acetaldehyde) and Monsanto processes (methanol carbonylation to acetic acid).³ Therefore, it can be understood why specialists have always looked for ways of developing catalysts of a new type that would combine the advantages of homogeneous and heterogeneous systems.

A new impetus for research along these lines was given by the discovery of unique catalytic properties for the systems prepared by grafting transition metal complexes to polymer supports. The knowledge coming from studies of the functional activity of MC in natural systems prompted the search for efficient heterogeneous catalyst systems to be focused on imparting certain mobility to the 'attached' catalytic sites. This is attained by immobilisation of functionalised MC on polymeric supports, which are most mobile. In what follows we restrict ourselves to considering this particular type of 'attachment'. This review discusses the set of problems associated with the development of catalyst systems based on immobilised porphyrins and metalloporphyrins (MP).

II. Immobilised metal complexes as fragments of natural systems

Fastening of low-molecular-weight compounds including MC to mineral or polymeric substrates and participation of these immobilised compounds in various processes are frequently encountered in animate and abiotic nature. The presence of ions in the inorganic natural sorbents occurring as parts of soils and natural sedimentary deposits dictates the dynamics of element redistribution in nature, ore-formation processes, the formation of carbon mineral products, and so on. The transport and assimilation of metal ions in animate

A B Solovieva N N Semenov Institute of Chemical Physics, Russian Academy of Sciences, ul. Kosygina 4, 119991 Moscow, Russian Federation. Fax (7-095) 938 24 84. Tel (7-095) 939 71 12. E-mail: anna@polymer.chph.ras.ru

S F Timashev State Scientific Centre of the Russian Federation 'L Ya Karpov Institute of Physical Chemistry', ul. Vorontsovo Pole 10, 105064 Moscow, Russian Federation. Fax (7-095) 916 14 25. E-mail: timashev@cc.nifhi.ac.ru

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nature determine almost all functions of native systems including enzymic, muscle, photosynthetic and other properties.^{1,2}

In particular, porphyrin metal complexes catalyse biochemical processes that provide for the vital activity of organisms. The specific activity of natural hemoproteins containing a protoporphyrin complex of trivalent iron (oxidase, monooxygenase, haemoglobin, myoglobin) is determined first of all by the spatial arrangement of the side functional groups of the polypeptide chain in the vicinity of the active site. In the best-studied monooxygenases, namely, cytochromes P-450, which oxidise xenobiotics such as steroids and cholesterol, within the microsomal system of the liver, the central Fe(III) ion of the haem is coordinated to the imidazole group of histidine and the thiol group of cysteine. The removal of these amino acid residues from the cytochrome active site results in enzyme deactivation. However, it is believed that in the haemoglobin molecule, iron protoporphyrin responsible for oxygen binding and oxygen transport to all organs and tissues of living creatures is coordinated to the imidazole groups of two histidine molecules. It should be noted that oxygen does not react with iron if iron is not coordinated to imidazole groups. In addition, strong binding between the haem and a protein is due to acid–base interaction of the carboxy groups of porphyrin with the side groups of the polypeptide chain.^{4,5}

As an example illustrating the possible conformational changes in the protein molecule in the vicinity of the metalloporphyrin active site, one can cite classical results of an X-ray diffraction study of ferro- and ferricytochrome *c* carried out by Dickerson and co-workers⁶ with a resolution of 0.245 (ferrocyclochrome) and 0.28 nm (ferricytochrome). Cytochrome *c* in mitochondrial membranes participates in the electron transport along the 'respiratory chain' and in oxidative phosphorylation of food, resulting in the synthesis of a versatile energy storage in the cell, namely, adenosine triphosphate (ATP), hydrolysis of which releases an energy of ~ 7 kcal mol⁻¹. The cytochrome *c* itself is a protein with a molecular mass of $\sim 123\,000$ containing 104 amino acid residues. Figure 1 sketches a stereoprojection of ferricytochrome *c*, indicating what types of rearrangement take

place in this system during the reduction of the central ion of the haem.⁷

It can be seen from Fig. 1 that the haem is linked to cysteines-14 and -17 of the protein by covalent sulfide bonds and to the imidazole nitrogen atom of histidine-18 and the sulfur atom of methionine-80 by coordination bonds *via* iron. The nitrogen atom of the imidazole ring of histidine-18 is involved in the hydrogen bond with the carboxy group of proline-30. On reduction of ferricytochrome *c*, the globule undergoes severe conformational changes (Fig. 1 *b*), only 21 amino acid residues of 104 remaining unaffected. Thus, the coordination properties of MP toward covalent binding to the fragments of biological systems are realised under dynamic variability of the 'environment' of the central ion and the porphyrin ring plane. The nature controls the catalytic or other properties of small molecules by 'attaching' them to supports, which formally do not participate in the process but indirectly influence it through the formation of non-covalent (coordination and hydrogen) bonds. This often changes the process direction and efficiency.

One more example of conformational rearrangements in biological macromolecules upon metal binding refers to the antibiotic valinomycin, first synthesised by M M Shemyakin in 1963. Valinomycin belonging to the class of cyclic depsipeptides can bind alkali metal ions (in particular, potassium ions) to give positively charged lipophilic complexes and perform the catalytic transport of these ions through hydrophobic zones of biological membranes. During this process, the valinomycin molecule undergoes complex conformational rearrangements, as shown in Fig. 2.⁸

It should be emphasised that the knowledge of dynamic aspects of the functioning of complex systems *in vivo* is not only of purely scientific but also of practical interest (we have in view the practical line of studies on metal complex catalysis, in particular, catalysis involving MP). Apparently, for efficient use of metalloporphyrins for practical purposes, it is necessary to follow nature's example, that is, to put them on various macromolecular supports.

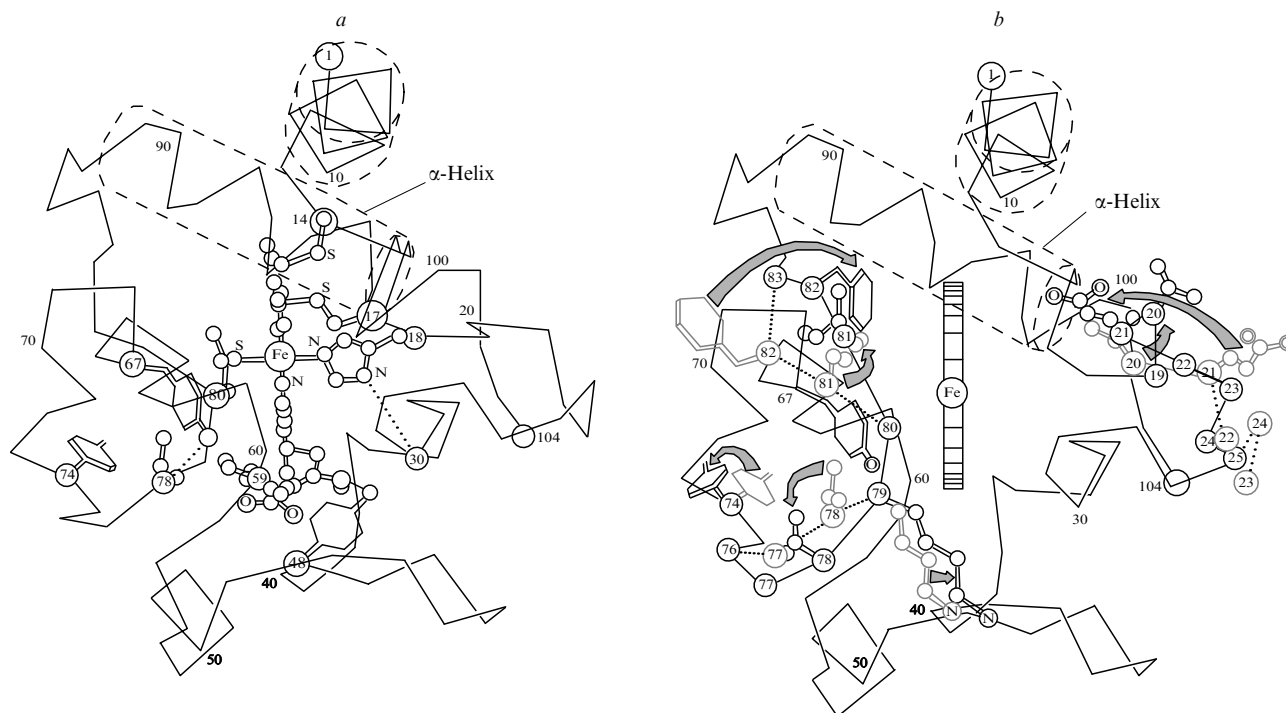


Figure 1. A stereoprojection of the schematically depicted molecule of ferricytochrome *c* (a) and main structural changes (shown by arrows) taking place upon reduction of ferricytochrome *c* (b).⁷

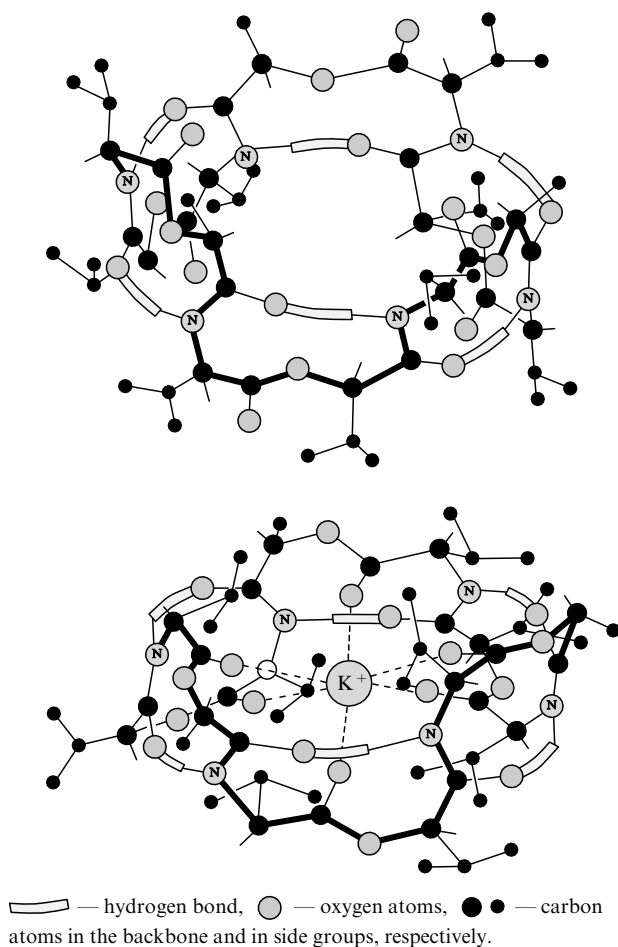


Figure 2. Conformational changes in the valinomycin molecule upon complex formation with the potassium ion.⁸

III. Immobilised metal complexes in catalysis

Apparently, the first attempts at using MC attached to a polymer support as catalysts date back to the late 1960s. By as soon as 1975, British Petroleum and Mobil Oil Corporation had received about 2000 patents for the use of such catalysts. The first publications devoted to the use of immobilised MP and metallophthalocyanines (MPc) in catalysis appeared 10 years later.¹

Immobilisation may both decrease and increase the specific (per active site) efficiency of metal complexes as catalysts. In particular, poor solubility of transition metal complexes is often responsible for their low catalytic activity in homogeneous catalysis, while immobilisation of MC on polymer supports soluble in the given reaction medium can markedly increase the MC concentration in the solution and, hence, the efficiency in catalysis. The change in the catalytic activity upon immobilisation can be due to specific rearrangements of the polymer chain, the change in the stereochemical environment of the metal ion, *etc.*, which take place in the reaction medium.

In the general case, immobilisation of metal complexes on a polymer support can redound to the combination of advantages and elimination of disadvantages of homogeneous and heterogeneous catalysts. Development of such catalyst systems is a fairly complicated task. In order to take advantage of the whole potential of the catalyst systems based on MC coupled with polymer supports, it is necessary to accumulate experience in selecting polymer supports and methods for grafting the MC. Moreover, in every stage of development of immobilised catalysts, one should take into account specific features of the interaction of MC with the macromolecular material.

Metalloenzymes are known to be polymers whose active sites incorporate transition metal complexes with porphyrins or other ligands. High catalytic activity of enzymes is due to the existence of a whole series of interrelated factors, first of all, to the enzyme–substrate structural compliance caused by enhanced affinity of some biopolymer fragments to the substrate. These fragments of protein macromolecules form a three-dimensional network around the active site, the shape and dimensions of the network being consistent with the substrate size. This promotes accumulation of the substrate near the active site (so-called substrate enrichment) and creates favourable orientation of the reactant molecules. In addition, enzymatic catalysis often involves so-called multicentre coordination, which arises upon additional activation of the substrate by functional groups of the biopolymer.⁹

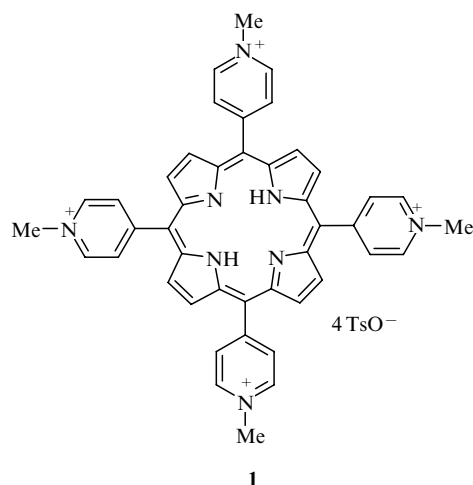
In the most general form, a polymer support suitable for chemical immobilisation of MC should meet the following requirements: (i) give a sufficient number of reactive functional groups; (ii) have a high specific (per unit volume) microporosity (iii) possess appropriate physical and mechanical properties; (iv) be chemically stable under catalysis conditions; and (v) be inert with respect to the reaction products. Depending on the type of catalytic process, polymer supports can be manufactured in different forms, in particular, as powders, granules, fibres, films (including membranes) or swollen gels. In terms of the degree of cross-linking of polymer supports, the metallopolymer catalysts (including those based on metal porphyrins) are classified into three groups — highly cross-linked beaded polymers approaching in properties inorganic substrates; lightly cross-linked swelling gel-type polymers; and linear soluble polymers whose macromolecular chain influences most appreciably the activity of the MC.

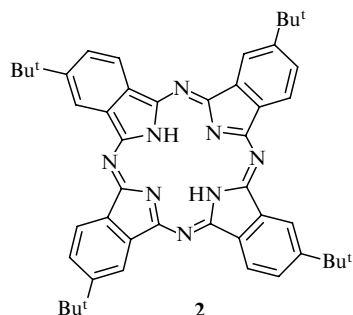
IV. Types of binding of porphyrins immobilised on polymer supports

1. Physical binding of MP to a polymer support

The ‘MP–polymer support’ systems in which the components do not form chemical bonds are usually prepared either by dispersing a polycrystalline porphyrin in a solution of the polymer (in the case of insoluble porphyrins) or by co-dissolution of the polymer and porphyrin followed by casting on an appropriate surface and solvent evaporation to prepare a film, or by impregnating a finished polymer film by a solution of porphyrin.

For example, for the preparation of bactericide photoreactive systems that generate singlet oxygen, metal-free 5,10,15,20-tetrakis(*N*-methylpyridinium-4-yl)porphyrin (**1**) as the tosylate was impregnated into regenerated cellulose films.^{10, 11} The films were 50 μm thick, the process was carried out in water or aqueous methanol at 50 °C.





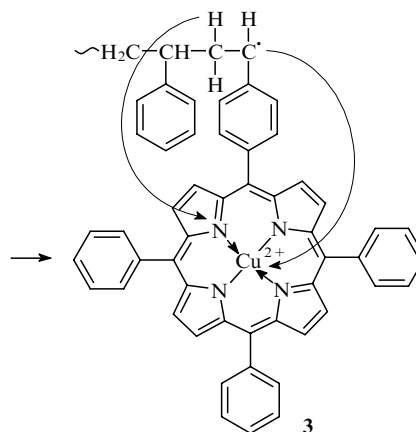
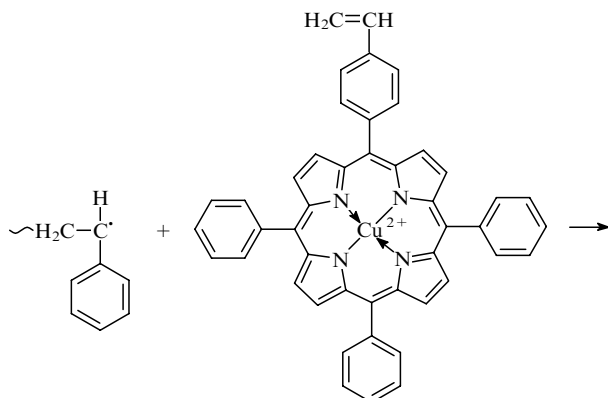
Films containing tetra(*tert*-butyl)phthalocyanine (**2**) were prepared by co-dissolution of phthalocyanine **2** and cellulose diacetate in wet acetone with subsequent casting on an appropriate surface.¹¹

Vankelecom *et al.*^{12–14} prepared porphyrin- and phthalocyanine-containing catalytically active membranes based on polydimethylsiloxanes (PDMS) by dispersing a porphyrin or phthalocyanine catalyst pre-deposited on an inorganic support (zeolites with different degrees of porosity) in a PDMS solution followed by casting a polymer film. The key prerequisite for uniform distribution of the catalyst in the matrix is the use of relatively dilute solutions of the polymer. The resulting polymer systems catalyse the selective epoxidation of hydrocarbons on treatment with *tert*-butyl hydroperoxide.

The same researchers^{15–17} proposed one more method for the preparation of porphyrin-containing membranes based on PDMS. To this end, a solution of the porphyrin complex of manganese or iron in dichloromethane was added to a mixture of prepolymer (RTV 615A) and a cross-linking agent (RTV 615B) in the same solvent. The mixture was stirred for 1 h at room temperature and left overnight. Polymerisation was carried out *in vacuo* at 150 °C. The catalyst systems prepared in this way proved to be efficient in epoxidation of enols and oxidation of alcohols to ketones.^{15–17} It was stressed that these composite catalyst systems containing iron porphyrins can be regarded as simple models of cytochrome P-450.^{18,19}

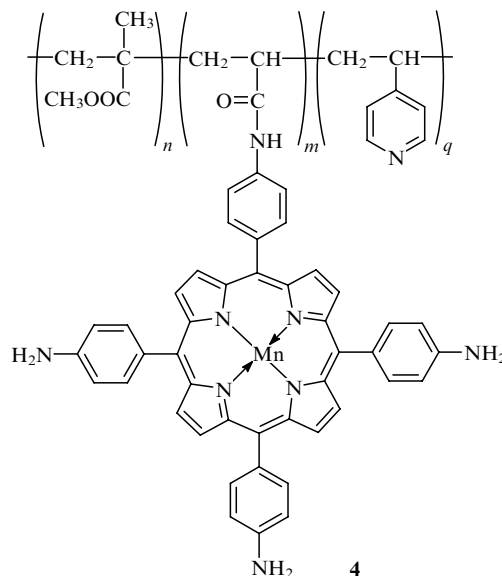
2. Covalently bound metalloporphyrins

Covalently bound metalloporphyrins are obtained most often by copolymerisation or polymerisation of porphyrin-containing monomers.^{20–31} In particular, the synthesis of THF-soluble copolymers of styrene with methyl methacrylate or acrylonitrile and vinyltetraphenylporphyrin has been reported.^{24–27} The scheme of preparation of copolymers **3** based on the vinylporphyrin complex of copper and styrene is shown below.



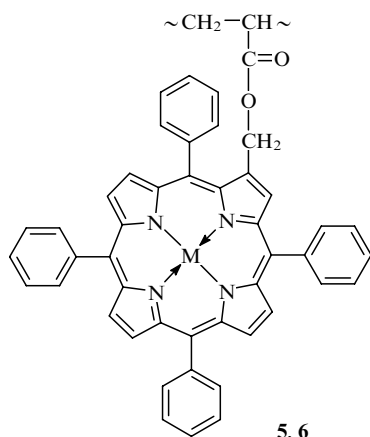
Neither vinylporphyrins themselves nor their metal complexes undergo homopolymerisation, which is due to either steric (bulky porphyrin substituents) or electronic factors (conjugation of the growing radical with the π -system of the porphyrin). The above procedure was used to obtain copolymers containing zinc and copper tetraphenylporphyrins. The content of MP in the polymer was 1 mol %–2 mol %, the molecular mass $M_w \approx 400\,000$. For increasing the content of porphyrin units in the copolymer, one should employ monomers in which the double bond is located far from the macrocycle.²⁸

The synthesis of copolymers **4** soluble in chloroform, based on mono-*N*-acryloylated [tetra(*p*-aminophenyl)porphyrinato]manganese (TAPPMn), vinylpyridine and methyl methacrylate, has been reported.²⁹



The content of TAPPMn in copolymer **4** was 3 mol %–7 mol %, $M_w \approx (2.5–4.0) \times 10^4$.

Benzene- and chloroform-soluble polyacrylates **5**, **6** with $M_w \approx (0.7–2.0) \times 10^4$ containing copper and vanadyl tetraphenylporphyrins (TPPCu and TPPVO) have been prepared by radical polymerisation of the corresponding monomers.³⁰ It was found that the molar extinction coefficient for the Soret band is lower for the polymer than for the monomer and a new absorption band appears at 630 nm. This may be due to electronic interaction of the porphyrin rings with fragments of the polymer chain.



5, 6

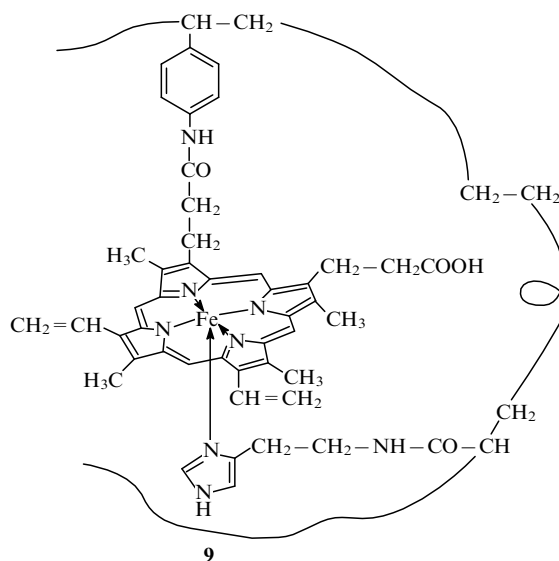
M = Cu²⁺ (TPPCu, 5), VO²⁺ (TPPVO, 6).

For the preparation of catalysts with controlled activity, one can use systems **7** and **8** formed upon polycondensation of pyrrole, sodium *o*-formylbenzenesulfonate and dipyrrolylethioporphyrim (Scheme 1).³¹ Using this reaction, it is possible to introduce a definite amount of porphyrin into the polymer to obtain a non-conjugated (**7**) or polyconjugated (**8**) porphyrin-containing polymer.

After metallation, such systems can be active in decomposition of hydrogen peroxide, oxidation of phenol and other processes that take place in aqueous media.

Mixed-type porphyrin-containing polymers (for example, **9**) have also been reported.³² In these polymers, MP are linked to the polymer support by covalent bonds through substituents present

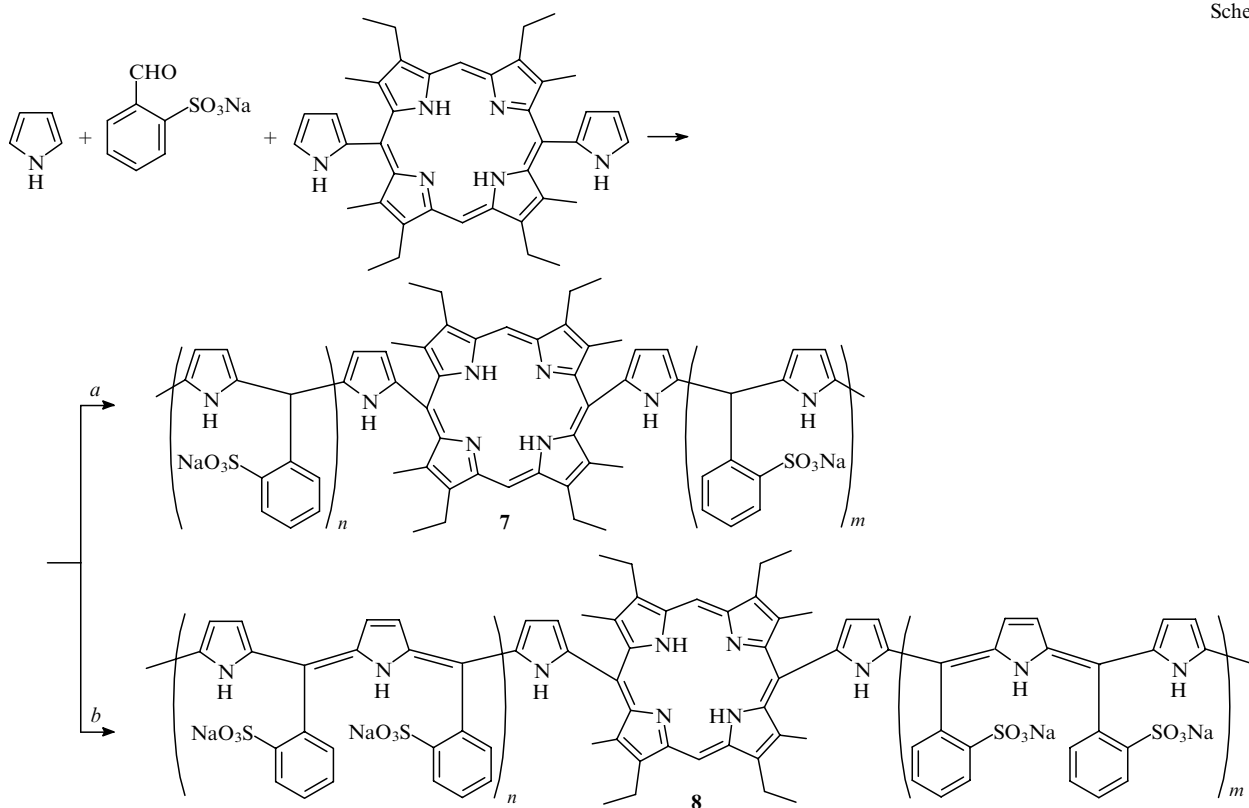
in the pyrrole rings of the porphyrin ligand; the central metal ion in the MP is additionally coordinated by the functional groups of the polymer chain. Shown below is the structure of the polymer modified with hemin, which is bound to the polymer chain by both covalent and coordination bonds (compound **9**).³²



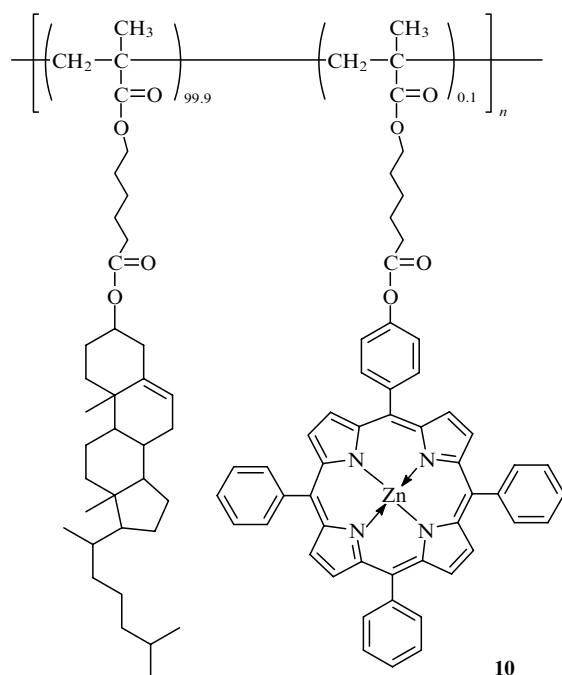
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Polymers **10**, containing zinc tetraphenylporphyrin (TPPZn) and cholesterol, were prepared by copolymerisation of (5-methacroyloxyhexanoyloxyphenyl-10,15,20-triphenylporphyrinato)zinc with cholesteryl methacroyloxyhexanoate.³³

Scheme 1



(a) H⁺ (Cat.), DMF, room temperature, N₂, 24 or 50 h; (b) H⁺ (Cat.), DMF, room temperature, O₂, 6 days.

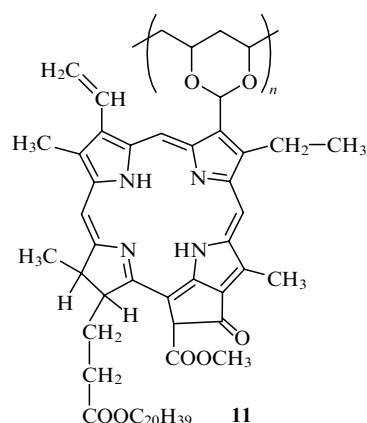


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The content of TPPZn in polymers **10** was 0.1 mol %. It was suggested³³ that in this copolymer, the cholesterol residues are involved in electronic interactions, resulting in the formation of 'cavities' which accommodate the porphyrin fragments.

Polymer systems containing covalently bonded porphyrins can be obtained by treatment of polymers having functional groups (carboxy, amino, hydroxy) with porphyrins containing reactive substituents in the ring. Thus the reaction of low-molecular-mass poly(ethylene glycol) with mesoporphyrin IX containing carboxy groups afforded porphyrin-containing polymers efficient in the photogeneration of singlet oxygen.³⁴

Some studies discuss the problems of polymer modification by metalloporphyrins. In particular, Govorov and co-workers^{35–38} described the synthesis of polymeric catalysts based on poly(vinyl alcohol) (PVA) and a number of natural porphyrins, namely, pheophytin *b* (catalyst **11**), rhodin *g*₇, and their copper and cobalt complexes.



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The resulting catalysts proved to be active in the decomposition of hydrogen peroxide in an aqueous medium.^{35,36}

A rather simple method for the preparation of porphyrin-containing insoluble polymers has been exemplified in tetra(aminophenyl)porphyrin (TAPP) modification of chloromethylated polystyrene³⁹ and polybenzaldehyde⁴⁰ cross-linked by divinylbenzene (Fig. 3). The subsequent metallation of these compounds by cobalt or aluminium salts resulted in the synthesis of polymeric MC used for reversible binding of molecular oxygen.

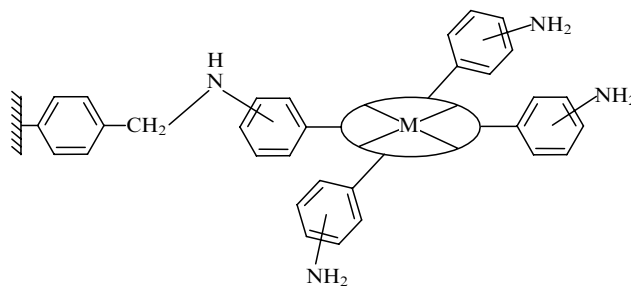
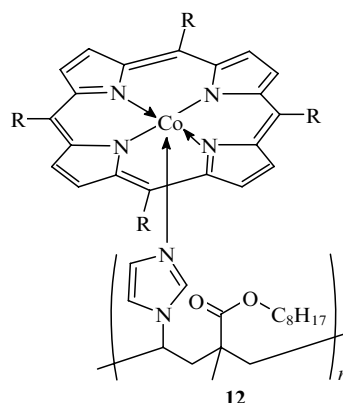


Figure 3. Structure of TAPP immobilised on chloromethylated polystyrene cross-linked by divinylbenzene.³⁹

A similar method has been used to prepare polymeric catalysts on the basis of chloromethylated polystyrene and TAPPMn.⁴¹ This catalyst proved to be active in the epoxidation of alkenes in the presence of imidazole or pyridine.

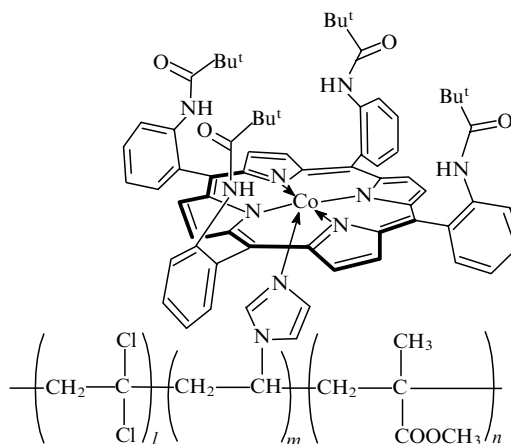
3. Metalloporphyrins bound to the polymer matrix by coordination bonds

The coordination of MP to polymers occurs most often through the central metal atom. Thus porphyrinatocobalt coordinated to the imidazole fragment of the octyl methacrylate–1-vinylimidazole copolymer (polymer **12**) has been used to prepare oxygen permselective membranes.⁴²



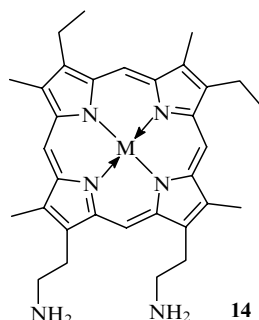
12

The membranes were prepared from a solution of these compounds in acetone. The same researchers obtained copolymers **13** of vinylidene dichloride, methyl methacrylate and vinylimidazole containing porphyrinatocobalt immobilised through coordination bonds.⁴³ Membranes composed of this material were also oxygen permeable (the oxygen molecules were transferred through the membrane by the hopping mechanism).



13

Development of water-soluble polymeric catalysts based on metalloporphyrins is the subject of one more study of the same groups of researchers,⁴⁴ which describes the synthesis of micellar systems from aminoporphyrins (for example, etioporphyrin **14** containing amino groups).



These micellar systems are stabilised by polyelectrolytes [polyallylamine or poly(vinyl sulfate)] through the formation of donor–acceptor bonds (Fig. 4).

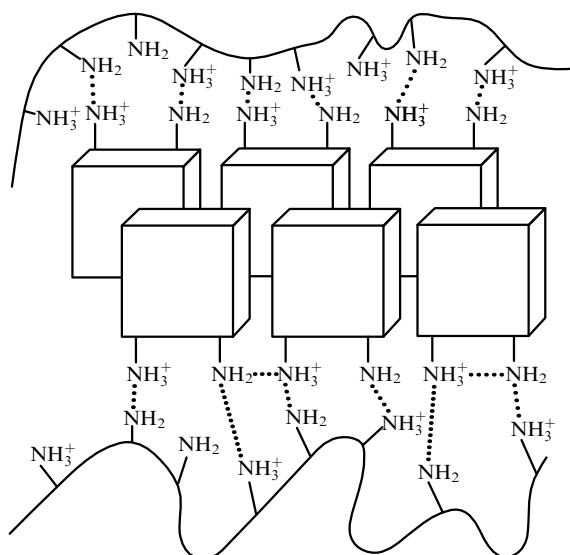
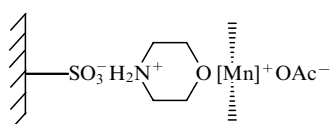


Figure 4. Structure of the complex formed by MP **14** and polyallylamine.⁴⁴

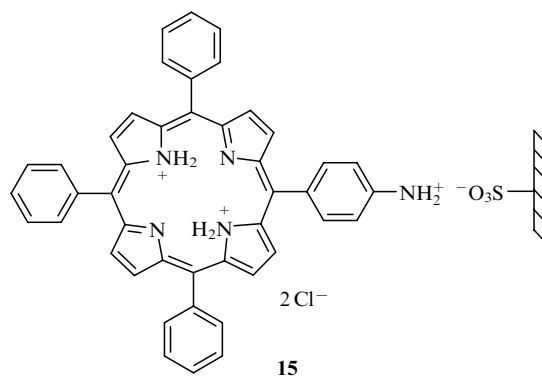
4. Polymeric catalysts with an ionic bond between metalloporphyrins and the matrix

The ionic interactions of MP with the polymer support can be found in the polymeric catalysts based on perfluorinated sulfonated cation exchange polymers (Nafion type) in the morpholine form and manganese porphyrins.^{45–47} Manganese porphyrins are immobilised on a sulfonate cation exchange membrane of the Nafion type through a morpholine bridge.⁴⁵



These systems exhibit catalytic activities toward hydroxylation of steroid alkenes in the presence of morpholine or imidazole.

It is noteworthy that metal-free porphyrins can also be fixed on sulfonate cation exchange materials (due to the formation of ionic bonds). For example, immobilisation of 5-(*p*-aminophenyl)-10,15,20-triphenylporphyrin (ATPP) in the protonated form on a sulfonate cation exchange matrix has given polymeric catalyst **15**,⁴⁷ active in the photogeneration of singlet oxygen.⁴⁶



V. Catalyst systems with metalloporphyrins embedded in micelles

Owing to the low polarity and the presence of charged groups and bound water, the structurally organised micellar aggregates can be used as analogues of a protein globule.⁴⁸ For example, in oxidation of organic substrates by oxygen-containing compounds in the presence of metalloporphyrins, phospholipid vesicles have been used as structure-forming agents,⁴⁹ resulting in a pronounced increase in the degree of conversion and a change in the reaction regiospecificity. Metalloporphyrins embedded in micellar structures were found to exhibit monooxygenase activity,⁵⁰ typical of P-450 type enzymes. Borovkova *et al.*⁵⁰ studied the kinetics of catalytic oxidation of unsaturated hydrocarbons with a system MP–reducing agent (NaBH₄)–dioxygen in the presence of micelle-forming agents, namely, Surf I (cetyltrimethylammonium bromide in a heptane–chloroform–ethanol mixture) and Surf II [sodium bis(2-ethylhexyl)sulfosuccinate in a heptane–ethanol mixture]. These systems displayed an extremal dependence of the specific rate constant k_s for the non-chain oxidation of cholesterol, anthracene and substituted naphthalenes on the concentrations of Surf I and Surf II (Fig. 5 and 6), the k_s value increasing significantly upon variation of the Surf I and Surf II concentrations in the ranges 0.05–0.30 mol litre^{−1} and 0.1–1.0 mol litre^{−1}, respectively. In the absence of surfactants, a certain contribution to the k_s value is apparently made by

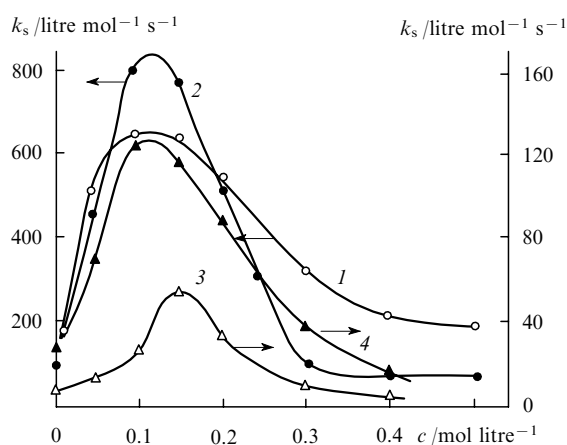


Figure 5. Dependences of k_s for oxidation of cholesterol (curves 1–3) and anthracene (curve 4) by the MP–NaBH₄–O₂ system on the concentration of Surf I in a chloroform–heptane mixture (1:1). MP = TPPMnCl (1, 2, 4) and TPPFeCl (3).⁵⁰ The concentrations of cholesterol, anthracene, TPPMnCl, TPPFeCl and NaBH₄ were 2.2×10^{-3} , 4.3×10^{-3} , 6×10^{-5} , 1.3×10^{-4} and 0.1 mol litre^{−1}, respectively.

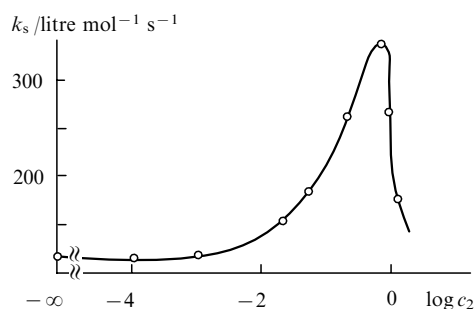


Figure 6. Dependence of k_s for the oxidation of cholesterol with the TPPMnCl–NaBH₄–O₂ system on the concentration of Surf II.⁵⁰ The concentrations of cholesterol, TPPMnCl and NaBH₄ were 2.2×10^{-3} , 6×10^{-5} and 0.1 mol litre⁻¹, respectively, and the concentration of EtOH was 2.65 vol. %.

diffusion restrictions; the reaction proceeds either in the diffusion or in the mixed diffusion and kinetic region.

The specific rate constant k_s in question was determined from the rate of formation of the product (v_p) at initial time instants

$$k_s = \frac{v_p}{[S][Cat]},$$

where $v_p = dQ/dt$ (Q is the concentration of the product, t is time), $[S]$ and $[Cat]$ are the substrate and catalyst concentrations, respectively. The catalysts used were tetraphenylporphyrin complexes with manganese, iron and cobalt (TPPMnCl, TPPFeCl and TPPCo). The manganese complex TPPMnCl was the most active in the oxidation of any of the studied substrates both in the presence and in the absence of surfactants. The specific rate constant for the non-chain oxidation of cholesterol increased 8–10-fold in the presence of Surf I and 10–18-fold in the presence of Surf II. The k_s value for the oxidation of anthracene increased by a factor of 5–8 when the system contained Surf I.

The products formed upon oxidation of cholesterol and anthracene were the same (3 β ,5 α -cholestanediol and 9,10-anthraquinone, respectively) as those formed in the absence of surfactants in the reaction mixture,⁵¹ while the ratio of the oxidation products of 2,6-dimethylnaphthalene and 2-methylnaphthalene (epoxytetralins and dihydroxytetralins) changed from 1 : 1 (without a surfactant) to 2 : 3 (with a surfactant).

The concentrations of Surf I and Surf II corresponding to a sharp increase in k_s were substantially higher than the critical micelle concentrations (CMC's) for both surfactants. Reverse micelles were formed with the polar tails of the surfactant molecules directed inwards. The observed extremal pattern of dependences $k_s = k_s([surfactant])$ can be attributed to redistribution of the catalyst and substrate molecules between the organic and micellar phases.⁵² An increase in the surfactant concentration is accompanied by an increase in the concentration of micelles and efficient accumulation of the substrate and the catalyst in the micelle bulk, which entails an increase in k_s (see Figs 5 and 6). Upon further increase in the surfactant concentration to values an order of magnitude greater than the CMC, phase separation with destruction of the reverse micelles starts in the reaction mixture, and process kinetics returns to the initial regime (observed in the absence of a surfactant).

The validity of the qualitative conclusions concerning the extremal dependence of k_s on c is also supported by the observed extremal dependence of k_s for the oxidation of cholesterol on the concentration of MP for surfactant concentrations exceeding the CMC (Fig. 7, curves 1 and 2) and by the fact that k_s almost does not depend on the MP concentration when no surfactant is present (Fig. 7, curve 3).

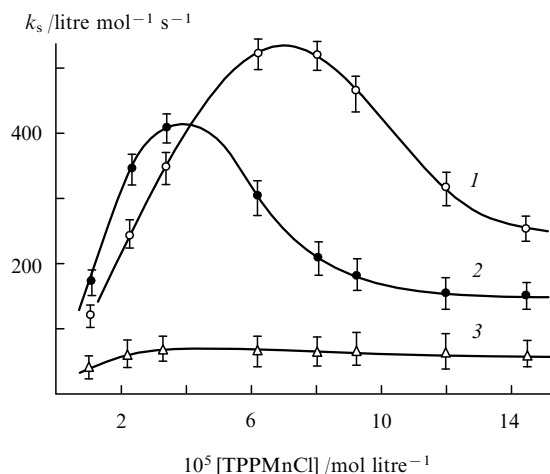


Figure 7. Dependence of k_s for the oxidation of cholesterol with the TPPMnCl–NaBH₄–O₂ system on the concentration of TPPMnCl in the presence of Surf II (curve 1), Surf I (curve 2) and in the absence of surfactants (curve 3) (in heptane).⁵⁰

The concentrations of Surf I, Surf II and cholesterol were 0.05, 0.5 and 2.2×10^{-3} mol litre⁻¹, respectively, the concentration of EtOH was 2.65 (1) and 4.42 vol. % (2, 3).

It is also evident that some concentration limit should exist for embedding of substrate molecules into the micellar phase. This is indicated by the dependences of the observed rate of cholesterol oxidation v_p in the presence of micelle-forming agents of both types on the cholesterol concentration shown in Fig. 8. The fact that the kinetic curves reach a stationary level (unlike the linear dependence of v_p on the cholesterol concentration in the absence of a surfactant) demonstrates the saturation effect in substrate embedding into the micelles.

The dependence of k_s values for these oxidation processes on the content of an aliphatic alcohol (or water) in the reaction mixture also deserves attention (Fig. 9). The necessity of introducing an alcohol (polar component) into the reaction mixture is due to the fact that sodium tetrahydroborate is insoluble in nonpolar

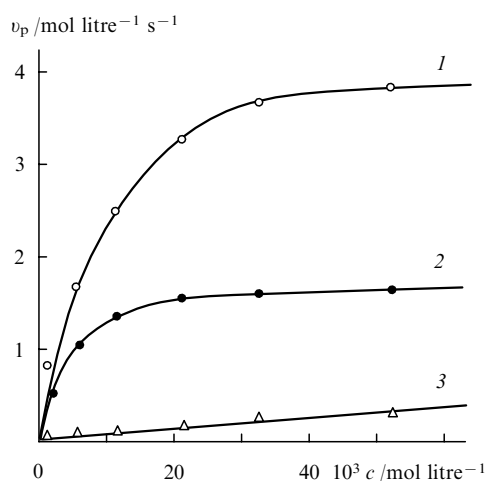


Figure 8. Rate of cholesterol oxidation v_p with the TPPMnCl–NaBH₄–O₂ system vs. cholesterol concentration in the presence of Surf I (curve 1), Surf II (curve 2) and in the absence of surfactants (curve 3) in a chloroform–heptane mixture (1 : 1).⁵⁰

The concentrations of Surf I, Surf II and TPPMnCl were 0.05, 0.5 and 6×10^{-5} mol litre⁻¹, respectively; the concentration of EtOH was 2.65 vol. %.

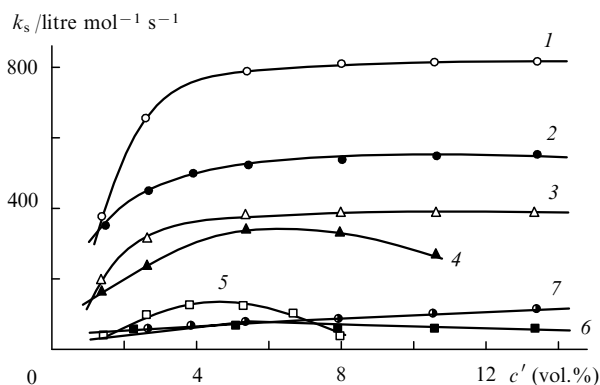


Figure 9. Dependences of k_s for cholesterol oxidation with the TPPMnCl–NaBH₄–O₂ system on the alcohol (or water) concentration (c') in the presence of Surf II (curves 1–6) and in the absence of Surf II (curve 7). The introduced alcohol (or water) used: ethanol (1–3), propan-2-ol (4), water (5), n-butanol (6).⁵⁰ The concentrations of cholesterol and TPPMnCl were 2.2×10^{-3} and 6×10^{-5} mol litre⁻¹, respectively, the concentration of Surf II was 0.2 (1), 0.1 (2), 0.05 (3–6) and 0 (7, in heptane) mol litre⁻¹.

solvents or chloroform. Depending on the nature of the alcohol, its concentration in the reaction mixture was 2.5 vol.%–3.0 vol.%. An increase in the content of alcohol (water) in the system resulted in a lower stability and a smaller size of the reverse micelles.

It was found that the rate of oxidation of cholesterol in the presence of Surf II decreases in the following sequence of the polar components added to the system: ethanol > propan-2-ol > n-butanol > methanol > water. The low k_s values observed with water and methanol are due to fast destruction of the reducing agent and loss in its activity.

It was also shown that the introduction of Surf I into the reaction system increases k_s for the oxidation of anthracene and the degree of its conversion (k_s increases 5–6-fold and the degree of conversion increases to 100%). Studies on the oxidation of substituted naphthalenes showed that the presence of reverse micelles formed by Surf I increases the specific rate constant for the oxidation of 2-methylnaphthalene in the presence of TPPCo by a factor of 4–6, and for 2,6-dimethylnaphthalene, this factor is 6–8. Simultaneously, the degrees of conversion increase from 10% to 30% and from 30% to 80%, respectively. The ratio of the oxidation products somewhat changes due to an increase in the yield of dihydroxy derivatives of tetralins (with respect to epoxy alcohols).

A significant feature found for the oxidation of hydrocarbons in the presence of surfactants is the substantial increase in the stability of the active form of the catalyst, which is more pronounced in the presence of Surf I than Surf II. It has been shown⁵⁰ for the oxidation of cholesterol in the presence of TPPMnCl that the turnover number of TPPMnCl until its complete decomposition ('discoloration') increased from 20–25 to 240–250 in the presence of Surf II and from 35–40 to 860–870 in the presence of Surf I. These data attest to a decrease in the rate of catalyst destruction. Apparently, this is related to a decrease in the probability that the intermediate complex $[MP]^{2+} - O_2$ –substrate involved in the oxidation⁵¹ would react with the hydroperoxide adducts formed during the reaction.

The above data provide grounds for treating MP solubilised by reverse micelles as a new type of porphyrin-containing catalyst for non-chain oxidation of alkenes characterised by enhanced efficiency and stability compared to monomer analogues.

VI. Catalytic activity of soluble and insoluble polymeric systems with immobilised porphyrins and their metal complexes

The catalytic activity of non-immobilised MP in the chain oxidation of unsaturated hydrocarbons by dioxygen in the presence of reducing agents has been described.⁵¹ It was shown that the Mn³⁺ and Fe³⁺ porphyrin complexes in the presence of sodium tetrahydroborate are efficient catalysts of the following reactions:

- regioselective oxidation of mono-, di- and trisubstituted aliphatic and trisubstituted steroid alkenes to ketones and secondary (or tertiary) alcohols (in the case of Δ^5 -steroid alkenes, the reaction proceeds with 100% stereo- and regioselectivities);
- oxidation of anthracene, its alkylated and phenylated derivatives and phenanthrene to the corresponding quinones; and
- oxidation of alkyl- and phenyl-substituted naphthalenes to dihydroxy- and epoxy-derivatives of tetralin.

A mechanism for the catalytic action of MP has been proposed. The mechanism is underlain by the view which implies the formation of an intermediate ternary complex MP–O₂–substrate where dioxygen is activated to a singlet-like state. Within the framework of this mechanism, it became possible to describe the whole set of data obtained for reactions of this type. New methods for the oxidation of cholesterol to 3 β ,5 α -cholestanediol (a new reaction in the chemistry of steroids) and oxidation of C₄–C₆ alkenes to tertiary alcohols have been developed.

1. Porphyrin-containing polymeric systems in the catalytic oxidation of steroid alkenes by dioxygen in the presence of reducing agents

This Section considers the results of studies^{29, 45, 46} dealing with oxidation of steroid alkenes with MP catalysts immobilised on polymers in the presence of sodium tetrahydroborate. The oxidation of these substrates by dioxygen was carried out in ethanol or its mixture with chloroform. The effective rate constants k_{ef} were found from the kinetic curves for oxygen absorption by the reaction system at the initial instants.

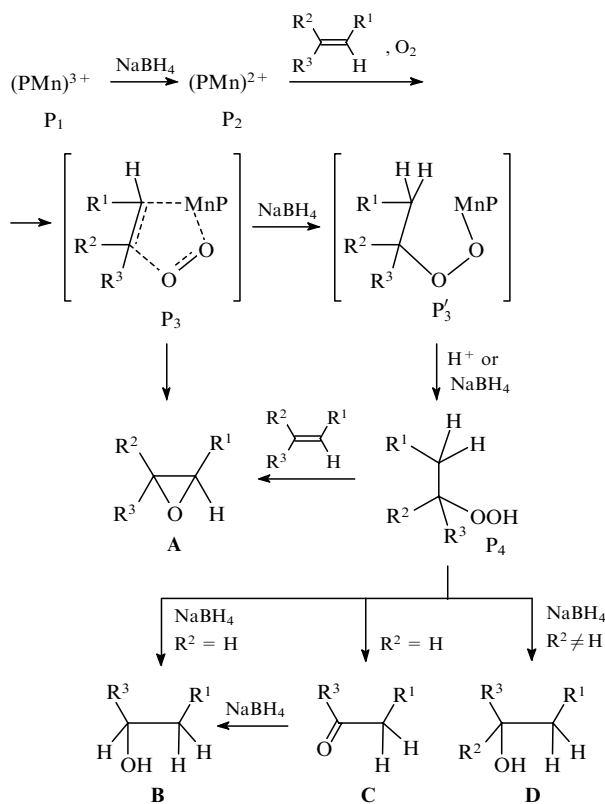
a. Oxidation of cholesterol in the presence of soluble polymeric catalyst systems

Soluble polymeric catalysts (PC) containing PMn were prepared by copolymerisation of methacrylates with the *N*-acryloyl derivative based on [tetra(*p*-aminophenyl)porphyrinato]manganese (PMn-AA) (the product of reaction between acryloyl chloride and TAPPMnOAc). The copolymers obtained in this way proved to be active catalysts for the oxidation of steroid alkenes (cholesterol, androstene). However, aliphatic, dienic, and fused aromatic hydrocarbons (ethylene, propylene, hex-1-ene, hex-2-ene, isoprene, anthracene and its derivatives or substituted naphthalenes) were not oxidised in the presence of these soluble PC. It was shown that oxidation of cholesterol to 3 β ,5 α -cholestanediol in the presence of soluble PC and NaBH₄ proceeds *via* the formation of cholesterol hydroperoxide, like oxidation in the presence of non-immobilised PMn,⁵¹ *i.e.*, the oxidation mechanism can be considered to remain the same on passing to soluble PC.

The scheme of catalytic action of MP in the presence of a reducing agent proposed in a number of studies^{51, 53–55} assumes the formation of an intermediate complex containing, apart from the reduced MP and dioxygen, a substrate molecule. It is significant that dioxygen and the alkene are coordinated on one side of the plane of the porphyrin ring. The possibility of this coordination is determined by the ability of the central ion of the MP occurring in the high-spin state to emerge from the plane of the porphyrin macrocycle by a distance of up to 0.05 nm. Previously, the existence of intermediate ternary complexes of this type has been postulated in the discussion of the oxidation mechanism of substrates involving haem enzymes.

It was assumed that the first stage ($P_1 \rightarrow P_2$) of the catalytic process (Scheme 2) is the reduction of the central ion in the MP molecule. The possible scheme of hydroxylation of substituted alkenes with the $\text{PMn}-\text{O}_2$ system in the presence of sodium tetrahydroborate is presented below.⁵¹

Scheme 2



The reaction of the reduced form of the catalyst (P_2) with the alkene and dioxygen molecules ensures the regioselectivity of the process and results in the intermediate product P_3 . Subsequently, under the action of the reducing agent, complex P_3 is converted into final products (A–D), possibly, *via* intermediate compounds P'_3 and P_4 . Depending on the alkene structure and the oxidation conditions, this can give ketones and secondary or tertiary alcohols. In the case of trisubstituted alkenes, the intermediate adduct P_3 with the tertiary carbon atom can be converted under the action of sodium tetrahydroborate (in particular, *via* hydroperoxide P_4) directly into tertiary alcohol. If complex P_3 contains a secondary carbon atom, *i.e.*, the initial alkene is disubstituted ($R^2 = \text{H}$), the hydroperoxide P_4 can either disproportionate to give ketones or be reduced on treatment with NaBH_4 to give secondary alcohols. According to this scheme, epoxides can be produced by two routes, namely, by disproportionation of the intermediate complex P_3 (this process predominates in the absence of hydride reducing agents) and by the reaction of hydroperoxide P_4 with a second alkene molecule (epoxidation of alkenes with hydroperoxides is a well-known reaction). Table 1 presents the effective 'specific' rate constants k_s for the oxidation of cholesterol related to the concentration of PC (for soluble PC) and the low-molecular-mass analogue (TAPPMnOAc) (*i.e.*, per catalyst molecule): $k_s = v_p / ([\text{MP}] \times [\text{substrate}])$, where v_p is the rate of transformation of cholesterol during the initial instants.

It follows from Table 1 that immobilisation can result in a substantial increase in the 'specific' TAPPMnOAc activity. This increase in the rate constants can be related to an increase in the local concentration of cholesterol near the active site caused by the participation of the macromolecular chain of the polymer catalyst in the effective sorption of the substrate. Evidently, in this case, the PC macromolecules should be sufficiently flexible. Indeed, an increase in the chain rigidity caused by introduction of a large

Table 1. Kinetic parameters of oxidation of cholesterol by dioxygen in the presence of copolymers of various acrylates and vinylpyridine (VP) with PMn-AA in a chloroform–ethanol mixture (1 : 1) at room temperature.²⁷

Second monomer ^a	[PMn] (mass %)	$10^5 [\text{PMn}]$ /mol litre ⁻¹	$10^5 v_p$ /mol litre ⁻¹ s ⁻¹	k_s /litre mol ⁻¹ s ⁻¹
MMA	0.3	1.87	1.14	60.9
MMA	1.0	6.14	1.90	32.4
MMA	3.5	21.8	2.21	10.1
BMA	0.5	3.12	0.31	9.8
OMA	0.1	0.62	0.01	1.6
4-VP	0.4	2.5	0.01	0.4
4-VP–MMA	0.6	3.74	0.47	12.7
Alkylated 4-VP–MMA	0.6	3.74	0.12	3.18
TAPPMnOAc (see ^b)	100	125	1.95	1.52

Note. The cholesterol and NaBH_4 concentrations were 1×10^{-2} and 5.5×10^{-2} mol litre⁻¹, respectively.

^a Designations: MMA is methyl methacrylate, BMA is butyl methacrylate, OMA is octyl methacrylate, 4-VP is 4-vinylpyridine; ^b non-immobilised complex.

amount of PMn into the polymer chain entails a decrease in the specific catalytic activity of copolymers based on MMA and PMn-AA, while the PC based on 4-vinylpyridine and PMn-AA, which exists in solution as a rigid solvated structure, is virtually inert in this process. However, the introduction of MMA fragments into this PC increases the catalytic activity of the resulting terpolymer. The copolymers of PMn-AA with BMA and OMA do not exhibit a catalytic activity, possibly due to the shielding of the MP active sites by bulky side groups of the polymer support.

The temperature dependence of the effective rate constant for the oxidation of cholesterol in the presence of PMn-AA copolymers with MMA and BMA passes through a maximum at about room temperature (Fig. 10, curves 1 and 2). It should be noted that upon a decrease in the molecular mass of the synthesised PC

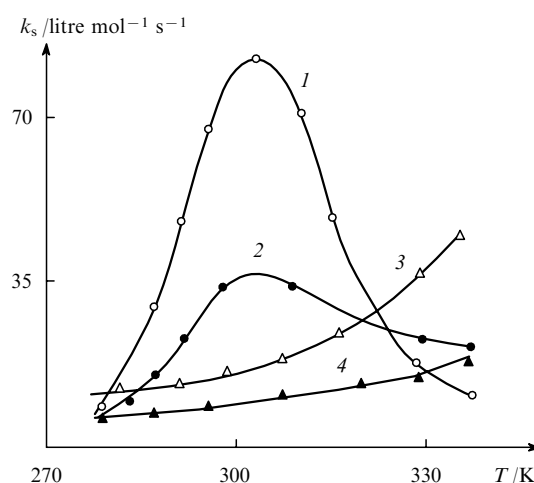


Figure 10. Temperature dependences of the rate constant for the oxidation of cholesterol in the presence of NaBH_4 and copolymers of PMn-AA with MMA (curves 1, 3) and BMA (curve 2) and also in the presence of non-immobilised TAPPMnOAc (curve 4).

The concentrations of cholesterol and NaBH_4 were 1×10^{-2} and 5.4×10^{-2} mol litre⁻¹, respectively. The concentrations of copolymers in relation to PMn were 1.8×10^{-5} (MMA) and 3.1×10^{-5} mol litre⁻¹ (BMA).

The molecular mass of MMA-based copolymers was 29 000 (curve 1) and 7 000 (curve 3).

(transition to oligomers), the k_s decreases and the temperature dependence acquires the Arrhenius form (curve 3 in Fig. 10).

This non-monotonic behaviour of k_s implies the possibility of temperature-induced conformational transitions in the system. In particular, this may be the rearrangement of the secondary structure of the polymer caused by the formation of hydrogen bonds. These processes are completed over a certain temperature range. Usually, rearrangements of this type are described using a cooperativity parameter depending on temperature (in the above-indicated temperature range) according to an activation law and defined as the equilibrium constant of the formation of one rupture in the sequence of hydrogen bonds. In the same temperature range, the intrinsic viscosity of the system (η) should also change according to the equation

$$\eta = \eta_0 \exp \frac{E}{RT},$$

where E is the activation energy for viscous flow. Indeed, the $\eta(T)$ dependences observed experimentally for the MMA copolymer with PMn-AA (the content of PMn was 0.3%), like those for poly(methyl methacrylate), were 'rectified' in the appropriate coordinates.²⁹ It is noteworthy that the introduction of 0.3% of porphyrin-containing groups in the copolymer changes the activation energy for viscous flow from 25.2 (for PMMA) to 50.4 kJ mol⁻¹ (for the PMn-AA copolymer).

b. Catalytic oxidation of cholesterol, substituted anthracene hydrocarbons and phenanthrene in the presence of metalloporphyrins immobilised on a perfluorinated sulfonate cation exchange copolymer

The insoluble PC containing MP were prepared by copolymerisation of methyl methacrylate with PMn-AA in the presence of a cross-linking agent (divinylbenzene) and by immobilisation of a number of monomeric PMn [P = TPP, tetra(*p*-methoxyphenyl)-porphyrin (TMPP) and hematoporphyrin (HP)] on insoluble polymeric supports at room temperature from solutions in dioxane in the presence of heterocyclic nitrogenous bases. Table 2

presents the data on the chemical structures and activities of the catalysts.

The insoluble copolymers of MMA and PMn-AA containing 3 mass %–5 mass % of TAPPMnOAc proved to be inert toward oxidation of cholesterol. The introduced PMn were easily washed out from the polymer matrices based on butadiene–styrene (**21**, **22**) and divinylbenzene–styrene (**19**, **20**) copolymers (see Table 2) under reaction conditions in a chloroform–ethanol solution. The low catalytic activity of the copolymers obtained by copolymerisation of PMn-AA with MMA or DVB (PC **23**–**25** in Table 2) became somewhat higher for lower degrees of cross-linking. This fact can be attributed to low accessibility of active sites of the catalyst in the cross-linked copolymer because the corresponding soluble PC (MMA copolymers with PMn-AA) exhibited high catalytic activities.

Catalysts **17** prepared by immobilisation of PMn on insoluble perfluorinated (sulfonate) cation exchange polymer films MF-4SK in the morpholine form manufactured at the scientific-production association Plastpolymer (St-Petersburg) exhibited a high catalytic activity towards the oxidation of cholesterol and anthracene. However, aliphatic alkenes were not oxidised in the presence of these catalysts. Note that if the central ion of the MP was linked to ionogenic groups of copolymers as a counter-ion, immobilisation resulted in the loss of the catalytic activity of PMn. This loss of activity can be attributed to the 'rigid' localisation of the Mn³⁺ in the vicinity of the ionogenic groups of the copolymers, which can prevent the reduction of the central ion and activation of oxygen. The 'rigid' fixing can be avoided by performing coordination of PMn through a bifunctional bridge, *i.e.*, heterocyclic nitrogenous base (morpholine, imidazole, piperazine). This type of immobilisation took place in the transformation of the sulfonate cation exchange copolymer into the morpholinium form (this process was monitored by IR spectroscopy based on the appearance of an absorption band at 3060 cm⁻¹ corresponding to the protonated form of morpholine in the spectra of copolymers) with subsequent treatment of this copolymer with a solution of PMn in dioxane (the absorption

Table 2. Some properties of insoluble polymeric catalysts.

Polymeric support	X (Y)	PC	Percentage of PMn washed out in 30 min	Content of PMn (mass %)	k_s /litre mol ⁻¹ s ⁻¹
$-(CF_2-CF_2)_n-(CF_2-CF-OCF_2O(CF_2)_2SO_3^-X)_m-$ (MP-4SK)	H ⁺ morpholine ^a	16 17	— —	2.5 3.0	10 ⁻⁵ 28–30
$-(CF_2-CF_2)_n-(CF_2-CF-OCF_2O(CF_2)_2COO^-X)_m-$	H ⁺ morpholine ^a	18	— 15–20	3.0 3.0	10 ⁻⁵ see ^b
$-(CH_2-CH(C_6H_4)-CH=CH_2)_n-(CH_2-CH(C_6H_4)-SO_3^-X)_m-$	H ⁺ morpholine ^a	19 20	2 20–25	2.5 2.0	10 ⁻³ see ^b
$-(CH_2-CH(C_6H_4)-CH=CH_2)_n-(CH_2-CH(C_6H_4)-SO_3^-X)_m-$	H ⁺ morpholine ^a	21 22	3–4 20–25	2.5 2.5	10 ⁻³ see ^b
$-(CH_2-C(CH_3)(COOCH_3))_n-(CH_2-CH(CONHTPPMn))_m-$	(0.1% DVB) ^c (0.3% DVB) ^c (0.6% DVB) ^c	23 24 25	— — —	1.2 1.5 2.0	10 ⁻³ 10 ⁻³ 10 ⁻⁴

^a Morpholine in the protonated form. ^b In experiments in which more than 5% of PMn contained in the PC passed to the solution, the k_s value was not calculated. ^c DVB is divinylbenzene.

band of the morpholinium ion was retained in the IR spectra of the copolymers).

The ability of the MF-4SK copolymer to bind PMn without the loss of catalytic properties of porphyrin is apparently due to the presence of fluorine-containing fragments in the α -position with respect to the SO_3^- groups, which causes migration of the electron density to the α -carbon atoms and thus enhances the acid properties of the copolymer sulfonic groups. In addition, the hydrophobicity of the fluorocarbon framework prevents the penetration of the polar solvent molecules into the diffusion channels of the copolymer;⁵⁶ as a consequence, the solvation environment of the ionogenic groups of MF-4SK differs substantially from that of the sulfo groups in other copolymers. The MF-4SK copolymer, unlike butadiene–styrene and divinylbenzene–styrene rubbers, has a rather ordered structure of simply connected channels along which the diffusion transfer of partially solvated ions and molecules takes place. This may stipulate high efficiency of the transfer of the initial reactants and products in MF-4SK along this system of channels.

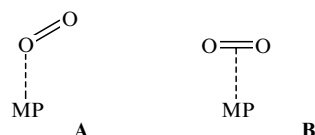
Experimental data related to the kinetics of oxidation of cholesterol by dioxygen in the presence of the MF-4SK polymeric catalyst and NaBH_4 are presented in Table 3.

It can be seen that the rate constants for the oxidation of cholesterol (k_s) in the presence of monomeric and immobilised PMn are of the same order of magnitude but for insoluble PC, the overall yield of the product per catalytic site markedly increases due to the increase in the turnover number (μ) of the catalyst. This parameter introduced during generalisation of the formal Michaelis–Menten kinetics⁵¹ characterises the number of product molecules formed per ‘catalyst molecule’ throughout the whole process until the catalyst has completely decomposed, which necessarily takes place due to oxidative destruction processes. As regards the data presented in Table 3, note that, whereas the rate constant for cholesterol oxidation in the presence of monomeric PMn is affected substantially by the nature of the substituents in the porphyrin macrocycle, in the case of immobilised HPMn and TPPMn, the k_s values are virtually the same. It has been shown above that the rate constants for the oxidation of substrates in the presence of soluble PC in a homogeneous catalytic process increase due to the ‘polymeric effect’, namely, due to the involvement of polymeric fragments in effective sorption of the substrate. However, a substantial increase in the turnover number of the insoluble PC (10–100-fold compared to that of monomeric HPMn) is apparently indicative of a substantially lower susceptibility of immobilised PMn to destruction.

The destruction processes that take place during the catalytic action of monomeric PMn and PFe and soluble PC containing them proceed apparently through bimolecular reaction of the reduced catalyst (P_2) with oxygen adducts (P_3 and P_3') or with the intermediate compound P_4 (see Scheme 2), resulting in cleavage of the conjugation chain of the porphyrin ring. With the above-described coordination of PMn near the sulfo groups of the

polymer matrix, these bimolecular destruction processes occur at a considerably lower rate, which is responsible for the longer service life of insoluble PC. It should be emphasised that the aggregative state of the catalyst may dictate the route of oxidation.⁵⁷ Indeed, cholesterol is oxidised to $3\beta,5\alpha$ -cholestanediol in the presence of both soluble monomeric PMn and insoluble PC, while anthracene is oxidised to anthraquinone in the presence of monomeric PMn, but only anthracene endoperoxide is formed in the presence of insoluble PC containing PMn. Alkyl-substituted anthracenes and phenanthrene are oxidised in a similar way (*i.e.*, to endoperoxides).

The whole set of results can be easily interpreted within the framework of the above Scheme 2 according to which oxygen reacts with reduced MP at initial stages of the process and then the ternary intermediate complex, $\text{MP}-\text{O}_2$ –substrate, is produced. According to Scheme 2, no noticeable transfer of charge or spin density to oxygen takes place in the adducts formed from PMn and PFe with O_2 , and oxygen passes into a reactive singlet-like state.⁵⁸ For the oxygen adducts PMn^{2+} and PFe^{2+} , two alternative structures were proposed, one with the terminal tilted attachment of the dioxygen molecule to the MP (structure **A**) where the Mn and Fe cations are linked to only one of the oxygen atoms and the $\text{M}-\text{O}-\text{O}$ angle is 120° and the other, with a symmetrical arrangement of oxygen (structure **B**) with the central cation coordinated to the oxygen double bond.



According to quantum-chemical calculations,⁵⁸ structure **A** is energetically favourable for isolated complexes. However, the complexes are stabilised in solutions due to solvation effects and the proportions of forms **A** and **B** do not necessarily correlate with the quantum-chemical estimates; therefore, in the general case, both structures should be taken into account.

When a catalytic reaction is carried out in a polar solvating solvent, the probability of interaction between the substrate and the catalyst in form **A** or **B** depends obviously on the nature of the substrate. The polar cholesterol molecules (dipole moment $\mu_C = 1.99$ D) should be coordinated preferably near complexes of type **A**. This type of interaction is responsible for the subsequent formation of 5α -hydroperoxycholesterol (**26**), which then reacts with sodium tetrahydroborate, being reduced to alcohol **27**.

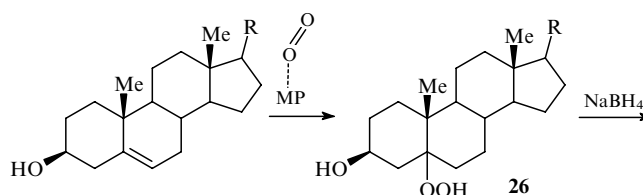
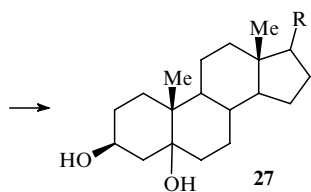


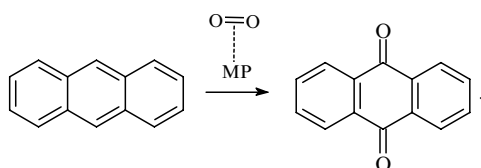
Table 3. Kinetic parameters of cholesterol oxidation in the presence of PMn immobilised on perfluorinated sulfonate copolymer MF-4SK and monomeric PMn in ethanol at 20°C .⁴⁵

Catalyst system	$10^2 [\text{Cholesterol}]$ /mol litre $^{-1}$	k_s /litre mol $^{-1}$ s $^{-1}$	$10^{-2}\mu$	Degree of conversion (%)
TMPPMnOAc	4.0	9	2	96
Immobilised TMPPMnOAc *	8.0	26	400	95
TPPMnOAc	4.0	8	2	95
Immobilised TPPMnOAc *	8.0	26	400	96
HPMnOAc	2.5	0.5	1.2	80
Immobilised HPMnOAc *	8.0	30	400	96

Note. The concentrations of NaBH_4 and PMn were 5×10^{-2} and 2.5×10^{-3} mol litre $^{-1}$, respectively. In the case of insoluble polymeric catalysts (asterisked), the conventional concentration [PMn] corresponding to the amount of PMn contained in the polymer per ml of the reaction mixture was calculated.



For the symmetrical anthracene molecules, having an extensive system of π -conjugation, the coordination and the formation of the intermediate ternary complex with form **B** of the catalyst are apparently more energetically favourable, although the content of this form in the solution may be lower than that of form **A**. Anthraquinone is produced according to the following scheme



An activated transition of form **A** into form **B** upon coordination of anthracene near the $\text{MP}-\text{O}_2$ complex is also possible. It is clear that for cholesterol the formation of this product is completely ruled out. However, at high PMn concentrations where the proportion of form **A** markedly increases, anthracene can also react with the 'asymmetrical' form of the oxygen adduct PMnO_2 , which leads to the appearance of anthracene endoperoxide in the reaction system. This is also facilitated by the large

bulk of the PMnO_2 complex with a tilted orientation of oxygen (form **A**).

When PMn is immobilised on insoluble polymer supports, the symmetry of the molecular fields of the above-described complexes decreases, which would suppress even more strongly the formation of symmetrical oxygen adducts (**B**), *i.e.*, the probability of formation of the corresponding oxidation products would diminish. Indeed, it has been noted above that oxidation of anthracene on insoluble immobilised PMn gives only anthracene endoperoxide.

2. Immobilised porphyrins and their metal complexes in hydroxylation, decomposition of hydrogen peroxide, electrooxidation, reversible binding of substrates, epoxidation and photocatalysis

Examples of the title processes catalysed by immobilised porphyrins and metalloporphyrins are given in Table 4. This list of reactions should be considered as a supplement (with some refinement) to the information on these reactions considered in the previous review.⁵⁹

Let us discuss in more detail the processes included in Table 4.

It has been shown that immobilisation of phaeophytin *b* and its cobalt and copper derivatives on PVA yields active catalyst systems used for H_2O_2 decomposition.^{36, 37} The catalytic activities of phaeophytin and its metal complexes in aqueous solutions of H_2O_2 are nearly equal. In the absence of porphyrin, with cobalt chloride dispersed in PVA, the reaction does not proceed. Cobalt complexes of phaeophytin dispersed in water do not initiate the reaction either. The mechanisms of these processes have not yet been elucidated; however, it has been suggested^{36, 37} that the

Table 4. Examples of processes catalysed by immobilised porphyrins and their metal complexes.

Catalysed process	Catalyst system ^a	Type of binding	Ref.
Decomposition of hydrogen peroxide	phaeophytin <i>b</i> (11), rhodin <i>g</i> ₇ , their Co and Cu complexes immobilised on poly(vinyl alcohol)	covalent	36, 37
Epoxidation of alkenes	TAPPMn (4) immobilised on chloromethylated polystyrene cross-linked by divinylbenzene	"	41
Photooxidation of hydrocarbons	TPPFe ^{III} –Nafion	ionic	60
Hydroxylation of cholesterol and alkenes	copolymers of TAPPMn with methacrylates (methyl, butyl, octyl) and 4-vinylpyridine	covalent	29
	TPPMn (TMPPMn or HPMn)–morpholine–Nafion	ionic	45, 46
Hydroxylation of aniline and oxidation of alkenes	TPPFe ^{III} –poly(γ -methyl-L-glutamate)	covalent	61
Electrooxidation of NO	glassy carbon electrode–polymeric TMHPP–Nafion	physical adsorption	62
Reversible oxygen binding	PCo–vinylimidazole copolymer with octyl methacrylate (sensor system)	coordination	42
	H ₂ TPP(2-NHCOBu ^t) ₄ –copolymer of vinylidene chloride, vinylimidazole and methyl methacrylate	"	43
	TAPPCo immobilised on chloromethylated polystyrene cross-linked by divinylbenzene	covalent	39
Photogeneration of singlet oxygen	TMPP tosylate (1)–regenerated cellulose	physical adsorption	10
	TMPPPd ^{II} –TDCPPFe ^{III} –Nafion	ionic	60
	MATPP (15)–Nafion	"	47
	(tetrapyrrolylporphyrinato)tin–silica	physical adsorption	63
Photoinduced modelling of oxygenase activity	TPPFe–Nafion	ionic	64

^a Designations: TAPP is 5,10,15,20-tetra(*p*-aminophenyl)porphyrin; TMHPP is tetrakis(3-methoxy-4-hydroxyphenyl)porphyrin, TMPP is tetrakis(*N*-methylpyridinium-4-yl)porphyrin, TDCPP is tetrakis(2,6-dichlorophenyl)porphyrin, MATPP is 5-(*p*-aminophenyl)-10,15,20-triphenylporphyrin.

mechanisms of decomposition of H_2O_2 in the presence of phaeophytin and its metal complexes are different.

The epoxidation of alkenes⁴¹ takes place with the participation of sodium periodate in acetonitrile in the presence of imidazole or another nitrogenous base. Due to the high degree of matrix cross-linking, the immobilised TAPPMn behaves as a typical heterogeneous catalyst where only near-surface layers are active. Immobilisation increases markedly the catalyst stability against degradation in the presence of sodium periodate, which is a strong oxidant. The degree of conversion reaches 95%.

The oxidation of a mixture of cyclohexene and cyclohexane by dioxygen on exposure to sunlight at 20 °C under atmospheric pressure has been studied.⁶⁰ In addition to the $\text{TPPFe}^{\text{III}}$ –Nafion system, the researchers used also chlorinated or fluorinated analogues of porphyrinatoiron immobilised on Nafion. The porphyrins were added to the reaction mixture after swelling of the resin in a mixture of dichloromethane and ethanol. The immobilisation of $\text{TPPFe}^{\text{III}}$ was found to result in a growth of the photocatalytic activity and stability of the catalyst. The ratio of the products formed in the catalytic reaction differed somewhat (from that obtained in the oxidation in the presence of non-immobilised porphyrinatoiron).

The covalent binding of TPPFe to poly(γ -methyl L-glutamate) afforded polymeric catalysts active in hydroxylation of aniline on treatment with hydrogen peroxide and in the oxidation of alkenes.⁶¹ Immobilisation was carried out in aqueous methanol. The catalyst obtained in this way was much more active than non-immobilised analogues.

Cizewski *et al.*⁶² developed a sensor device for determination of nitrogen oxide based on its anodic oxidation. The catalyst was prepared by successive deposition *via* electropolymerisation of tetrakis(4-hydroxy-3-methoxyphenyl)porphyrin (or its nickel complex) and Nafion film layers onto the surface of a glassy carbon electrode. The oxidation proceeded throughout the whole bulk of the film. The limit of determination of nitrogen oxide by this method was 10^{-4} mol litre⁻¹.

It should be noted that metalloporphyrins and metallophthalocyanines deposited on graphite or carbon electrodes are often used in electrooxidation or electroreduction processes (for example, proton to hydrogen). The use of Nafion films containing metalloporphyrins, in particular TPPCo , for coating the electrodes increases the efficiency of this process.^{65–68}

Membrane systems selectively permeable for oxygen have been prepared using cobalt porphyrin complexes and polymer supports.^{39, 42, 43} The polymeric systems based on vinylimidazole copolymers proved to be most efficient. The introduction of Co into the polymer increased the membrane permeability by a factor of 25. The ratio of the oxygen and nitrogen permeability coefficients of the membranes reached several hundreds.

The photogeneration of singlet oxygen upon photoexcitation of regenerated cellulose films containing adsorption-bound porphyrins has been studied.¹⁰ The photogeneration of singlet oxygen to the gas phase has been studied in the presence of protonated MATPP immobilised on the Nafion film and on quartz⁴⁷ and in the presence of (tetrapyridylporphyrinato)tin supported on silica gel.⁶³ The process was more efficient with MATPP immobilised on a polymer support. The efficiency of generation of singlet oxygen was found to increase with an increase in the temperature of the support. The TPPFe immobilised on the Nafion film was used to model the oxygenase activity exhibited by the system on photoexcitation.⁶⁴

To summarise the data, it can be stated that immobilisation of MP on insoluble polymeric supports results most often in a higher stability of the catalyst. This may also change the selectivity and increase the efficiency of the catalysed processes compared to the processes taking place in the presence of free MP. If the substrate is a bulky molecule, as is the case for hydroxylation of cholesterol, the MP molecule should retain some mobility during the catalytic transformation. However, in other cases, there is no need for MP

mobility (the case of photogeneration of singlet oxygen on MATPP immobilised on Nafion).

Some publications deal with the redox reactions taking place in metalloporphyrin (Co, Zn, Mn, *etc.*) molecules immobilised on poly-4-vinylpyridine and Nafion. In this case, polymeric films with immobilised MP were applied on glass electrodes,^{69–73} which were immersed into an electrolyte solution. The electrochemical charge transfer to the polymeric film was studied in a three-electrode system.

VII. Photochemical processes involving deposited layers of porphyrins

In recent years, the possibilities of functional use of not only porphyrin-containing polymer systems but also molecular aggregates and supramolecular ensembles formed with participation of porphyrin molecules and metalloporphyrins have been found. Scanning probe microscopy (SPM) and its versions — scanning tunnelling (STM), atomic-force (AFM) and scanning magnetic (SMM) microscopies — allow one not only to examine the arising structures at the atomic and subatomic levels but also to transfer and isolate separate molecules on a solid surface.^{74–78} These techniques cover the scale from fractions of a nanometre to several micrometres. The appropriate instruments allow one to control the ‘assembly’ and the structural organisation of molecular and supramolecular ensembles. In particular, recently STM has been used to elucidate the supramolecular aggregation on the surface of gold of the molecules of substituted tetraphenylporphyrin containing cyanophenyl substituents, which initiate the aggregation. This aggregation gave di-, tri- and tetrameric (*cis* and *trans*) aggregates.⁷⁹ The STM technique was also used to visualise *in situ* the process of formation of highly ordered structures of tetramethylpyridiniumporphyrin (in the form of tosylate) on an iodine-modified gold surface.⁸⁰ The process was performed in 0.1 M solutions of perchloric acid.

The new potential of nanotechnology can be associated with the use of deposited molecular layers formed under self-assembly conditions where the structural organisation of the layers (for nanometre to fractions of micrometre levels) is dictated by the structure of the molecules and interactions between them. Porphyrins and related molecules can be used for deposition, as they are capable of aggregation upon both precipitation from solutions and sputtering onto various substrates. In this Section, we present the results of investigation of the structure of vacuum deposited layers of tetraphenylporphyrin and some of its derivatives over a broad range of surface concentrations N_{tot} ($N_{\text{tot}} \approx 10^{-11} - 10^{-9}$ mol cm⁻²) of deposited molecules.⁸¹ These layers proved to be functionally active for generation of the singlet oxygen $^1\text{O}_2$ to the gas phase upon the photosensitised excitation of the molecular oxygen $^3\text{O}_2$ adsorbed on the deposited TPP layer. The rate of generation of $^1\text{O}_2$ depended on the structure of deposited layers on scales of about fractions of a micrometre. The conclusions concerning the structure of porphyrin layers on different spatial scales were drawn from the micrographs obtained by transmission electron and atomic-force microscopy. The recent interest in the photogeneration of singlet oxygen to various media is related to the possibility of initiating the photosensitised oxidation of biologically active substrates and to the problem of photodynamic therapy in medicine.

Here, it is pertinent to note that SPM analysis of the surface structure is based on the processing of digitised ‘roughness profiles’ along the scans obtained from a surface section with characteristic dimensions ranging from tens of nanometres to tens of micrometres. As a rule, the results are represented as images of fragments of the surface structure (for example, molecular aggregates) or the general surface morphology under conditions of ‘model highlighting’;^{82, 83} the appearance of images can depend appreciably on the type of this highlighting and, at the operator’s option, pictures different in kind (from the Carpathians to the Himalayas) can be obtained from the same section of the surface.

No routine and generally accepted methods for the processing of digitised data in order to derive parameters generally characterising the key features and peculiarities of the surface under study have been developed as yet. The purely statistical processing methods giving the average roughness and the corresponding variances and semiinvariants are barely used now, because they do not provide information on a significant feature of the structures, namely, the correlations in the spatial organisation of fragments with different spatial scales. The Mandelbrot fractal dimension^{84,85} proved to be inadequate for correct representation of the differences between complex surface structures. New prospects for parametrisation have appeared due to flicker-noise spectroscopy (FNS),^{86–88} which is based on the views on the information significance of the irregularities in real structures ('spikes', 'jumps' and discontinuities of derivatives) on different spatial scales and the degree of correlation of these irregularities (connectivity) over the surface.

Photogeneration of singlet oxygen to the gas phase was studied in an all-soldered glass setup⁸¹ in the presence of tetraphenylporphyrin and other porphyrin photosensitisers. Porphyrins were sputtered onto quartz plates with an area of 20 cm². The surface concentration of porphyrin was determined from the intensity of the Soret band in the electronic spectra of solutions of TPP in chloroform recorded after washing the porphyrin off the surface of quartz plates. The lowest detectable surface concentration was 5×10^{-12} mol cm⁻². The ¹O₂ concentration was determined using semiconductor sensors.⁴⁷ The working pressure of dioxygen in the setup was maintained at 0.1 Torr. A DRSh-500 mercury lamp with a BS-8 light filter was used as the light source. The efficiency of photogeneration of singlet oxygen was estimated from the steady-state concentration c_S of singlet oxygen in the setup bulk under continuous photoexcitation of the system (in the absence of a photosensitiser deposited on quartz, no generation of singlet oxygen was detected upon photoexcitation). The data were presented as the reduced bulk concentrations $c_{S_0}^{\text{red}} = c_S/c_{S_0}$, the concentration of singlet oxygen formed in the setup at a temperature of 20 °C being taken as c_{S_0} . The c_{S_0} value was estimated using decomposition of 9,10-diphenylanthracene endoperoxide yielding a controlled amount of ¹O₂.⁸⁹ According to this estimate, $c_{S_0} \approx 10^{-13}$ mol cm⁻³ ($\sim 10^{11}$ particles cm⁻³).

Electron microscopy data were obtained using a JEM-2000 EX-II transmission electron microscope. The samples were prepared by depositing TPP on a NaCl single crystal and then carbon replicas were formed from the deposited surface. The generation of singlet oxygen was studied for samples prepared by depositing TPP onto quartz. The surface reliefs were analysed for TPP layers deposited onto mica plates. A Solver P47 atomic force microscope (NT-MDT, Zelenograd) was used. The studies were carried out in the semicontact mode, the surface concentration of porphyrin (N_{tot}) being varied in the range of 10^{-11} – 10^{-9} mol cm⁻². Electronic absorption spectra were recorded on a Specord UV-VIS spectrophotometer.

Figure 11 presents the dependence of the efficiency of generation of singlet oxygen on the overall surface concentration of TPP. It can be seen that this dependence has a broad maximum in the concentration range $N_{\text{tot}} \approx (4–12) \times 10^{-11}$ mol cm⁻². The photosensitised generation of singlet oxygen is known to start with excitation of the sensitizer molecules and includes several steps.⁹⁰ Under experimental conditions, the surface layer of the deposited porphyrin films exists in the stationary photoexcitation state in which electronic-vibrational transitions take place in the molecular-crystalline fragments of the porphyrin layer. The porphyrin molecules in the initial singlet state ¹Π pass into the excited ¹Π* states upon photon absorption. Under the conditions of electronic-vibrational transitions, intersystem crossing becomes possible in the molecular-crystalline fragments giving excited porphyrin molecules in the ³Π* triplet spin state. The photosensitisation of the triplet ³O₂ molecules, which are coordinated most probably near the porphyrin macrocycles, can be accomplished through these excited states. In this case, the oxygen

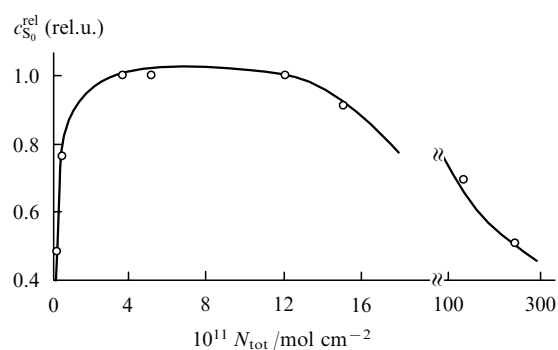


Figure 11. Efficiency of generation of singlet oxygen by deposited TPP layers at different average surface concentrations of porphyrin.

molecules ¹O₂ in the singlet excited state formed upon energy transfer are also coordinated at the porphyrin molecules. This means that the generation of singlet oxygen to the gas phase is possible only in the case where the characteristic time of desorption of the coordinated ¹O₂ molecules does not exceed their deactivation time in the coordinated state.

Within the framework of a formal kinetic scheme, from which some of the above-described intermediate steps have been eliminated, the process of ¹O₂ generation to the gas phase induced by a light quantum $h\nu$ can be represented as the following set of transitions:



Here k_1 , k_2 , k_3 and k_4 are the rate constants for processes (1)–(4), respectively, namely, the formation of porphyrin molecules in the triplet spin state ³Π*, generation of the ¹O₂ molecule to the gas phase, deactivation of the porphyrin molecule in the ³Π* state and deactivation of the ¹O₂ molecule on the surface sites, in the chamber bulk and on the chamber walls. It is evident *a priori* that chemical transformations (1)–(3) occur on the surface of the porphyrin film; therefore, the rate of these chemical processes should be determined by the surface concentrations of the reactants. However, to simplify the subsequent analysis and to obtain analysable final relations, we shall write the equations of formal kinetics for the concentrations of oxygen molecules in the singlet and triplet states (c_S and c_T) in the gas phase assuming that the necessary equilibrium between the adsorbed and free forms of oxygen is attained over a short period of time. Therefore, all constants appearing in the set of equations of formal kinetics should be taken as effective values. In the stationary case, this set assumes the form

$$\frac{dN^*}{dt} = k_1 w N - k_2 c_T N^* - k_3 N^* = 0, \quad (5)$$

$$\frac{dc_S}{dt} = k_2 c_T N^* - k_4 c_S = 0, \quad (6)$$

$$N_0 = N + N^*, \quad (7)$$

$$c_0 = c_T + c_S, \quad (8)$$

where w is the parameter characterising energy absorption by the deposited layer under photoexcitation conditions (determined by the product of the incident luminous flux, the extinction coefficient and the effective thickness of the absorbing layer); N and N^* are the surface concentrations of the porphyrin molecules in the ¹Π and ³Π* states, respectively, efficiently involved in the photo-

generation of singlet oxygen; N_0 is the overall surface concentration of the TPP molecules participating in the photosensitised generation of singlet oxygen; and c_0 is the total concentration of oxygen in the gas phase.

The solution of the set of equations (5)–(8) for the steady-state concentration c_S in the gas phase has the form

$$c_S = \frac{k_1 k_2 w N_0 c_0}{k_3 k_4 + k_1 w (k_4 + k_2 N_0) + k_2 k_4 c_0}. \quad (9)$$

It is worth noting that under the experimental conditions, $c_S/c_T \approx 10^{-4}$, which implies fulfilment of the inequality

$$\frac{k_1 k_2 w N_0}{k_3 k_4 + k_1 w (k_4 + k_2 N_0) + k_2 k_4 c_0} \ll 1. \quad (10)$$

When comparing the obtained expression (9) with the experimentally observed dependence $c_S = c_S(N_{\text{tot}})$, one should take into account the effective dependence of the rate constants k_1 , k_2 , k_3 and k_4 on N_0 . It is natural to suggest that $N_0 = \theta N_{\text{tot}}$, where θ is the fraction of porphyrin molecules participating in photosensitisation processes. Before discussing these dependences, we shall consider the experimental results of analysis of the structure of porphyrin polymolecular layers formed upon vapour deposition of porphyrin on a quartz substrate.

With low concentrations of the deposited TPP ($N_{\text{tot}} \ll 10^{-9} \text{ mol cm}^{-2}$), porphyrin islands are formed on the mica and quartz surfaces, the number and the dimensions of the islands being different for different N_{tot} . As follows from the transmission electron microscopy data, when $N_{\text{tot}} = 1.8 \times 10^{-11} \text{ mol cm}^{-2}$, TPP forms particles with linear dimensions 15–50 nm, the distances between them being greater than the particle size by a large factor. The increase in the surface concentration of TPP to $4.1 \times 10^{-11} \text{ mol cm}^{-2}$ results in the growth of both the dimensions of porphyrin particles (30–100 nm) and their number per unit area. Further increase in N_{tot} to $1.5 \times 10^{-10} \text{ mol cm}^{-2}$ induces mainly an increase in the linear dimensions of the islands to 100–150 nm. Figure 12 shows typical images of the porphyrin islands for $N_{\text{tot}} = 4.1 \times 10^{-11} \text{ mol cm}^{-2}$. These micrographs demonstrate that the particles formed are inhomogeneous as regards both their internal structure and the elevation above the support level. When $N_{\text{tot}} > 10^{-9} \text{ mol cm}^{-2}$, continuous porphyrin layers are formed.

The tentative inferences concerning the crystal structure of porphyrin ‘macroislands’ were drawn from analysis of the X-ray diffraction patterns obtained using an electron microscope in the microdiffraction mode.⁸¹

When N_{tot} is low and the deposited layer is mainly composed of small islands, these islands (the seeds for larger aggregates) are crystalline. As the island dimensions increase (with an increase in the surface concentration of porphyrin), the proportion of the amorphous component increases (the number of crystal reflections located on concentric circles diminishes and the amorphous halo grows). When the islands grow to their maximum size, the crystalline component becomes less pronounced. Presumably, the growth of the islands ceases when the crystalline seeds have been coated by an amorphous layer of porphyrin. Thus, upon an increase in the surface concentration N_{tot} , the overall degree of the layer crystallinity decreases and, hence, the degree of amorphisation increases.

The conclusions drawn about the morphology of the deposited TPP layers are confirmed by the data from atomic-force microscopy. The results are presented in Fig. 13 *a–c*, which show the typical surface reliefs of deposited TPP for different surface concentrations N_{tot} . The formation of a TPP layer on the support starts with the appearance of relatively small particles with a height of up to 5 nm. When the surface concentration of porphyrin increases to $N_{\text{tot}} = 2.0 \times 10^{-11} \text{ mol cm}^{-2}$, the height of some aggregates of porphyrin molecules reaches 80 nm, the diameter being 10–50 nm (Fig. 13 *a*), which is in line with the electron microscopy data. Further increase in N_{tot} induces mainly an increase in the number of new (small) seed islands formed on the defects of the mica surface, while the growth of particle height virtually ceases. As the surface concentration reaches $N_{\text{tot}} \approx 10^{-9} \text{ mol cm}^{-2}$, bridges between the separate aggregates of TPP molecules appear, which gives rise to a continuous layer (Fig. 13 *b*). Figure 13 *c* shows an enlarged image of a surface section obtained at $N_{\text{tot}} = 1.5 \times 10^{-12} \text{ mol cm}^{-2}$ with a separate large porphyrin particle. It can be clearly seen in the relief that the particle is non-uniform in height.

The atomic-force microscopy data were processed in terms of a special programme of flicker-noise parametrisation of chaotic surfaces.^{86,91,92} The parameters used for the quantitative description of the surface included the average roughness height of the surface h , the correlation length L_1 for the types of surface irregularities (jumps), and the dimensionless parameter n , which is a factor of Fourier spectra in the flicker-noise section describing the rate of loss of the correlation links in the sequence of spike-type irregularities. Table 5 presents the calculated flicker-noise parameters.

The structural features of the porphyrin (TPP) layers deposited on NaCl identified on the basis of electron-microscopy images of the layers recorded at different surface concentrations of TPP, including the high surface concentrations N_{tot} (the region of

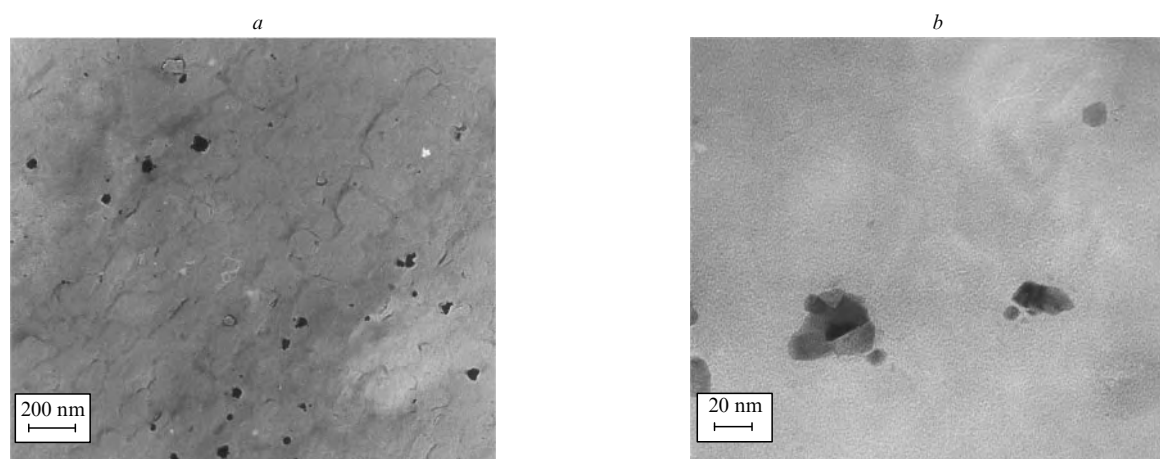


Figure 12. Typical electron micrographs of samples of deposited TPP at a surface concentration of $4.1 \times 10^{-11} \text{ mol cm}^{-2}$. Magnification (a) $\times 50\,000$, (b) $\times 500\,000$.

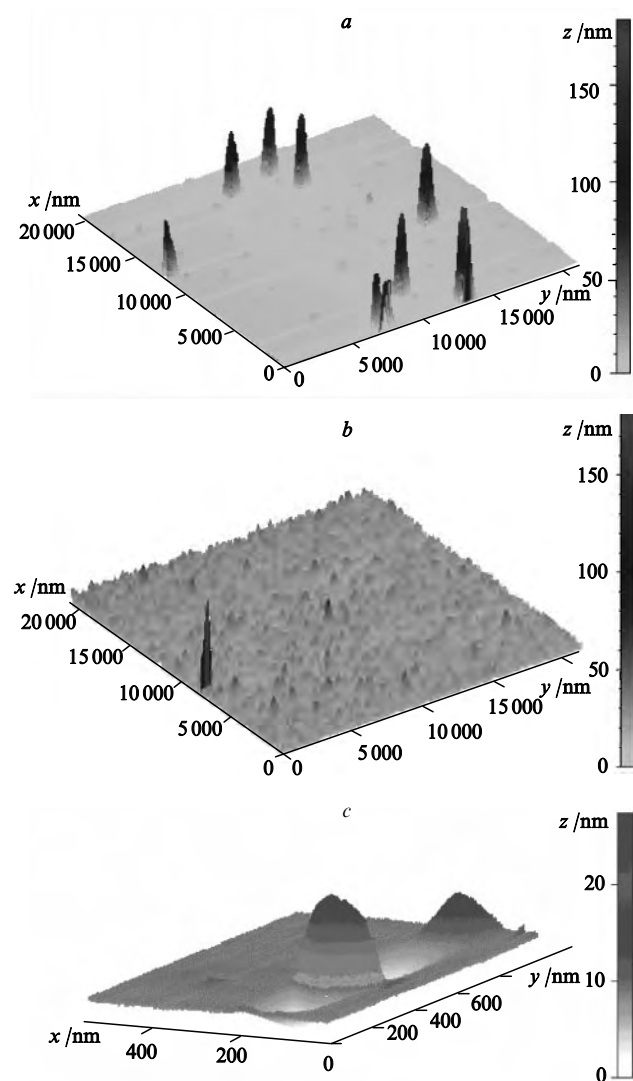


Figure 13. Typical surface reliefs of deposited TPP (a, b) and a separate island of deposited TPP (c).

Dimensions of sections: $20 \times 20 \mu\text{m}$ (a, b) and $600 \times 1000 \text{ nm}$ (c). The surface concentrations of TPP were 2.0×10^{-11} (a), 1.3×10^{-9} (b), $1.5 \times 10^{-12} \text{ mol cm}^{-2}$ (c).

continuous layer) are in good agreement with the structural features of mica-deposited TPP layers determined using atomic-force microscopy data on scales of tens and hundreds of nanometres. In other words, the structure of deposited porphyrin layers on submicro- and microscopic scales is determined to a higher extent by the interaction of the porphyrin molecules with one another and, to a lower extent, by the effect of the support (quartz or mica). This conclusion is very significant for the subsequent analysis because the photosensitised generation of singlet oxygen to the gas phase was studied taking TPP layers deposited on quartz as an example. In view of the foregoing, we assume that the pattern of variation of the flicker-noise parameters following an increase in N_{tot} , revealed in analysis of the structure of mica-deposited porphyrin layers, is similar to the pattern of variation of the corresponding parameters of the layers deposited on quartz.

In the analysis, we shall proceed from the data presented in Table 5, which demonstrate how the parameters L_1 and n , which characterise, on the nanometre and submicrometre scales, the structural organisation of the molecular crystals of porphyrins formed upon sputtering onto the quartz support, depend on the surface concentration N_{tot} of porphyrin. In particular, the decrease in the correlation length L_1 and the increase in the

Table 5. Quantitative parameters of deposited TPP layers characterised by flicker-noise spectroscopy.

$N_{\text{tot}} / \text{mol cm}^{-2}$	$L_1 / \mu\text{m}$	n	$h / \mu\text{m}$
5.2×10^{-11}	0.332	2.85	0.0182
1.3×10^{-9}	0.190	2.86	0.0236
2.4×10^{-9}	0.0623	3.32	0.0316

parameter n with an increase in N_{tot} in the film continuity region attest to the loss of correlation relationships in the film structure following an increase in the surface concentration of porphyrin. This fact may be responsible for the experimentally observed (see Fig. 11) decrease in the rate of generation of singlet oxygen to the gas phase with an increase in N_{tot} in the region of high surface concentrations ($N_{\text{tot}} > 10^{-10} - 10^{-9} \text{ mol cm}^{-2}$).

It has been noted above that the formation and the subsequent desorption of $^1\text{O}_2$ occur under continuous excitation of the deposited crystalline porphyrin layers. The experimental data obtained in recent years, most often using scanning atomic-force and tunnelling microscopy, confirmed the earlier hypotheses^{93,94} concerning the substantial length of the solid-phase surface regions (from several nanometres to hundreds of nanometres) involved in structural rearrangements after chemisorption of simple gases (H_2 , O_2) and the relative retardation (to times of $\sim 10^{-11} \text{ s}$ or longer) of the relevant electronic and conformational rearrangements.^{95,96}

As applied to the problem we are considering, this means that the structural features of the molecular crystalline porphyrin layers identified on nanometre scales by FNS analysis of atomic-force microscopy data^{91,92} and determining the transfer of the electronic-vibrational excitation in the surface layers can affect the rate of $^1\text{O}_2$ generation to a vacuum upon photoactivation of the surface layers of porphyrin crystals. In particular, a decrease in the degree of correlation of fragments of the crystal structure of the surface layers determined by a decrease in L_1 and an increase in n may be expected to result in lower effective rate constants k_1 and k_2 , whereas the constants k_3 and k_4 may, on the contrary, increase [see reactions (1)–(4)]. These assumptions, which imply the introduction of effective dependences $k_i = k_i(N_0)$, because the parameters L_1 and n vary with N_{tot} according to a known pattern (see Table 5), provide a natural interpretation for the concentration dependences $c_s = c_s(N_{\text{tot}})$ for the steady-state $^1\text{O}_2$ concentration presented in Fig. 11 (linear increase in c_s at low N_{tot} , reaching a maximum and a decrease at high N_{tot}) and allow one to estimate the parameters appearing in Eqn (9).

The correlation of the flicker-noise parameters with the surface concentration, which reflects quantitatively the degree of chaotisation of the deposited layer, is in full conformity with the trend of the rate of generation of singlet oxygen to decrease. Attention is drawn first of all by the non-trivial character of the result obtained, in particular, under the conditions of photo-excitation of deposited TPP layers considered here, the rate of generation of singlet oxygen is determined by the structural features of such layers revealed on scales exceeding by two orders of magnitude the proper atomic scale (fractions of a nanometre). Thus, in the heterogeneous photogeneration of $^1\text{O}_2$, the crucial role is played by the dynamics of redistribution and accumulation of the excitation energy of polymolecular porphyrin layers with the formation of local dynamic fluctuations sufficient for the generation of singlet oxygen molecules followed by their injection to the gas medium.

In connection with this result, we would like to note the following. The problems associated with the role of heterogeneity of the surface structure at the atomic or molecular level in heterogeneous catalysis have long been debated in the literature. From Temkin's standpoint (cited from Ref. 97), the surface of a heterogeneous catalyst is inhomogeneous in the adsorption capacity. According to Ostrovskii,^{98,99} the surface involved in heterogeneous catalysis is effectively 'homogeneous' in reactivity

of the chemisorbed phase ('chemadphase'), which is largely due to the diffusion transfer of components over the surface. Both suggestions are hypothetical because they are based on analysis of the kinetics of heterogeneous catalytic transformations (in particular, for the synthesis of ammonia) rather than on direct experiments on the measurement of surface diffusion or identification of surface heterogeneity on the basis of reactivity on the atomic level. The more so, because the formal kinetics equations give in both cases the same or similar dependences (see Ref. 98). The concept we develop here concerning the role of dynamic rearrangements of the surface (upon photoexcitation under conditions of heterogeneous catalysis) in the formation of local excitations determining the kinetics of chemical reactions and the efficiency of sorption-desorption processes, actually 'reconciles' these opposite viewpoints. Indeed, the effects of structural rearrangements with reorganisation of metastable fragments of a real surface with external excitation actually 'homogenise' the surface with dimensions of tens or hundreds of nanometres with respect to the kinetics of chemical processes taking place on this surface even when the surface is initially heterogeneous on the atomic level.

In conclusion, it should be noted that photosensitised generation of $^1\text{O}_2$ upon photoexcitation of deposited layers proved to be dependent on the chemical structure of the porphyrin molecules. This is demonstrated in Fig. 14, which presents the data on the steady-state concentrations of the singlet oxygen in the gas phase under conditions of photoexcitation of deposited layers of different porphyrins with the surface concentrations $N_{\text{tot}} \approx 10^{-11} - 10^{-9} \text{ mol cm}^{-2}$ corresponding to the maximum $^1\text{O}_2$ generation upon photoexcitation of TPP.

The reduced values of the steady-state concentrations are related to the corresponding value of the concentration of singlet oxygen upon TPP photoexcitation. It follows from Fig. 14 that the efficiency of generation of $^1\text{O}_2$ on the photoexcitation of different porphyrins can differ by an order of magnitude: the lowest activity is found for deuterioporphyrin, while the highest one is found for dicarboranylporphyrins CP3 and CP2.⁸¹ The apparent paradox of this result lies in the fact that the dicarboranylporphyrins CP3 and CP2, which form the most active deposited layers, were obtained by introducing carborane substituents into deuterioporphyrin molecules, which not only form the 'least active' layers for the photogeneration of $^1\text{O}_2$ but also

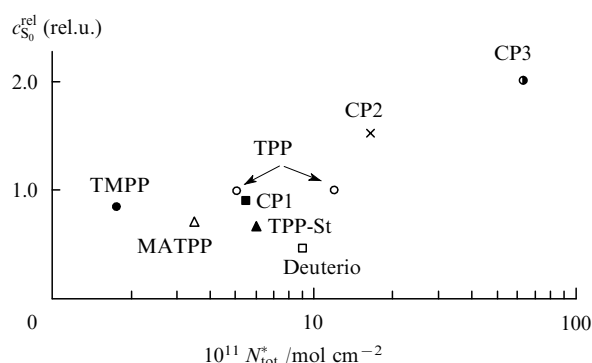


Figure 14. Comparative chart of the efficiency of generation of singlet oxygen by various porphyrins.

The following abbreviations are used: TPP is tetraphenylporphyrin, TMPP is tetra(*p*-methoxyphenyl)porphyrin, MATPP is 5-(*p*-amino-phenyl)-10,15,20-triphenylporphyrin, TPP-St is 5-(*p*-stearoylamino-phenyl)-10,15,20-triphenylporphyrin, Deuterio is dimethyl ether of deuterioporphyrin, CP1 is 1,3,5,8-tetramethyl-2,4-divinyl-6(7)-[(2-benzoyloxycarbonyl)ethyl]-7(6)-[2-(*m*-carboran-9-yl)oxycarbonyl]porphyrin, CP2 is 1,3,5,8-tetramethyl-6,7-di[2-(*o*-carboran-3-yl)carbamoyl]porphyrin, CP3 is 1,3,5,8-tetramethyl-6,7-di[2-(*m*-carboran-9-yl)methoxycarbonyl]porphyrin.⁵¹

demonstrate the least photosensitising activity (of all the porphyrins we studied) in the generation of singlet oxygen in homogeneous processes.⁸¹

The resolution of this paradox can be attributed to the specific structural organisation of porphyrin layers on the nanometre and submicrometre levels produced by packing of the porphyrin molecules deposited on a support under slow deposition conditions. Here, it is pertinent to note that the change in the angle (to 45°) at which the flux of porphyrin molecules is directed on the support has virtually no influence on the efficiency of the resulting layers towards photosensitised generation of singlet oxygen. This means that with the deposition conditions used, one can speak about realisation of quasi-steady-state conditions for the formation of film structure on different spatial scales, where the critical role is played by steric factors and intermolecular interactions. Evidently, the relatively bulky carboranyl substituents in the porphyrin molecules (especially in CP2 and CP3, whose molecules contain two such substituents) favoured the formation of less dense and 'more organised' (less 'chaotised') structures of deposited films under conditions of slow quasi-equilibrium deposition where a great free space ensured the possibility of more equilibrated adjustment of the porphyrin molecules getting on the surface to the structure of the layer. It is noteworthy that elucidation of the features of generation of singlet oxygen to the gas phase upon photoexcitation of deposited layers of various porphyrins allows a targeted search for efficient porphyrin-containing sensitising systems for liquid-phase oxidation of organic compounds.

VIII. Conclusion

The development of efficient catalytic systems based on immobilised metal complexes of porphyrins for specified chemical processes is faced with two types of problem. First of all, it is necessary to know the dynamics of an elementary catalytic event with allowance for all the key factors that influence the process kinetics (here, we mean the influence of electronic and conformation structures of MP, including the type of the central ion and side groups, the environment, and the dynamics of its fragments). Evidently, homogeneous catalyst systems based on MP and the systems with MP immobilised on soluble polymer supports should serve as model systems for the kinetic studies. It is necessary to take into account the role of the solvent and the functional groups (for example, amino acids) of the polymer in the catalytic activity of these systems. Recall that an amino acid residue (histidine) localised in place of one of the haem axial ligands regulates the enzymic activity of cytochrome *c*. A solvent that solvates the MP molecules can also affect appreciably the specific (per MP molecule) catalytic activity due to specific 'heterogeneity' of the solvation shell formed.

The second type of problem encountered in the development of immobilised metalloporphyrin systems is associated with elucidation of the role of the polymeric surrounding of MP. Although immobilisation of MP on a polymeric support results in all cases in lower mobility of the environment fragments near the MP, the choice of the matrix for immobilisation (polymers with functional groups, gels) leaves a place for variation of the local mobility of such fragments. The main point is to understand what positive effects can be attained and what type of labile environment (polar groups, amino acid residues, *etc.*) should be created.

A decrease in the mobility of fragments of the environment in the vicinity of the porphyrin ligand can bring about positive effects, in particular, decrease the probability that destructive factors would occur in the vicinity of the porphyrin ring. Perhaps, this accounts for the substantial increase (compared to the homogeneous case) in the turnover number of PMn immobilised on Nafion film until its degradation during non-chain hydroxylation of cholesterol.

It can be suggested that the search for new efficient porphyrin-containing polymeric systems will also continue along other routes. In our opinion, the main avenue of this research should be development of a fairly controllable labile environment of the porphyrin ligand — in conformity with the key principles of functioning of natural systems.

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Modern methods for the determination of physicochemical states of microelements in natural waters

E V Polyakov, Yu V Egorov

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Abstract. The state-of-the-art in studies on the determination of ion – molecular and colloidal forms of microelements in aqueous solutions is analysed. Instrumental and hyphenated methods for the determination of such forms of microelements as aqua-ions, complexes, true and adsorption colloids are considered. The bibliography includes 153 references.

I. Introduction

The methods used to monitor the concentrations of microelements in aqueous media, determine the sources from which they enter the hydrosphere and predict the dynamics of migration of separate physicochemical forms of microelements in the hydrosphere are of importance for studies in environment protection.^{1–5} A survey of publications on this subject over the past 10–15 years revealed considerable changes in the instrumentation and theoretical generalisation of methods used to determine the physicochemical state of microelements in aqueous media. We intend to analyse these changes in the present review.

The role of microelements in environmental objects is estimated by determining their concentrations in samples. If the content is low, concentration and separation methods based on distribution of microelements between phases, *viz.*, ion exchange, sorption, extraction, precipitation and coprecipitation, flotation, electroprecipitation, filtration, distillation, sublimation, dialysis, *etc.* are used, depending on the analysis scheme. Each of the methods listed above involves trans-phase interaction of separate chemical forms of a microelement; therefore, knowledge of the physicochemical state of a microelement in a sample is required in order to maximise its concentration and/or separation from admixtures. In the laboratory, this is achieved by converting the existing form of a microelement to a chemical form convenient for concentrating. Under field conditions, correction of the state of a microelement is often impossible or inefficient; therefore, the selection of a chemical analytical method for the determination requires independent information about both the chemical and

phase compositions of all the forms of the extracted microelement in the medium of interest.⁵

This problem has been studied insufficiently, so difficulties of a methodological nature exist. First, the physicochemical processes involving microelements and occurring in industrial and natural aqueous systems are complex indeed. Second, the development of the interphase distribution-based theory of reactivity in interrelated systems of ionic, molecular, colloidal and suspended forms of microelements in solution is in its infancy. Third, for field conditions (unlike laboratory conditions), there is a lack of approved methods for the determination of the chemical and phase compositions of microelements in natural aqueous media; approved test procedures and standard samples of their separate chemical forms are also unavailable.^{6–10} Fourth, it is necessary to consider the factors affecting the violation of equilibrium and/or steady states of microelements in a sample when it is transferred from a natural medium to a laboratory.^{1–9, 11}

Not only analytical chemists, but also heads of enterprises and bodies involved in environmental monitoring, are interested in development and perfection of methods for analysis of the physicochemical state of microelements in the hydrosphere.¹² The most promising methods result from combinations of column chromatography with high-performance spectrometric detection of separate elements. Analyses can be made less expensive by using combined methods of selective oxidation – reduction, coprecipitation, membrane extraction, dialysis and stripping voltammetry.^{12–18}

The relationships between the transport properties of microelements in the aqueous phase and the content of specific organic and inorganic components of soils or bottom sediments are studied using selective dissolution of groups of compounds, anion-exchange and distribution chromatography and ultrafiltration.^{1, 7, 9, 19} A sample can contain coexisting microelements as suspensions and colloids along with truly dissolved forms, including molecular, cationic and anionic complexes with inorganic and organic ligands.^{1, 19} Colloidal forms of microelements can be detected by sequential filtration of a liquid sample through membranes with pore sizes from 0.5 μm to 1 nm. Ionic compositions are determined by electrophoresis and ion-exchange chromatography after separation of the suspended fraction.^{20, 21}

In the early 1990s, the interest of researchers in the forms in which inorganic compounds exist in solutions increased due to the aggravation of global environmental problems (Fig. 1). As a result, new instrumental and combined physicochemical methods appeared; these methods made it possible to monitor not only the analytical concentrations of microelements in aqueous solutions, but also their chemical and phase compositions.

E V Polyakov Institute of Solid State Chemistry, Urals Branch of the Russian Academy of Sciences, ul. Pervomaiskaya 91, 620219 Ekaterinburg, Russian Federation. Fax (7-343) 249 35 91. Tel. (7-343) 274 48 14. E-mail: Polyakov@ihim.uran.ru

Yu V Egorov Urals State Technical University USTU-UI, ul. Mira 19, 620002 Ekaterinburg, Russian Federation. Fax (7-343) 274 38 84. Tel. (7-343) 275 48 92

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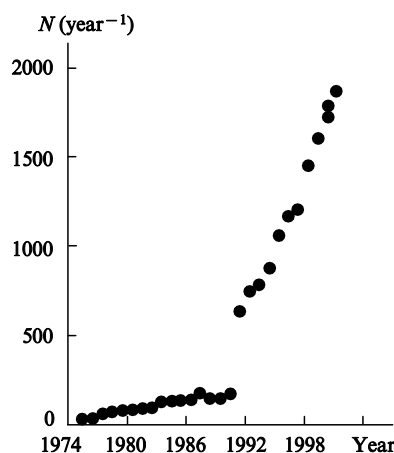


Figure 1. Data from the Institute of Scientific Information (USA) on the worldwide statistics of publications dealing with studies on the chemical state of inorganic compounds in solutions. N is the number of papers on the subject.

II. Instrumental methods

1. Time resolved laser fluorescence spectroscopy

Time Resolved Laser Fluorescence Spectroscopy (TRLFS) is a popular modern instrumental method used to determine the state of microelements in solutions.^{22–26} Neodymium lasers with a pulse energy of 2.5–2.7 mJ and adjustable frequency are the main elements of setups that implement this method. For example, the wavelength of 266 nm was selected to excite the fluorescence of UO_2^{2+} ions; pulse excitation is followed by a decay of the fluorescence signal in the wavelength range from 407.0 to 634.0 nm. This is measured by scanning at discrete times in the range from 0.1 to 15 μs . Each spectrum in this time range is obtained by averaging the results from 100 laser-induced excitations.²² This method was used to determine the interaction between uranium(VI) ions and silicic acid in model solutions of sodium perchlorate. Analysis showed²² that the red shift in the fluorescence spectrum is caused by chemical reaction of UO_2^{2+} with $\text{Si}(\text{OH})_4$.

According to the theory of fluorescence signal formation, the overall amplitude (A_0) and the amplitudes of signals from various complexes (A_i) are related by the following expression:

$$A_0 = \sum_{i=1}^n A_i e^{-t/\tau_i}, \quad (1)$$

where t is the signal relaxation time and τ_i is the characteristic time of fluorescence decay. It was shown²² that uranyl silicate complexes comprise species of a single type with the ratio $\text{UO}_2:\text{UO}_2\text{Si}(\text{OH})_3^+ = 1:0.95$. By decomposing the fluorescence spectrum into components, one can determine the stability constants of complexes directly in solution (without concentrating). By combining TRLFS and thermodynamic simulation methods, it is possible to use characteristic fluorescence spectra and τ_i values in order to identify uranium complexes (Fig. 2), including $\text{Ca}_2\text{UO}_2(\text{CO}_3)_3(\text{aq})$ in mine waters,²³ and determine the compositions and stability of complexes of trivalent actinides with natural analogues of fulvic and humic acids in model solutions^{24,25} and in hot brines.²⁶ The theory and potential of the TRLFS method are described in detail elsewhere.²⁷

2. Laser induced breakdown spectroscopy

Laser Induced Breakdown Spectroscopy (LIBS)^{28–30} is among the most promising instrumental methods for the study of the state of inorganic compounds in solutions. The method is based on controlled excitation of characteristic emission spectra. Plasma

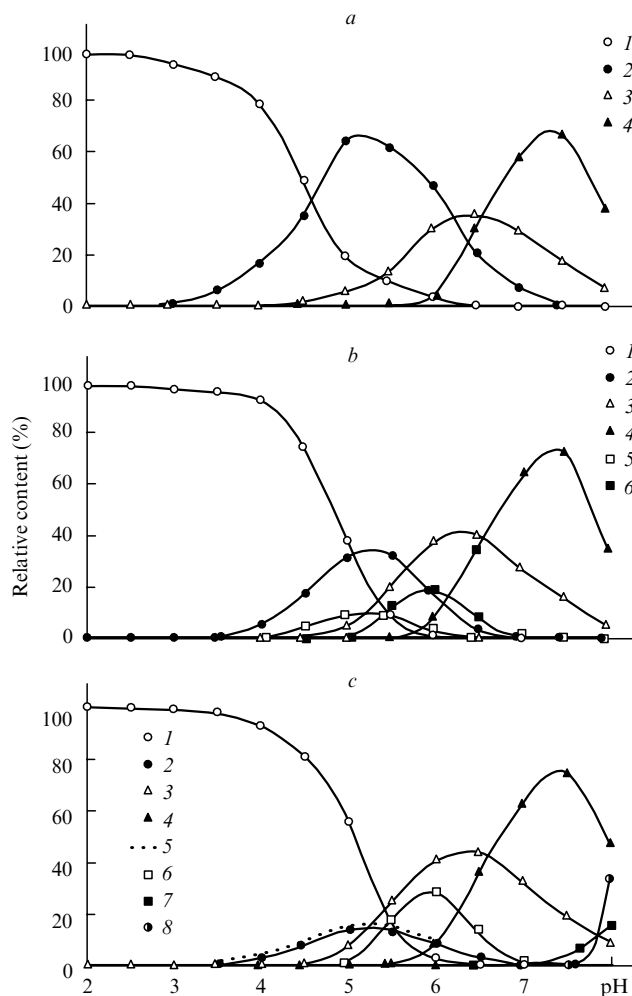


Figure 2. Results of TRLFS determination of the compositions of uranium complexes (a–c);²² (1) UO_2^{2+} , (2) $\text{UO}_2\text{OSi}(\text{OH})_3^+$, (3) $\text{UO}_2(\text{OH})_2(\text{aq})$, (4) $(\text{UO}_2)_2\text{CO}_3(\text{OH})_3^-$, (5) UO_2OH^+ , (6) $(\text{UO}_2)_3(\text{OH})_5^+$, (7) $(\text{UO}_2)_2\text{CO}_3^{2-}$, (8) $\text{UO}_2(\text{CO}_3)_3^{4-}$.

with a temperature of 2500–25 000 K is formed by focusing a pulsed laser beam on the solution studied; the beam has a power density of $10^{15} \text{ W cm}^{-2}$ and creates an electrostatic field of up to $10^{11} \text{ V cm}^{-1}$ in the focal plane.²⁸ As the plasma temperature is lowered and the intensity of the continuous spectrum from the microsample within the sample decreases, characteristic lines of elements appear in the emission spectrum; they are analysed using a special detector.

The LIBS method is used to perform elemental analyses of solid samples (alloys, soils, minerals, microelectronic devices), liquids (milk) and gases (air, aerosol particles). The application of this method to analysis of liquids opens up new prospects in chemical analytical studies.^{28,30} Transformation of an aqueous solution or droplet-sized samples to plasma by a laser beam with a wavelength of $\sim 500 \text{ nm}$ with beam focusing makes it possible to obtain signals from microelements that exist as colloidal phases or adsorption colloids (in this case, the intensity of emission lines is 10^3 times higher than that from ionic and molecular forms of the same element).

The use of the method under consideration in studies of uranium, americium and plutonium migration with ground waters makes it possible to determine the amounts of colloidal fractions of these elements in complex natural objects. By varying the power of the laser beam, it is possible to determine the phase compositions and sizes of colloid particles of hydroxycarbonates of certain transuranium elements [e.g., $\text{Am}(\text{OH})\text{CO}_3$] at their

solution concentrations of 10^{-5} – 10^{-6} mol litre $^{-1}$. The LIBS method is most sensitive to low concentrations of colloid particles typical of natural waters. In the case of high concentrations of such particles (*e.g.*, in aqueous carbonate solutions of uranium and plutonium), the intensity of emission lines of an element decreases due to secondary oxidation of metal atoms in hot plasma and due to multiple scattering effects. To determine the phase composition and size distribution of colloid particles, it is recommended that the LIBS method be combined with other colloid fractionation methods.^{28,29}

3. Laser photo-acoustic spectroscopy

The potential of a new highly sensitive method for the determination of the state of ionic and colloidal forms of microelements in solutions, *viz.*, laser photo-acoustic spectroscopy (LPAS), is based on the absorbing ability of species being studied and on the power of the available pulse laser with adjustable wavelength.³¹ The intensity of the photo-acoustic signal in this method is proportional to the power density absorbed by particles. The method is based on the determination of characteristic changes in the volume of molecules of a compound of interest (that are in contact with solvent molecules) caused by emission of thermal energy upon transition from an excited state to a ground state following selective absorption of laser irradiation quanta.

The selectivity of LPAS is determined, first, by the high conversion efficiency of absorbed energy of monochromatic irradiation into thermal energy; second, the possibility of recording (using high-precision piezoelectric sensors and detection circuits with high time resolution) a sound wave that appears due to changes in the volumes of molecules upon their deactivation.^{31–38} In addition to a laser, the main elements of a photo-acoustic registration system comprise a cell for the solution being studied, a transducer of ultrasonic waves to voltage pulses, and an electronic system for starting the registration scheme, digitising and storing of data that arrive from the ultrasonic transducer. The construction of miniaturised photo-acoustic cells allows one to study microsamples (down to 10^{-7} dm ^{3}) in real-time mode.^{32,33}

The LPAS method can be used to determine a microelement concentration down to 5×10^{-6} mol litre $^{-1}$ and to monitor its variations in time, both in homogeneous and heterogeneous samples. The LPAS method has the advantage that it allows one to determine the physicochemical state of elements in aqueous solutions simultaneously containing molecular forms as well as true and adsorption colloids of microelements.^{31,35–38} This method was used to study the state and sorption behaviour of Cr(VI) microquantities on hematite under competitive sorption of phosphate ions,^{35,39} to determine the concentration and sizes of Tc(IV) colloid particles^{36,38} and to reveal the physicochemical state and nature of Np(IV) colloids.³⁷

4. X-Ray absorption spectroscopy

X-Ray spectroscopic absorption methods with the use of synchrotron radiation are widely used to study the nearest environment of atoms of a microelement in aqueous and heterogeneous electrolyte–solid systems.^{40–67} Data on the structure and short-range order of microelement compounds in a suspended adsorbed state can be obtained by EXAFS (Extended X-Ray Absorption Fine Structure) and XANES (X-Ray Absorption Near Edge Structure) methods.⁴¹

The EXAFS method provides extended data on the local environment of an absorbing atom, namely, the type and number of its nearest neighbours, interatomic distances in a sphere with a radius of 5–6 Å; furthermore, information on bond angles can be obtained based on multiple diffusion of photoelectrons and on data for near-edge absorption of several different elements in a compound studied. The EXAFS oscillation structure originating from diffusion of photoelectrons on atoms of the local environment is usually observed in the range of 100–1000 eV above the absorption edge.

The XANES method is used to study the electronic structures of compounds. Using this method, one can obtain information, *e.g.*, about the oxidation state of the absorbing atom and on the symmetry of its coordination sphere. An XANES structure occupies the range from ~ 50 eV before the absorption edge to 100–150 eV after the edge. The resonance bands generated by electron transitions from the core level to vacant levels up to removal of the electron from the atom (photoionisation) are comparatively narrow; the bands after the absorption edge, which correspond to electron transitions to quasi-bound states, are broader.

Both methods are used to study the state of elements in bulk samples and in surface phases that are formed due to sorption processes involving microelements and surface sorbents, *i.e.*, soils and colloid particles.

If traditional instrumental methods are used to study the state of microelements in a liquid phase (*e.g.*, UV and IR spectroscopies), distinguishing individual signals corresponding to a compound of interest from those corresponding to the support without their chemical separation is the main difficulty.⁴¹ After chemical separation, it is incorrect to apply data on the composition of chemical forms of a microelement to the original natural solution or heterogeneous system.

The EXAFS method is devoid of such restrictions, because, as noted above, the spectra contain information about the chemical environment, interatomic distances and the number of the closest neighbours of a microelement atom.⁴¹ In fact, it was noted in an EXAFS study on the identification of the state of hardly soluble lead compounds in soil that it was possible to decrease the detection limit of chemical compounds (below 10^{-3} mass%) at a relative measurement error of 5%.⁴¹

By combining the EXAFS method with free boundary electrophoresis, it is possible to reach sensitivity of 10^{-5} – 10^{-8} mol litre $^{-1}$. It was shown using these methods that the sorption of uranium by hematite at pH 4.5 is caused by partial binding of carbonate (hydrogencarbonate) anions with uranyl cations in monomeric carbonate uranium complexes. However, it is dimeric complexes that are responsible for the sorption of uranium on the surface around pH 6.5. Based on this fact, it was concluded that the mobility of U(VI) tricarbonates complexes in ground water is low.⁴³

Studies on the state and sorption behaviour of actinides with different oxidation states showed that their mobilities were considerably affected by the redox potential of the solution. Foster *et al.*³⁵ and Antonio *et al.*⁴⁴ developed a procedure to determine the formal redox potentials of neptunium in soil and ground waters for the Np(IV)/Np(V) and Np(IV)/Np(III) pairs and formulated the objectives for subsequent EXAFS studies on the sorption behaviour of neptunium complexes in natural waters. This method was used to study the coordination environment of Cd(II) sorbed by goethite in the presence of sulfate, oxalate and citrate ions and anions of humic acids; it was shown that cadmium atoms are surrounded by six oxygen atoms in the first coordination sphere and by two iron atoms in the second sphere.⁴⁵ In oxalate and citrate solutions, precipitation of a sparingly soluble cadmium compound on goethite facets occurs. A drawback of the latter study⁴⁵ is that the results obtained for cadmium concentrations of 10^{-3} – 10^{-4} mol litre $^{-1}$ in solution were extrapolated to the region of microconcentrations typical of soil and ground waters.

The EXAFS method was used to obtain structural information on the composition of cadmium, zinc and copper complexes with organic ligands in non-aqueous solutions;⁴⁶ data on the composition and structure of chloride Cu(II) complexes at ordinary and elevated temperatures in solutions simulating sodium chloride thermal water by matrix elements are reported by Collings *et al.*⁴⁷ It was shown that copper chloride complexes are not formed in the temperature range of 25–75 °C at sodium chloride concentrations in the range of 0.2–2.2 mol litre $^{-1}$; under hydrothermal conditions, the CuCl^+ and CuCl_2^0 species

start to predominate as the temperature is increased from 125 to 175 °C; at chloride concentrations up to 5 mol litre⁻¹ in the temperature range of 25–75 °C, the CuCl₃⁻ and CuCl₄²⁻ species predominate, but the CuCl⁺ and CuCl₂⁰ species start to predominate again at 175 °C (due to the formation of Na–Cl ion pairs).

The EXAFS method was used to study the state of AuCl₃ in chloride solutions.⁴⁸ Sherman *et al.*⁴⁹ analysed the state of different-valent tin chloride complexes in 0.5–2.5 mol litre⁻¹ sodium chloride solutions in the temperature range of 25–250 °C. Data on the coordination of copper, zinc and arsenic ions in sodium hydrosulfide solutions were reported.^{50, 51} Seward *et al.*^{52–54} used EXAFS to determine the state of AgNO₃, CdCl₂, AgClO₄ and SrCl₂ in aqueous solutions. Mosselmans *et al.*⁵⁵ studied the coordination of molybdenum, cobalt and cadmium aqua-complexes; the state of antimony and yttrium in chloride solutions was studied in a number of works.^{47, 48, 56, 57} The compositions of metal complexes (in particular divalent and tetravalent tin complexes) found by EXAFS sometimes noticeably differ from the compositions obtained by thermodynamic simulation:⁴⁹ in the chloride concentration range 0.5–2.5 mol litre⁻¹ and the temperature range of 25–350 °C, an increase in chloride concentration increases the numerical value of factor *n* in the formula SnCl_n²⁻ⁿ from 3.4 to 3.9, which suggests that the SnCl₃⁻ and SnCl₄²⁻ complexes predominate. If the temperature has been increased from 250 to 350 °C, the SnCl₄²⁻ complexes are mainly present. The SnCl₆²⁻ complex predominates in oxidising media; this implies higher solubility of SnO₂ (in comparison with that obtained by thermodynamic calculation) in this medium and the possibility of efficient transport of di- and tetravalent tin in hydrothermal processes.

It is particularly efficient to use EXAFS spectroscopy in combination with molecular dynamics methods in studies on the polymerisation of aqua complexes in solutions, because it is possible to register changes in the inner coordination sphere (metal–ligand–metal) directly. In this way, the polymerisation of SrCl₂ in concentrated chloride solutions was confirmed directly.⁵²

This method is efficient in studies on ion–molecular and other forms of elements in solutions. However, its use in ecological studies of natural waters that have complex microelement compositions is presently limited by the low sensitivity and selectivity, as well as by the necessity of preliminary withdrawal and conservation of samples.

The XANES method, which is being intensely developed at present, is much more sensitive.^{58–67} Using this method, one can analyse the chemical bonds between atoms, oxidation states and chemical compositions of compounds formed by microelements at their solution concentrations of about 10⁻⁶ mol litre⁻¹. The theory of the method has been described in a number of publications.^{65–67} The XANES method was used to obtain data on the sorption behaviour of lead in soils,^{62, 63} the physicochemical state of arsenic in bottom sediments,^{59, 60} the mechanism of Cr(VI) reduction in natural solutions⁶¹ and also to study the state and sorption behaviour of separate valent forms of plutonium in the water–soil system.⁶⁴

5. Mass spectrometric methods

The Laser Microprobe Mass Spectrometry (LMMS) and especially the Static Secondary Ion Mass Spectrometry (SSIMS) methods are used as direct instrumental methods for determination of the physicochemical state of microelements that predominantly exist in the adsorbed state. The characteristic mass spectra of simple ions and ion clusters serve as the main source of data on the chemical composition of compounds being studied.⁶⁸

The use of LMMS mass spectrometers with Fourier transform of the signal provides a mass resolution of 10⁵ with a sensitivity of about 1 ppm for separate ions.⁶⁸

The instrumental potential of Secondary Ion Mass Spectrometry (SIMS) for chemical analysis of microquantities of inorganic compounds is more versatile, since the signal results from

bombardment of the surface of a sample of interest by a primary ion beam (*e.g.*, Ar⁺, O⁻) with an energy of several kiloelectronvolts. This increases considerably the intensity of the secondary beam of ions (both positive and negative) from the sample and the overall sensitivity of the method. The static version of this method, *viz.*, SSIMS, employs a low-intensity beam of primary particles, thus making it possible to study compositions of compounds with extremely high mass numbers. The sensitivity of the SSIMS method can range within 10²¹–10¹⁵ atoms cm⁻². Time of Flight Static Secondary Ion Mass Spectrometry (TOF SSIMS) makes it possible to identify the molecular composition of a compound of interest based on the set of secondary ion clusters, which is unique for each compound.^{68, 69} Therefore, when analysing biological and natural solid samples, compounds can be identified by matching the sample composition with the secondary ion spectrum.⁶⁸

Mass spectrometric methods are used in high-precision studies on the molecular composition of microcomponents with concentrations below 10⁻⁶ mol litre⁻¹. These methods are primarily used to assess the state of adsorbed compounds. A mass spectrum obtained by SSIMS is a superposition of spectra corresponding to original molecular states of microelements and to their reaction products with stable ions in the gas phase. In the LMMS method, the possibility of obtaining mass spectra of molecules of interest is based on the specific features of the signal formation. An advantage of the LMMS method is that it provides a relatively high spatial resolution on the sample surface (0.1–10 μm); the SSIMS method makes it possible to perform sequential in-depth analysis of a sample at molecular resolution. Owing to the high signal-to-noise ratio, the LMMS method provides direct (that is, without the use of composition standards) data on the molecular composition of samples. To obtain such data by SSIMS, one has to compare the mass spectra of a sample in question with the mass spectra of samples with standard compositions. Evidently, the two methods complement each other. They can be modified in order to study the chemical composition of microelements in solution, provided that the relationship between the composition of the solid sample being analysed and the composition of the original sample is established when the solution is being prepared for analysis.

The problem of sample preparation for mass spectrometric studies on the composition of complex compounds of microelements in solutions is solved, to a considerable extent, by using Electrospray Mass Spectrometry (ESMS).⁷⁰ It is used for quantitative determinations of metal ions in inorganic, organometallic and complex compounds and is based on a genuine way of generating ionic clusters.

The experimental value of the ESMS method is that electro-spraying of a sample transfers ions and molecules existing in the original solution to be studied to the gas phase. This occurs due to two main processes, *viz.*, creation of charged micro-droplets of the solution and transfer of ions of elements from the micro-droplets to the gas phase. The original information on the chemical composition and oxidation state of an element is preserved in these processes. Charged micro-droplets are formed on passing a solution of interest through a conductive capillary with an inner diameter of ~ 100 μm kept under a 2–4 kV voltage relative to the counter-electrode, as a rule, the mass spectrometer sampler (the tool for introducing a sample into the mass spectrometer). Under an electric field gradient, separation of charges occurs in the surface layer of electrolyte micro-droplets; as a result, it acquires an excess positive charge leading to intense carryover of positive ions from the surfaces of micro-droplets and evaporation of the surface layer of the liquid meniscus in the capillary (Taylor's cone).⁷¹ Owing to the electrophoretic motion of the liquid in the near-surface region, the charged surface layer stretches as a thin (1–10 μm) fibre towards the sampler of the mass spectrometer, breaks into positively charged micro-droplets and forms a cone in a stable electro-spraying mode.⁷²

The field of application of ESMS includes studies on molecular reactions in the gas phase and formation of bioorganic and organometallic complexes in non-aqueous solvents.⁷⁰ The drawbacks of the method include the complexity of sample preparation from natural objects and the necessity of maintaining reproducible instrumental conditions when mass spectra are recorded. An advantage of the method is that information on the oxidation states of metals (microelements) in aqueous solutions and on the presence of mono- and polyatomic anions (nitrates, thiocyanates, chromates, permanganates, oxohalides, various sulfur anions, *etc.*) and transition metal complexes with inorganic and organic ligands can be obtained. The limitations of the quantitative version of this method include the dependence of the reproducibility and sensitivity in the determination of clusters of microelements on the solution electrical conductivity and the narrow signal range (3–4 orders of concentration). These limitations can be eliminated by simultaneous spraying of an additional background electrolyte solution. This will make it possible to determine the chemical composition of microelements at concentrations $\sim 10^{-8}$ mol litre⁻¹ (see Ref. 70).

Determination of the state of microelements by ESMS in real natural solutions is complicated by the noise that appears in the mass spectra. Preliminary separation of elements and their chemical forms, *e.g.*, by high-performance liquid chromatography and other methods, is used to increase the signal-to-noise ratio.^{70, 73}

6. Voltammetry methods

Electrochemical methods are among the most convenient instrumental methods for the study and determination of the ion-molecular state of microelements in natural aqueous solutions; of these, Stripping Voltammetry (SV) is worth special attention.⁷⁴ The main advantage of this method in studies of natural waters is its selectivity with respect to separate chemical forms of microelements and low detection limits of microelements. The relatively low cost of analysis, the possibility of its automation and the small size of the instruments make it possible to use the stripping voltammetry under field conditions, in particular, in prolonged continuous analyses and when composing distribution maps of separate forms of microelements in seawater and fresh water as part of above-water and underwater experiments.⁷⁴ After preliminary concentration of a microelement from the aqueous phase, the SV method can be combined with subsequent cathodic or anodic dissolution of the analyte accumulated on the working electrode.

The multi-element version of the accumulation method makes it possible to reach detection limits of microelements in seawater as low as 10^{-10} – 10^{-12} mol litre⁻¹ (Ref. 74). Up-to-date polarographs are three-electrode systems (working electrode, auxiliary electrode and reference electrode); a dropping mercury electrode, a hanging mercury drop electrode or a thin rotating film mercury electrode is used as the working electrode. In the former case, measurements are carried out on a continuously renewed surface of the working electrode; this is advantageous as high analysis reproducibility is ensured. The second version is usually implemented by electrodeposition of mercury on surfaces of glassy carbon, graphite, metallic conductors (gold, iridium), graphite fibre; this enhances the sensitivity owing to high ratios of the working electrode surface to the solution volume.

In recent years, mercury (deposited on carbon fibre or iridium wire) and gold microelectrodes with sizes < 10 μ m have become more and more popular. They are characterised by a much weaker effect of capacitance current and an increased signal-to-noise ratio; these electrodes allow microelement concentrations $< 10^{-10}$ mol litre⁻¹ to be determined owing to an improved efficiency of deposition on the working electrode and the suppression of diffusion effects.

Stripping voltammetry with anodic polarisation (Anodic Stripping Voltammetry, ASV) is used successfully to analyse relatively high (due to adverse effects of overlapping of signals from interfering elements) concentrations of copper, cadmium, lead, zinc and thallium in seawater.⁷⁴ It is recommended to

increase the negative potential in the metal deposition stage so as to make it 0.3–0.4 V higher than the reduction potential. After accumulation of a microelement of interest as an amalgam in the reduction stage, subsequent anodic polarisation of the working microelectrode results in oxidation of the reduced form of the microelement, thus providing both quantitative and qualitative information (as the oxidation potential is a specific characteristic of an element) about the metal on the electrode. The method requires additional analytical operations, *viz.*, calibration and standardisation of measurements.

The SV version with cathodic polarisation and adsorption of the sample (Adsorptive Cathodic Stripping Voltammetry, AdCSV) is a more sensitive method used as an alternative to traditional inversion voltammetry. The sensitivity is increased by introducing a specific ligand into a solution. The role of the ligand is to form a relatively stable complex ion with the microelement being determined which can be adsorbed on the working electrode surface at constant potential and then be involved in the reduction process. The reduction is generally carried out with linear sweep of the signal amplitude; if the discharge electrochemical stage is reversible, a square high-frequency AC component is applied. This suppresses the interfering capacitance currents, slows down the competing step of adsorbed oxygen reduction and shortens the analysis duration. The techniques described above create conditions for reaching very low detection limits of metals (10^{-12} mol litre⁻¹ for cobalt, platinum, titanium) in seawater.⁷⁴

The high sensitivity for trace amounts of compounds makes SV a convenient method to study forms of existence of microelements in aqueous solutions. For example, the concentrations of many transition metals (cobalt, copper, iron, zinc) in natural water (river, lake, seawater) are generally extremely low but they can considerably affect biochemical processes involving hydrobionts.^{75–77} Simple aqua ions are the most bioactive and toxic forms as they easily penetrate cell membranes of phytoplankton and algae. Complexes with organic ligands (humic and fulvic acids, ethylenediaminetetraacetic acid, *etc.*) are devoid of this ability, and the susceptibility of micro-organisms to these metals decreases if such ligands are present in aqueous solutions.

In studies on exchange processes, the SV method is one of the few instrumental methods that make it possible to determine the valence of microelements in solutions, as well as the fractions of separate microelements in the free form and as organic complexes at concentrations around 10^{-9} mol litre⁻¹ in natural water (see Refs 78–92). For example, it was shown using the AdCSV method that the natural state of Cr(VI) in Mediterranean Sea water matches the data from thermodynamic calculations of the concentration of the most stable form of chromium, CrO_4^{2-} , in an oxygen-saturated solution. However, determination of the overall chromium content in seawater after decomposing its organic complexes by UV irradiation and sorption separation of Cr(III) showed that it contains tri- and hexavalent chromium ions (Fig. 3). The presence of trivalent chromium is explained by the photochemical reduction of the CrO_4^{2-} ions in the seawater surface layer.⁷⁹

The ratio of free metal forms to those bound in complexes can be found using the ASV and AdCSV methods. The equilibrium concentrations of an aqua ion and its labile complexes with inorganic and organic ligands are determined using the ASV method. The AdCSV method is used to establish the chemical nature of organic ligands. To do so, it is necessary to provide conditions for competitive complexation of an added ligand (with a known complexation scheme) and natural ligands in a solution of interest. Based on results of concentration measurements for the free and bound forms of a microelement, the concentration complexation constant with natural ligands is calculated. The true compositions of organic (primarily bioorganic) complexes of the majority of microelements in seawater and fresh water are unknown; algae and products of phytoplankton biodegradation are believed to be the main sources of organic ligands.⁷⁴ For example, it was found by means of SV that over 99% of dissolved

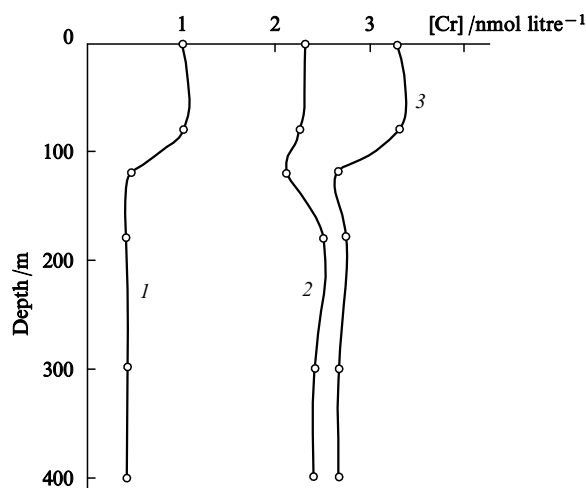


Figure 3. Concentration profiles of Cr(III) (1), Cr(VI) (2) and total chromium (3) at different depths of the western part of the Mediterranean Sea determined by AdCSV.⁵⁵

iron is bound with organic ligands and is characterised by an arbitrary complexation constant of $\sim 10^{18}$. Using SV combined with direct determination of microelement concentrations and preliminary filtration-based fractionation, it is possible to determine the ratio of ion–molecular and colloidal forms of a metal of interest.

III. Hyphenated methods

At present, studies on the physicochemical state of microelements in solutions combining techniques for separation of individual microelement forms with high-sensitivity instrumental methods for detection of separated microelements have become one of the leading directions.^{7,9,93–102} In favour of this is the appearance of high-sensitivity instruments for electrochemical, emission and mass spectrometric analyses.

1. Chromatographic methods

Numerous procedures have been developed based on chromatographic methods including a procedure for the determination of hexavalent chromium and tungsten by extractive isolation of their ternary complexes with rutin (quercetin-3 β -rutinoside) in the presence of cetyltrimethylammonium and procedures for determination of the valence and chemical composition of molecular and cationic complexes of tri- and pentavalent arsenic (mono- and dimethylarsonium, arsenobetaine and some other arsenic compounds), organic and inorganic derivatives of tetra- and hexavalent selenium, divalent lead and mercury, di- and tetravalent tin, tri- and hexavalent chromium.¹⁰³ The multistage separation and independent determination of the forms of state of these microelements in aqueous media are carried out by automated control of the chromatographic process, using standard samples of the states and compositions of microcomponents in the medium of interest or in some other similar medium. The sensitivity of hyphenated methods with respect to separate chemical forms can reach $10.0\text{--}0.01\text{ }\mu\text{g litre}^{-1}$ for media in which the chemical compositions of the complexes to be analysed are known beforehand.

In their review, Vanhaecke and Moens⁹⁴ analysed works published in the past decade and dealing with chromatographic methods with mass spectrometric detection for the determination of the chemical composition of microelements in natural objects. Of these, column separation with reversed phases, ion-exchange sorption, ion pair sorption and gel filtration are the most popular methods. The latter method can be used to determine simulta-

neously the behaviour and degree of complexation of metal ions in natural waters in the presence of dissolved organic compounds. This is achieved by combining gel filtration and mass spectrometry with simultaneous determination of the total carbon content (e.g., by UV spectroscopy) in the fractions eluted from a chromatographic column.⁹⁴

Today, the analytical instrumentation market offers transportable toolkits for the analysis of the chemical state of separate microelements. A toolkit comprises a microcolumn of specific type for high-performance liquid chromatography (HPLC) combined with a mass spectrometer; this allows one to determine the concentration of separate valence forms of such microelements as chromium, selenium and arsenic.

Hyphenated methods based on chromatography are beginning to compete with traditional radiochemical methods for the analysis of the isotopic and elemental composition conventionally used in technologies of processing and burial of spent nuclear fuel. Using the methods considered here, one can determine the forms of migration of both radionuclides corresponding to the middle of the Periodic System (s-, p-, d- and f-elements) and trans-actinide elements.^{104–110} The possibility of using inductively coupled plasma mass spectrometry and thermal-ionisation mass spectrometry was shown: preliminary HPLC separation of ionic complexes of uranium, americium, and curium is followed by determination of the $^{241}\text{Am}/^{238}\text{U}$ and $^{244}\text{Cm}/^{238}\text{U}$ isotope ratios in separate chemically pure fractions with the use of the double isotope dilution method.¹¹¹ The chemical separation of uranium and plutonium was performed in an anion-exchange column; that of americium and curium, by HPLC (stationary phase, Nucleosil SA; 0.14 M 2-hydroxy-2-methylbutyric acid, pH 4.1 as the eluent). The use of the hyphenated method provides a relative determination error of 2.5% in the isotope ratio range from 1 to 0.001.

Hyphenated methods are generally used with standard samples of states of the microelements studied (e.g., alkyl derivatives of tin, mercury and arsenic). Their kinetic inertness makes it possible to neglect the effects of foreign components, that is, potential ligands and competing complexing agents, when an aliquot of the standard is added to the solution under study.¹¹²

An example of the use of hyphenated methods for determining the states of labile organic and inorganic metal complexes is given by Pesavento *et al.*¹¹³ who studied the formation of manganese, nickel, cadmium, and copper complexes with ligands of unknown composition. The Chelex-100 chelating resin with iminodiacetate groups was used as a selective ion exchanger. The state of ions of these elements in seawater (samples from Ligurian Sea, Italy) was determined by ion-exchange titration of the solution with a selective ion-exchange resin under static conditions. Based on the results of titration, the content of the elements sorbed by the ion-exchange resin was determined from the ratio of the volumes of the solution and the resin. The total concentrations of an element in a system with standard composition and in a natural system being studied, as well as the coefficient of side reactions were found from experimental data using the Schubert method. The agreement between the results of measurements served as a criterion that the degree of complexing of a microelement with ligands of unknown nature in seawater was determined correctly. Seawater was initially purified from suspended matter and (partially) from colloidal particles. Therefore, one can characterise the ratios of simple and complex ions of manganese, nickel, cadmium and copper in seawater, but not the composition and nature of these complexes, based on information obtained. Pesavento *et al.*¹¹⁴ also studied the physicochemical state of aluminium in potable water by ion exchange titration and found that very stable aluminium complexes with complicated composition were present at pH 6–7 in addition to aquahydroxo complexes.

The application of chromatography-based hyphenated methods makes it possible to carry out detailed studies on the state of microelements, identify their oxidation states and determine their environment in both simulated and natural aqueous systems.^{114–117}

2. Electrophoresis

Methods for the determination of the state of stable and radioactive microelements based on the analysis of electrophoretic mobilities of ions and colloidal particles in a free electrolyte and in a porous medium have been used for a long time. Both theoretical and methodical approaches have been developed for these methods.^{7,9,95,96} The application of such methods has broadened considerably over the past decade. Instruments based on the principle of capillary electrophoresis are now commercially available.^{118–121} These instruments are successfully used in radiochemistry and in ecological and biochemical studies in order to determine the charges of individual ions, oxoanions, as well as inorganic and organic metal complexes.^{119–121}

Separation by capillary electrophoresis is based on differences in the migration of ions of microelements along a capillary filled with a solution of an electrolyte. The capillary diameter is close to the thickness of the dense part of the double electric layer at the capillary walls; therefore, the resulting mobility of ions in the capillary is concurrently affected by the electrophoretic and electroosmotic flows of the electrolyte.

Two versions of capillary electrophoresis are used, *viz.*, zone electrophoresis in free electrolyte and electrokinetic micellar chromatography. The first version is used to separate individual chemical forms of a microelement in ordinary solutions. In this case, separation depends primarily on the ratio of the charge of a solvated ion to the size of its solvate shell. The second variant is intended for separation of microelements in micellar (colloidal) solutions; its efficiency is mainly determined by the micelle charge and the mechanisms of distribution of the molecular forms of the microelement between the electrolyte and micelles.¹²⁰ Capillary electrophoresis is particularly efficient if the element being determined is present as both charged complexes and colloidal particles. As in the case of free boundary electrophoresis, the efficiency of separation of individual microelement forms is strongly affected by kinetic factors of the reaction of the complex-forming ion with the ligands.^{112, 119, 120}

A number of publications are available^{119–122} on the results of separations and determinations of metals in various oxidation states by combined methods based on capillary electrophoresis on quartz glass microcolumns. For example, the following elements were separated and determined: selenium, arsenic, tin, mercury, chromium, iron, platinum and vanadium; trivalent iridium, europium, cadmium and tetravalent rhodium, $\text{Al}^{3+} - \text{F}^-$ complexes, divalent zinc, di- and trivalent cobalt and a number of their alkyl derivatives, amino, cyano, chloro, and acetate complexes, both in artificial solutions and in river water, seawater and rainwater, as well as in soil extracts, liquid radioactive waste and biological environments. The following issues were noted: insufficient sensitivity of detecting instruments, necessity of using spectral detection methods, improvement of sampling methods and methods for preparation of media for sampling, improvement of procedures for checking the quality of analytical data obtained, and creating a base of standard samples of particular microelements and media in various states.

3. Filtration methods

In the past decade, there has been an increasing number of studies on the role of the colloid-dispersed state of microelements in their migration in water.^{123–153} The usual method of studying the colloidal state of microelements employs the principle of ultrafiltration. Chemically inert filtering materials with pore size from a few nanometres to tens of nanometres have been developed. Filtrating devices using both ordinary frontal filtration and cross-flow filtration (CFF) are now commercially available. Owing to the more favourable flow dynamics, the latter variant provides considerable advantages in studies on the size of colloidal particles, their charge and chemical nature.^{130–140}

The CFF principle involves the separation of colloidal particles with a volume concentration c_B on a membrane filter surface.¹³⁸ The movement of the incoming colloidal solution

occurs laterally with respect to the porous membrane surface, while the filtration occurs tangentially with respect to the wall due to the hydrostatic pressure gradient, which appears in the near-the-wall liquid film because of the concentration polarisation, and a change in the penetrating filtration flow (J). The J value depends on the concentration parameters of a colloid solution by the relationship

$$J = k \ln \left(\frac{c_w - c_p}{c_B - c_p} \right), \quad (2)$$

where k is the mass-transfer coefficient determined experimentally or from empirical hydrodynamic relationships; c_w is the concentration of colloidal particles near the wall; and c_p is the concentration in the flow that has passed through the membrane. The initial flow of a liquid being analysed is divided into two flows during cross-flow filtration: the penetrated and delayed flows. It is the ratio of concentrations in these flows that carries information about the content of the colloid fraction, for which the rejected particle size is equivalent to the membrane pore diameter, in the original flow.¹³⁸

A comparison of cellulose- (Millipore Pre-scale CFF) and polysulfone-based (Amicon CFF) commercial filters in the cross-flow filtration mode¹³⁹ showed their similar efficiencies: both filter types retain up to 91% of colloidal particles with rejected sizes shown in the filter passports. The major fraction of standard colloidal dextrin solution with a nominal molecular mass of 3000 is removed from water by filters with a rejecting mass of 1 kDa; up to 30% of colloidal dextrin particles are lost in the case of polysulfone-based membranes owing to the sorption in the filter material. Losses of protein colloids (in particular, lactalbumin) are considerable on both filters. The content of colloidal particles of organic carbon introduced in seawater as a standard is determined without a systematic error. However, when seawater is analysed using cross-flow filtration, 'breakthrough' of some fractions of both low- and high-molecular fractions is observed.^{140, 141}

For example, in a study of organo-inorganic colloids of ^{230}Th and ^{234}Th in seawater by ultrafiltration it was found that physical separation of the ionic and colloidal fractions of thorium on membrane filters with rejecting mass < 10 kDa is accompanied by adsorption of micro-quantities of thorium and mechanical interaction with the membrane material (polysulfone, polypropylene, *etc.*).¹⁴⁰ The adsorption losses increase with a decrease in the organic carbon concentration; they cannot be suppressed by acid treatment of the membranes. In total, the changes in the fraction of the colloidal fraction of ^{234}Th coincide with the changes in the concentration of the colloidal fraction of organic carbon with molecular masses > 10 kDa.

Using frontal or cross-ultrafiltration in combination with monitoring the sizes and charges of particles by dynamic light scattering methods (laser photon-correlation spectroscopy) and Doppler electrophoresis, it is possible to determine not only the usual characteristics of colloids but also their acid–base properties. These methods were employed¹³⁰ to show the possibility of transferring natural colloidal particles from an estuary (river–sea hydrochemical border) to an electrolyte solution followed by determination of the acid–base properties of the colloids that have been concentrated. Furthermore, a conclusion about the nature of an organic colloidal compound in river water was drawn, and the range of organic colloid sizes (2–3000 nm) in the electrolyte solution after filtration concentrating was determined. It was found that the particle size increases with time and decreases with an increase in pH of the electrolyte. The acid–base properties of freshly prepared concentrates of a natural organic colloid differ from the acid–base properties of humic acids. This fact was explained¹³⁰ by possible formation of organo-mineral colloids involving large particles of colloidal iron hydroxide.

Sorption of humic acids on the surface of boehmite ($\gamma\text{-AlOOH}$) particles involves a similar interaction mechanism of

colloidal particles: anion exchange of ligands occurs in the initial stage; after that, the organic acid undergoes condensation on the hydroxide surface as its concentration increases.¹⁴² The ion-exchange mechanism of interaction of organic and inorganic colloids is considered as a complex variety of the metal–ligand coordination interaction¹⁴³ characteristic of microcomponents with high hydrolysis constants (in particular, for high-charged ions of transition metals and actinides).^{131, 144, 145} In radiochemistry, such interaction occurs during the heteronucleation of colloids present in trace amounts.⁹

The real picture of stepwise colloidal interactions in natural aqueous systems is complicated by the fact that colloids of inorganic hydroxides of the majority of transition metals present in trace amounts are nano-sized particles,^{107–114} migration of which in natural waters increases considerably in the presence of humic acids. The migration of microelements mainly occurs by this mechanism.^{123, 124, 131, 146}

The discreteness of fractional analysis of the colloidal state of microelements in frontal and cross-ultrafiltration methods does not allow the size distribution of colloid particles to be estimated and hence prevents a comprehensive explanation of the effects of size on the physicochemical state and migration. The drawbacks of filtration methods also include poor resolution of particles according to size and frequent fouling of filter pores.

These drawbacks are eliminated in a hyphenated method uniting sedimentation separation of colloids in a centrifugal field with mass spectrometric detection of the elemental compositions of separate colloidal fractions in the stream (Sedimentation Field-Flow Fractionation, SdFFF).^{128, 147–153} According to this method, the capillary with the colloid solution of interest is simultaneously affected by a tangential centrifugal field and a longitudinal axisymmetrical pressure field. The effect of these fields on the flow results in separation of particles into fractions, which are successively eluted from the capillary. The concentration of colloidal particles in the eluate is determined by inductively coupled plasma mass spectrometry or by UV spectroscopy. The method makes it possible to concentrate colloidal fractions. The eluate fractions can be passed for a more thorough study of the composition of colloidal particles by scanning tunnelling microscopy, X-ray diffraction analysis and X-ray fluorescence spectroscopy.^{128, 148–153} Based on SdFFF data, one can plot a differential curve of distribution of colloidal particles against eluate fractions (volumes) or elution time, and then according to the diameters of spherically similar particles with concentrations $< 100 \mu\text{g litre}^{-1}$. By comparing distribution curves for organic carbon and separate elements, particles are identified as true colloids or pseudo-colloids (of organic or mineral nature). This method is particularly efficient in studies of the state of colloidal forms of microelements.

* * *

By now, studies of physicochemical states of microelements in aqueous media have become an independent scientific direction of interdisciplinary type that combines problems and methods of analytical and physical chemistry of ultra-dilute solutions, radiochemical and geochemical analysis of the ion–molecular and phase analysis of compounds. It is obvious that the instrumental base is growing rapidly, and ample new information is therefore appearing about the chemical, phase and dispersion composition and reactivity of separate forms of stable microelements both in natural systems and their geochemical combinations.

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^a — *J. Anal. Chem. (Engl. Transl.)*

^b — *Mendelev Chem. J. (Engl. Transl.)*

^c — *Radiochemistry (Engl. Transl.)*

Modern magnetic chemistry of exchange clusters

V T Kalinnikov, Yu V Rakitin, V M Novotortsev

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Abstract. The review concerns the state-of-the-art in studies on the magnetic chemistry of exchange clusters (polynuclear transition-metal complexes in which the unpaired electrons of particular sites are involved in magnetic exchange due to both direct or indirect, *via* bridging ligands, interactions of their wave functions). Particular emphasis is placed on (i) theoretical models that can be used to interpret experimental data in terms of the effective Hamiltonians and chemical bonding theory and (ii) molecular nanomagnets (complexes containing a large number of magnetic atoms and possessing unusual properties). The bibliography includes 158 references.

I. Introduction

Magnetic chemistry studies the interrelations between the magnetic properties of chemical compounds and their molecular and electronic structures. Creation of a theoretical basis for magnetic chemistry is intimately associated with the development of quantum mechanics.^{1,2} Current progress in magnetic chemistry is due to improvement of its theoretical foundations and posing new problems of preparative chemistry.^{3–25}

The first advances in magnetic chemistry were due to the discovery of correlations between the magnetic properties and the type of chemical bonding in diamagnetic crystals and organic molecules.³ Studies on the splitting of transition-metal atomic orbitals (AOs) in mononuclear complexes^{4–7} became even more important, because prediction of these effects belongs to the key results obtained using the ligand field theory, which is the main model in the theory of electronic structure of transition-metal compounds.

In 1952, it was found that the interactions between paramagnetic metal atoms in polynuclear complexes can cause a

pronounced temperature dependence of the magnetic moment.⁸ This class of compounds is called ‘exchange clusters’. The spin–spin correlations in the exchange clusters are due to the same exchange interactions as in the magnetically ordered crystals; however, they occur within isolated molecules. Therefore, detailed interpretation of experimental data based on the conventional molecular orbital (MO) theory is an easy task in the case of clusters. In magnetically ordered crystals the microscopic nature of magnetic interactions is masked by a continuous spectrum of elementary excitations. Such continuum systems have been the subject of solid state physics,^{2,26} which uses methods based on consideration of translational symmetry of crystals rather than specific features of pair atom–atom interactions in them to interpret the properties.

At the same time, the border between the physics of magnetic phenomena and magnetic chemistry is rather conventional. In particular, complexes containing a large number of paramagnetic atoms exhibit a magnetic memory effect,^{22–25} which is characteristic of crystals. At the same time, computational methods based on division of crystals into small clusters proved their efficiency in the case of magnetism.²⁷

Usually, the magnetic properties of exchange clusters smoothly depend on temperature and the corresponding curves can hardly be used to assess particular characteristics of the electronic structure. Because of this, interpretation of experimental data in magnetic chemistry is based on two related but clearly distinct divisions of theory.

The object of a phenomenological theory is to determine the form of model Hamiltonians and to develop relevant methods of solution in order to find the parameters of such Hamiltonians by comparing the calculated and experimental characteristics. Phenomenological theories are usually based on some general considerations. Therefore, treatment of experimental data as a set of parameters of the model Hamiltonian can be considered correct. Calculations of the parameters of the Hamiltonian using particular versions of the theory of electronic structure is the object of microscopic theory.

In accord with the aforesaid, in this review we will briefly outline the theoretical methods of modern magnetic chemistry, which are employed to interpret the experimental data, and then dwell on some applications of these methods to molecular nanomagnets, the most complex and promising class of polynuclear complexes.

V T Kalinnikov, Yu V Rakitin I V Tananaev Institute of Chemistry and Technology of Rare Elements and Raw Mineral Materials, Kola Scientific Centre of the Russian Academy of Sciences, ul. Fersmana 14, 184200 Apatity, Murmansk Region, Russian Federation. Fax (7-815) 557 64 25. Tel. (7-815) 557 93 16 (V T Kalinnikov).
E-mail: rakitin@chemy.kolasc.net.ru, Apa7tit@mail.ru (Yu V Rakitin)
V M Novotortsev N S Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninsky prosp. 31, 119991 Moscow, Russian Federation. Fax (7-095) 954 12 79.
Tel. (7-095) 952 39 48. E-mail: vmnov@igic.ras.ru

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II. Phenomenological theory

1. Exchange effect and the exchange Hamiltonian

The simplest way of introducing the notion of exchange interaction is to consider the interaction between a pair of atoms containing one unpaired electron each. Using the spin functions of two electrons, $|\alpha\rangle$ and $|\beta\rangle$, it is possible to derive the following functions of the total spin S

$$|1\rangle = \left(\alpha\alpha, \frac{\alpha\beta + \beta\alpha}{\sqrt{2}}, \beta\beta \right)$$

and

$$|0\rangle = \frac{\alpha\beta - \beta\alpha}{\sqrt{2}}.$$

Then, the total wave functions can be written as

$$\begin{aligned} \psi(1) &= \varphi_- |1\rangle, \\ \psi(0) &= \varphi_+ |0\rangle, \end{aligned} \quad (1)$$

where φ_- and φ_+ are the corresponding radial components.

The spin functions $|1\rangle$ and $|0\rangle$ are of different symmetry. According to the Pauli principle, the functions φ_- and φ_+ should also be of different symmetry and, hence, describe the states characterised by different Coulombic energies (E). The exchange effect consists of the appearance of energy difference (splitting), which is usually denoted as

$$-2J = E(S=1) - E(S=0), \quad (2)$$

where J is the exchange parameter.

Depending on which has a lower energy, the magnetic triplet ($-2J < 0$) or the non-magnetic singlet ($-2J > 0$), one deals with ferromagnetic or antiferromagnetic exchange, respectively. As the temperature decreases, the magnetic moment increases in the former and decreases in the latter case. The rate of the change in the magnetic moment depends on the parameter $|-2J|$. This dependence serves as the basis for the determination of the parameters of exchange interactions in clusters.

Formally [see relation (2)], the exchange effect can be treated as some 'interaction', which causes orientation of the spins $\mathbf{S}_1$ and $\mathbf{S}_2$. The corresponding spin Hamiltonian has the form

$$\hat{H} = -2J \mathbf{S}_1 \mathbf{S}_2. \quad (3)$$

Since

$$-2J \mathbf{S}_1 \mathbf{S}_2 = (\mathbf{S}_1 + \mathbf{S}_2)^2 - \mathbf{S}_1^2 - \mathbf{S}_2^2 = \mathbf{S}^2 - \mathbf{S}_1^2 - \mathbf{S}_2^2, \quad (4)$$

passing from operators to their eigenvalues, we get

$$E(S) = -J[S(S+1) - S_1(S_1+1) - S_2(S_2+1)]. \quad (5)$$

From this it follows that

$$E(S=1) = -\frac{1}{2}J,$$

$$E(S=0) = \frac{3}{2}J,$$

$$E(S=1) - E(S=0) = -2J,$$

which coincides with relation (2).

Compared to the simple expression (2), relationship (3) for the spin Hamiltonian has advantage consisting of the possibility of generalisation to the multi-centre systems with arbitrary spins of the paramagnetic particles.

From general considerations^{14, 20, 28} it follows that in the absence of orbital degeneracy the interaction between localised spins can be described using the spin Hamiltonian

$$\begin{aligned} \hat{H} = & -2 \sum_{ij} J_{ij} \mathbf{S}_i \mathbf{S}_j + \sum_{ij} \mathbf{G}_{ij} [\mathbf{S}_i \times \mathbf{S}_j] + \sum_{k \geq 2} \sum_{\gamma} J_{\gamma}^{(k)} \mathbf{O}_{\gamma}^{(k)} + \\ & + \sum_{ij\alpha\beta} J_{ij}^{(d)} (\mathbf{S}_{\alpha i} \mathbf{S}_{\beta j} + \mathbf{S}_{\beta i} \mathbf{S}_{\alpha j}) + \sum_i \mu_B \mathbf{S}_i \mathbf{g}_i \mathbf{H}. \end{aligned} \quad (6)$$

Here, the subscripts i and j denote paramagnetic ions, α and β are the spin components; $-2J_{ij}$ are the Heisenberg isotropic exchange parameters; $\mathbf{S}_i$ and $\mathbf{S}_j$ are the spin operators of the magnetic atoms; $\mathbf{G}_{ij}$ are the vector parameters of antisymmetric exchange; and $J_{ij}^{(d)}$ are the anisotropic exchange parameters. All higher-order isotropic exchange operators $\mathbf{O}_{\gamma}^{(k)}$ can be derived by summing similar terms in the expressions $(\sum_{ij} \mathbf{S}_i \mathbf{S}_j)^k$. The last term in relationship (6) describes the Zeeman interaction with external magnetic field $\mathbf{H}$, $\mathbf{g}_i$ are the g -tensors and μ_B is the Bohr magneton. Usually, the Heisenberg term predominates.

2. General relations of theory of magnetism

In the approximation of isotropic g -factors the static magnetic susceptibility of orbitally non-degenerate exchange clusters is given by²⁰

$$\begin{aligned} \chi_m &= \chi'_m + N\alpha = \\ &= \frac{N_A \mu_B^2 \sum_{\gamma, S} g^2(\gamma, S) S(S+1)(2S+1) \exp[-E(\gamma, S)/kT]}{3kT \sum_{\gamma, S} (2S+1) \exp[-E(\gamma, S)/kT]}. \end{aligned} \quad (7)$$

Here χ'_m is the magnetic susceptibility per mole of paramagnetic molecules, $N\alpha$ is the correction for temperature-independent paramagnetism of the metal ions and for diamagnetism of ligands, N_A is the Avogadro constant and $\sum_{\gamma, S}$ denotes summation over all quantum numbers.^{4, 13, 20}

Often, construction of temperature dependences of the magnetic properties of real clusters requires the inclusion of corrections for the monomer impurity

$$\chi = (1-\eta)\chi_m + \eta\chi_{\text{mono}}, \quad (8)$$

(η is the monomer fraction and χ_{mono} is the magnetic susceptibility of the monomer) and for intermolecular exchange²⁹⁻³¹

$$\chi_{\text{cl}} = \frac{\chi'_m}{1 - 2z'J'\chi'_m/Ng^2\mu_B^2}, \quad (9)$$

where z' is the number of nearest neighbours and χ'_m and $2J'$ are the parameters of intermolecular exchange.

The magnetic susceptibilities of polyatomic clusters χ'_m can reach very high values, so that intermolecular exchange can strongly affect the magnetic properties even at rather small values of the intermolecular exchange parameters $-2z'J'$.

For mononuclear complexes characterised by the only spin state S and $E(\gamma, S) = \text{const}$, Eqn (7) takes the form

$$\chi'_{\text{mono}} = \frac{N_A g^2 \mu_B^2 S(S+1)}{3kT} \quad (10a)$$

or

$$\chi'_{\text{mono}} T = \frac{N_A g^2 \mu_B^2 S(S+1)}{3k}. \quad (10b)$$

Hence, for such systems the right side of this equation is temperature independent.

In the high-temperature limit $|E(\gamma, S)| \ll kT$, Eqn (7) is the sum of the contributions of n paramagnetic atoms in a molecule

$$\chi'_m = \sum_i^n \chi'_{\text{mono}}(i), \quad (11a)$$

or

$$\chi'_m T = \sum_i^n \chi'_{\text{mono}}(i) T. \quad (11b)$$

Relationships (10b) and (11b) show the advantages of using the parameters $\chi'_m T$ instead of χ'_m in the analysis of experimental data. The high-temperature values $\chi'_m T$ permit the spins of the metal ions to be determined by simple summation of n constant contributions (10b). If one knows the trend and rate of changes in $\chi'_m T$ on lowering the temperature, it is possible to determine the sign and estimate the magnitude of exchange interactions. If, at low temperatures, the parameter $\chi'_m T$ corrected for the monomer impurity and intermolecular exchange takes some nonzero value, relationship (10b) also allows the ground-state spin to be evaluated.

Often, the ratio

$$\chi'_a = \frac{\chi'_m}{n} \quad (12)$$

is used instead of χ'_m and $\chi'_m T$ (here, n is the number of atoms; usually, χ'_a is denoted as χ'_m !). Then, the effective magnetic moment is given by

$$\mu_{\text{ef}}^2 = \frac{3kT\chi'_a}{N_A\mu_B^2} \approx 7.991\chi'_a T. \quad (13)$$

For mononuclear complexes, the parameter

$$\mu_{\text{ef}} = g[S(S+1)]^{1/2} \quad (14)$$

is temperature independent and can be used in analysing the experimental data in nearly the same way as the parameter $\chi'_m T$. However, this is less convenient because μ_{ef} (in contrast to $\chi'_m T$) is a non-additive quantity.

The $\chi'_{\text{mono}} T$ and μ_{ef} values for all realistic S at $g = 2$ are as follows:

S_i	1/2	1	3/2	2	5/2	3	7/2
$\chi'_{\text{mono}} T / \text{cm}^3 \text{ K}$	0.375	1.000	1.875	3.001	4.377	6.002	7.898
μ_{ef} / μ_B	1.732	2.828	3.873	4.899	5.916	6.928	7.937

3. The energy level and magnetic susceptibility calculations

The shape of the curves $\chi(T)$ is highly 'sensitive' to the magnitude and sign of the parameters $-2J_{ij}$, which mainly depend on the energies of the levels $E(\gamma, S)$.³² Therefore, the parameters $-2J_{ij}$ can be determined using best-fit procedures for the experimental and calculated $\chi(T)$ values. Clearly, the reliability of a particular procedure depends on the correctness of the theoretical model employed. The formalism of deriving correct spin Hamiltonians has been well developed.¹⁴ Because of this, the most important problem is to calculate the eigenvalues (energies) of such spin Hamiltonians.

A method of finding the simplest analytical solutions to the spin Hamiltonians of a large number of types of cluster structure was reported.³³

a. Analytical solutions to the spin Hamiltonians

Theorem. Consider a system that can be divided into two subsystems, L and M , such that (1) the spin Hamiltonians of the subsystems L and M have the solutions $E_L(\gamma_L, S_L)$ and $E_M(\gamma_M, S_M)$, respectively; and (2) all particles of one subsystem interact with particles of the other subsystem in an identical manner. Then, the solution of the total spin Hamiltonian has the form

$$E = E_L + E_M - J_{LM}[S_{LM}(S_{LM} + 1) - S_L(S_L + 1) - S_M(S_M + 1)], \quad (15)$$

where S_L and S_M are the spins of the subsystems, $-2J_{LM}$ is the parameter of the exchange interaction between particles of the

subsystems and S is the total spin, which can take the following values

$$S = S_L + S_M, S_L + S_M - 1, \dots, |S_L - S_M|. \quad (16)$$

In the simplest case (binuclear complexes) from Eqns (15) and (16) one gets

$$E = -J_{12}[S_{12}(S_{12} + 1) - S_1(S_1 + 1) - S_2(S_2 + 1)], \quad (17)$$

$$S_{12} = S_1 + S_2, S_1 + S_2 - 1, |S_1 - S_2|. \quad (18)$$

Equation (5) is a particular case of Eqn (17).

The equilateral triangle (Fig. 1a) meets the conditions of the theorem mentioned above. According to Eqns (15) and (16), here one has

$$E = -J_{12}[S_{12}(S_{12} + 1) - 2S_1(S_1 + 1) - J_{123}[S_{123}(S_{123} + 1) - S_{12}(S_{12} + 1) - S_3(S_3 + 1)], \quad (19)$$

where

$$S_1 = S_2,$$

$$J_{123} = J_{13} = J_{23},$$

$$S_{123} = S_{12} + S_3, S_{12} + S_3 - 1, \dots, |S_{12} - S_3|. \quad (20)$$

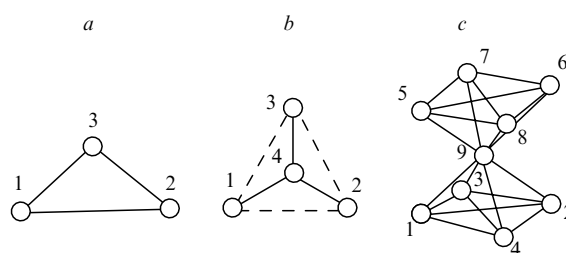


Figure 1. Schematic view of the structures of triangular (a), trigonal (b) and nonanuclear (c) clusters for which analytical solutions of the spin Hamiltonian exist.

Among tetramers, the theorem is applicable to, *e.g.*, a trigonal pyramid (Fig. 1b), which can be represented as a combination of a regular triangle 123 and a mononuclear species 4. Therefore, taking into account Eqns (15) and (19), one has

$$E = -J_{123}[S_{123}(S_{123} + 1) - 3S_1(S_1 + 1)] - J_{1234}[S_{1234}(S_{1234} + 1) - S_{123}(S_{123} + 1) - S_4(S_4 + 1)], \quad (21)$$

where

$$S_1 = S_2 = S_3,$$

$$J_{1234} = J_{14} = J_{24} = J_{34},$$

$$S_{1234} = S_{123} + S_4, S_{123} + S_4 - 1, \dots, |S_{123} - S_4|.$$

Other solutions can be obtained using the next terms of the expansion. For instance, an analytical solution for the nonanuclear cluster shown in Fig. 1c can be found by simply representing the system as a combination of two square fragments 'linked' by the interaction parameters $J_{ij} = 0$. Then, the eight-particle subsystem interacts with the symmetrically arranged central species. Solving this simple problem using general methods requires considerable efforts.³⁴

To interpret the magnetic properties of various types of polynuclear complexes based on the theory outlined above, a software library was developed.²⁰

b. Method of irreducible tensor operators and consideration of spatial symmetry

If the system under study does not meet the conditions formulated in the theorem given in Chapter II.3.a, one should numerically solve the corresponding spin Hamiltonian. For small molecules, the solutions can be obtained by diagonalisation of the matrix of the operator (6), written in the complete basis set of the product functions:

$$|S_1 m_1\rangle |S_2 m_2\rangle \dots |S_n m_n\rangle. \quad (22)$$

However, the number of such functions,

$$N_f = \prod_{i=1}^n (2S_i + 1)$$

rapidly increases as the number and magnitude of the spins S_i increase. For instance, even for a relatively simple Fe(III) complex with $n = 8$ and $S_i = 5/2$ the order of the matrix in the basis set of the functions (22) is $N_f = 1\,679\,616$. Computer diagonalisation of matrices of so high an order is currently impossible.

The situation is significantly simplified if we take into account only the Heisenberg exchange, which usually predominates. Indeed, the first term in expression (6) can be represented as the sum of zero-rank irreducible tensor operators³⁵

$$\sum X_{ij} = -2 \sum J_{ij} S_i S_j = \quad (23)$$

$$= 2\sqrt{3} \sum J_{ij} \{ \dots [(S_1^{(k_1)} S_2^{(k_2)})^{(k_{12})} S_3^{(k_3)}]^{(k_{123})} \dots S_n^{(k_n)} \}^{(0)},$$

where, e.g., the contribution $-2J_{13} S_1 S_3$ corresponds to the tensor operator with $k_1 = k_{12} = k_3 = 1$ (all other $k_\alpha = 0$). Other 'multiplication' schemes that obey the quantum vector addition rule^{1,2} can also be applied to Eqn (23). Based on the Wigner–Eckart theorem,³⁶ in the basis set of the total spin functions one can write

$$\langle \dots SM | \sum X_{ij} | \dots S' M' \rangle = \delta(M, M') \delta(S, S') \times \quad (24)$$

$$\times 2\sqrt{3} (2S + 1)^{-1/2} \times \sum J_{ij} \langle \dots SM | X_{ij} | \dots SM \rangle,$$

where $\langle \dots SM | X_{ij} | \dots SM \rangle$ are the reduced matrix elements, which can be calculated with ease.^{35–37}

Thus, the method of irreducible tensor operators (ITO) involves division of the isotropic spin Hamiltonian matrices into blocks corresponding to particular S and M values. In particular, for the above-mentioned octanuclear complex of trivalent iron the maximum order of the matrix in the basis set of the functions $|\dots SM\rangle$ is only 16 576. This allowed the software library²⁰ to be extended by including some modules written to interpret the magnetic properties of rather large clusters ($n \leq 16$) possessing no particular symmetry.

More detailed analyses of applications of the ITO method to the phenomenological theory of magnetism are available.^{7, 14, 20, 38}

The inclusion of spatial symmetry of molecules allows the orders of the matrices to be significantly reduced even in the case of low symmetry. To this end, it is sufficient to go from the basis set of the functions $|\dots SM\rangle$ to the functions $|\dots I^{(\alpha)} q_\alpha SM\rangle$, which are transformed by rows q_α of irreducible representations of the $I^{(\alpha)}$ point group.³⁹ For instance, in the case of an octanuclear Fe(III) complex⁴⁰ of a rather low symmetry (D_2), this passage causes the maximum order of the matrix to reduce from 16 576 down to 4170. This means that the required computer memory and the diagonalisation time are reduced by a factor of nearly 16.⁴¹

c. Cyclic clusters and linear chains

There is a large family of n -nuclear cyclic clusters, for which the Heisenberg spin Hamiltonian has the form

$$\hat{H} = -2J \sum_i S_i S_{i+1}, n+1 \equiv 1 \quad (25)$$

The most thoroughly studied uniform chains ($n \rightarrow \infty$) have the same spin Hamiltonian.

The J - and S -alternating chains with the spin Hamiltonian

$$\hat{H} = -2J \sum_i S_{2i} (S_{2i-1} + \alpha S_{2i+1}) \quad (26a)$$

(α is the alternation constant) and

$$\hat{H} = -2J \sum_i S_{2i} (s_{2i-1} + s_{2i+1}), s \neq S, \quad (26b)$$

(S and s are the spins in the alternated chain), respectively, have also been studied.

There is an analogy between cyclic clusters and linear chains. In both cases, the spin Hamiltonians depend on the single parameter, $-2J$, so the theoretical curves once calculated can be then used for all chains of a given type. Besides, cyclic clusters and linear chains possess a translational symmetry, which corresponds to periodic boundary conditions $n+1 \equiv 1$.

It should be noted that the magnetic properties of chains and other infinite systems are described using the quantity χ'_a [see Eqn (12)], because χ'_m is not defined in these cases.

In spite of considerable interest in linear chains as candidates for molecular magnets^{19, 22–25} and models of superconducting cuprates,⁴² there are few calculations of the magnetic properties of linear chains.

Numerical calculations of uniform chains with $S_i = 1/2$ and $n \leq 11$ were reported.⁴³ The possibility of approximation of infinite chains using finite ones was first demonstrated, the quality of approximation being significantly improved when using periodic boundary conditions. The effect of the chain length on the energy spectrum was first reported by Tsukerblat *et al.*⁴⁴ and on the magnetic properties by Hatfield *et al.*³⁸ Studies^{45–48} in which exact numerical solutions of functions $\chi'_a(T)$ for antiferromagnetic and ferromagnetic chains with $S_i = 1/2$ were obtained deserve particular attention. The $\chi'_a(T)$ plots for uniform chains with $S_i = 1$ were reported.⁴⁹ Theoretical dependences $\chi'_a(T)$ were also obtained for all S_i values ranging from $1/2$ to $7/2$ obtained by the high-temperature expansion method⁵⁰ and in the classical spin approximation.⁵¹ A review⁵² provides a comprehensive consideration of theoretical results for uniform and J -alternated chains with $S_i = 1/2$. Based on these results, one can no longer use the popular theoretical Weng curves⁵³ the plotting of which is based on rather rough assumptions.⁵⁴

The results of numerical calculations^{17, 55–57} of J -alternated chains with $S_i = 1/2$ and 1 were presented in the form of fractional rational functions. For $S_i = 1$, the $\chi'_a = f(\alpha, J, T/J)$ plots were reported.⁵⁸ These calculations were performed for finite cycles; however, the results obtained must also correctly describe the magnetism of infinite chains, because the $\chi'_a(T, n)$ curves rapidly match the limiting $\chi'_a(T, n \rightarrow \infty)$ curves at $\alpha \neq 1$.⁵⁹

The results of magnetic susceptibility calculations for S -alternated chains with $s_{2i} = 1/2$ and $S_{2i+1} \leq 5/2$ were briefly outlined.^{60, 61} The case for $s_{2i} = 1/2$ and $S_{2i+1} = 5/2$ has been studied in more detail.⁶² Analytical solutions for the systems with $s_{2i} \ll S_{2i+1}$ and the parameters S_{2i+1} approximated by classical spins were also reported.^{18, 63}

The limited number of theoretical $\chi'_a(T)$ curves for cyclic and quasi-one-dimensional systems is to a great extent due to the little amount of attention paid to the possibilities of symmetrisation of the basis set. In particular, for a real cyclic cluster Fe₁₀ (see Ref. 64) on going from the complete basis set to the $|\dots SM\rangle$ -representation and then to the $|\dots I^{(\alpha)} q_\alpha SM\rangle$ functions symmetrised in the C_{10v} group, the maximum order of the secular equation is reduced from 60 466 176 to 484 155 and then down to 48 480, which seems to be quite acceptable for being solved with modern computers.

4. Non-Heisenberg exchange

Higher-order isotropic exchange operators in Eqn (6) cause insignificant modification of the intervals between the spin levels. They have little effect on the magnetic properties, the more so if the parameters $J_\gamma^{(k)}$ are small.^{14, 20} Because of this, we will not dwell on them.

a. Antisymmetric exchange

The notion of antisymmetric (AS) exchange, $\sum G_{ij}(\mathbf{S}_i \times \mathbf{S}_j)$, was phenomenologically introduced by Dzyaloshinskii.⁶⁵ The energy,

$$|G| \sim \frac{J(g-2)}{2}$$

of this interaction estimated by Moria⁶⁶ was found to be relatively low. However, if isotropic exchange favours alignment of spins or their antiparallel orientation, the AS exchange favours a perpendicular alignment of spins. In crystals, this leads to formation of non-collinear magnetic structures, which was called 'weak ferromagnetism',^{2,65} and in clusters, to manifestation of nontrivial magnetic and spectroscopic properties.¹⁴ Magnetic measurements⁶⁷ carried out using a specially synthesised trinuclear complex of divalent copper seem to remain the most reliable confirmation of the Moria estimate as yet.

b. Anisotropic exchange. Molecular magnetic memory effect

If Z is the molecular axis of light magnetisation, the major contribution to the operator of anisotropic exchange has the form DS_Z^2 (see Ref. 68). Because of this, in the magnetic field $H \parallel Z$ for any (in particular, for the lowest well separated level $|S\rangle$) the solution to the spin Hamiltonian has the form:

$$E = DM^2 - g\mu_B H M, \quad (27)$$

where $M = S, S-1, \dots, -S$; $g \sim -g_e > 0$.

Consider the behaviour of the lowest energy level $|S\rangle$ of such a system with $D < 0$ in the magnetic field (Fig. 2a). Application of an external $H > 0$ followed by slow reduction of temperature will make only the lowest level $M = -S$ populated. Let us reduce the field H down to zero. From Fig. 2a it can be seen that at $H \rightarrow 0$ the levels $M = -S$ and $M = S$ become degenerate. However, no instantaneous equalisation of the level populations will occur because the transition $| -M \rangle \rightarrow | M \rangle$ is forbidden for $H \parallel Z$.⁶⁸ Hence, at $H = 0$ the system under study will retain its magnetisation corresponding to $M = -S$. This is the essence of the molecular magnetic memory effect.

An increase in the ground-state spin S is accompanied by an increase in the energy difference, $\Delta M = 2S$, between the two

lowest-lying levels, a decrease in the transition probability between them and, hence, a slowing down of relaxation of the magnetisation.

Another mechanism of relaxation of the magnetisation involves successive thermal population of higher levels. The nearest of them, $|M = \pm(S-1)\rangle$, is separated from the ground-state energy level $|M = \pm S\rangle$ by an interval of $D(-2S+1)$. Therefore, slowing down relaxation of the magnetisation favours an increase in not only S but also $|D|$. Complete thermalisation of the system corresponds to the overcoming of the barrier between $M_{\max}$ and $M_{\min}$

$$\Delta E \approx |D|S^2,$$

which confirms the conclusion drawn.

At rather large S values, not only the level $M = -S$ but also the levels $M = -S+1, -S+2$ can have long lifetimes. The latter levels can be individually populated by selective excitation. Thus, multilevel molecular magnetic memory is possible.

If $D \geq 0$, different levels with close M values cross one another at $H \rightarrow 0$ (see Fig. 2b), which leads to unavoidable rapid thermalisation and the absence of magnetic memory effect. A similar situation is typical of systems with any D , if the ground state forms a group of spin levels: numerous crossings of the levels with close moments inevitably lead to fast relaxation of the magnetisation.

In all cases, acceleration of relaxation is also favoured by the anisotropic exchange operators of the type $E(\mathbf{S}_X^2 - \mathbf{S}_Y^2)$, which appear at symmetries lower than axial symmetry.⁶⁸

The anisotropic exchange parameters are combinations of dipole-dipole, pseudodipole and single-ion contributions;^{19,68} therefore, their estimates are usually based on experimental data.

III. Microscopic theory

Targeted synthesis of compounds with predictable magnetic properties (design of molecular magnets) is mainly based on the calculated and experimentally confirmed 'structure-magnetic property' correlations.^{15,19-21} Because of this, in this section the emphasis is placed on theoretical description of such correlations, the more so as this problem is somewhat simpler than calculations of numerical values of the exchange parameters.

Microscopic models in modern magnetic chemistry of exchange clusters are based on Anderson's theory of magnetism (see, e.g., Refs 9 and 69). In particular, most models use the magnetic orbital approximation.¹⁹ In essence, this approximation is the same as that used in the ligand field theory,^{7,20,21} namely, only those nonbonding and antibonding orbitals are considered, which mainly belong to the metal atoms and can contain unpaired electrons.

1. Natural orbital approximation

The natural orbital approximation is based on the assumption that a polynuclear complex can be represented as a system composed of mononuclear fragments. Quantitatively, the validity of the natural orbital approximation is determined by the possibility of division of the system under study into weakly interacting mononuclear fragments. However, this approximation is convenient for qualitative analysis of exchange effects, because it allows well-known concepts of the ligand field theory^{6,7,20,21} to be used.

a. Ferromagnetic and antiferromagnetic exchange

In Anderson's theory, the expression for the parameter of exchange interaction between the unpaired electrons localised in the natural orbitals, Φ_a and Φ_b , of two sites a and b has the form

$$-2J_{12} = -2\langle \Phi_a \Phi_b | \frac{e^2}{r_{12}} | \Phi_b \Phi_a \rangle - 4\delta \langle \Phi_a | V | \Phi_b \rangle. \quad (28)$$

Here $\langle \Phi_a \Phi_b | e^2/r_{12} | \Phi_b \Phi_a \rangle$ is the Coulombic energy of two-electron charge distribution (this energy is always positive; i.e., it corresponds to the ferromagnetic contribution $-2J^f < 0$). In the

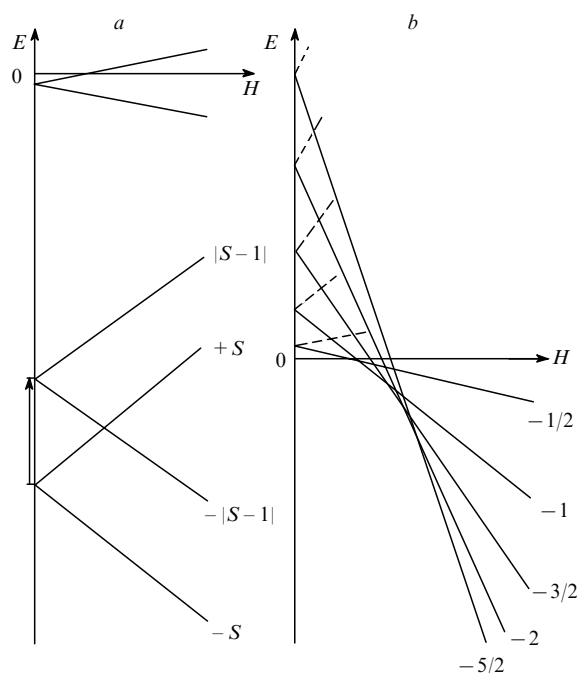


Figure 2. Splitting of the spin level S due to the action of the anisotropic exchange operator DS_Z^2 and magnetic field at $D < 0$ (a) and $D > 0$ (b).

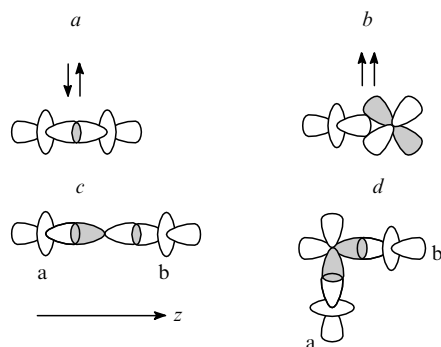


Figure 3. Schemes of direct and indirect electron–electron interactions favouring antiferromagnetism (*a*, *c*) and ferromagnetism (*b*, *d*).

second term δ is the overlap integral $\langle \Phi_a | \Phi_b \rangle$, and $\langle \Phi_a | V | \Phi_b \rangle < 0$ is the matrix element of effective one-electron Hamiltonian V . This term appears only in the case of non-orthogonal orbitals ($\delta \neq 0$). In the Heitler–London scheme, it is responsible for the formation of chemical bonds involving paired electrons. Therefore, $-2J_{12} < 0$ only at $\delta \sim 0$.

The aforesaid serves as the theoretical basis for the well-known Goodenough–Kanamori rules.⁹ They can be exemplified in the simplest way by considering a direct interaction between d-orbitals of two neighbouring metal atoms. Figure 3 *a* presents a scheme of the formation of the metal–metal bond involving paired electrons in the case of strong antiferromagnetism. If, from symmetry considerations, $\delta = 0$ (Fig. 3 *b*), the resulting effect is ferromagnetism. A more complicated situation is observed when direct interaction is absent but a bridging ligand *L* is available. However, this can be simplified by considering that the predominant contribution to the antiferromagnetic exchange is due to the interaction of unpaired electrons on the bridge.⁷⁰ Indeed, in this case the natural orbitals (with inclusion of the bridging ligand only) take the form

$$|\Phi\rangle \sim d + \alpha\varphi_L,$$

where α is the covalency. Figure 3 *c* illustrates the case where the orbital φ_L is common to both centres. Here, one has

$$\delta = \langle \Phi_a | \Phi_b \rangle \sim \langle \alpha\varphi_L | \alpha\varphi_L \rangle = \alpha^2 \neq 0,$$

which corresponds to indirect antiferromagnetic exchange. The case where

$$\delta \sim \langle \Phi_{La} | \Phi_{Lb} \rangle = 0$$

corresponds to indirect ferromagnetic exchange (Fig. 3 *d*).

b. The bond covalency and bond length effects

From the aforesaid it follows that an increase in the bond covalency (α) must cause an increase in the parameter $|-2J|$. Indeed, this holds for compounds with the F^- , O^{2-} , S^{2-} and Se^{2-} bridges.¹¹

At long metal–bridging ligand distances (R), the site–site interactions vanish; therefore, the fact that the dependence $|J(R)|$ has a decreasing character is not in doubt. This dependence was revealed^{71,72} by analysing experimental data for oxides and fluorides and a quantitative correlation was established

$$-2J \sim R^{-m}, m = 10-12. \quad (29)$$

c. Angular dependence of superexchange

Using the natural orbital approximation, it is an easy matter to derive an expression for the angular dependence of superexchange on a monatomic ligand.

Let the sites *a* and *b* (Fig. 4) contain one unpaired electron in the orbitals d_{z^2} , the lobes of which are directed at the bridging ligand *L* and overlapped with its valence orbitals *s* and *p*. Then,

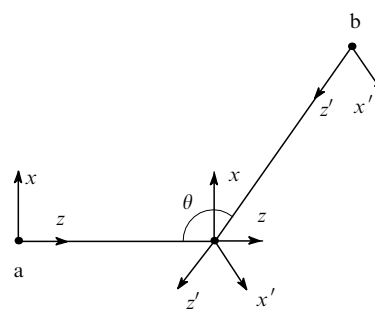


Figure 4. Directions of the local axes in the fragment M–L–M.

the natural orbitals in the local system of coordinates have the form

$$\Phi_a \sim d_{z^2} + \alpha p_z - \beta s, \quad (30a)$$

$$\Phi_b \sim d_{(z')^2} + \alpha p_{z'} - \beta s, \quad (30b)$$

where α and β are the covalency parameters. By substituting relations (30a) and (30b) into (28), we get the expression for the antiferromagnetic contribution with inclusion of the interaction on the ligand only⁷⁰

$$-2J^{af} = -4\alpha^4 V_1 \cos^2 \theta - 4\alpha^2 \beta^2 (V_1 + V_2) \cos \theta - 4\beta^4 V_2. \quad (31)$$

Here

$$V_1 = \langle p_z | V | p_z \rangle < 0,$$

$$V_2 = \langle s | V | s \rangle < 0$$

and it is considered that

$$p_{z'} = p_z \cos \theta - p_x \sin \theta.$$

Since α^2 is nearly an order of magnitude greater than β^2 (see Ref. 73), the major contribution to Eqn (31) comes from the first term at all angles except for the range $\theta \approx 90^\circ$. The presence of the angle independent term causes the minimum of $-2J^{af}$ to be attained at $\theta \approx 95-100^\circ$ rather than $\theta = 90^\circ$.

As for the ferromagnetic contribution, after substituting expressions (30a) and (30b) into the relationship

$$-2J^f = -2 \langle \Phi_a \Phi_b | \frac{e^2}{r_{12}} | \Phi_b \Phi_a \rangle$$

one gets the sum of terms of the same order of magnitude, which only slightly depends on the angle θ . This conclusion was proved by direct numerical estimates (see, e.g., Ref. 74). In addition, usually $|-2J^f| \leq -100 \text{ cm}^{-1}$ (see Ref. 19), whereas $-2J^{af}(\theta)$ can take values ranging from 0 to $\sim 2000 \text{ cm}^{-1}$ (see Refs 20 and 75). Thus, to an accuracy of relatively small and nearly constant contribution, the expression (31) provides a correct explanation for the angular dependence of superexchange. Usually, Eqn (31) is used in the parametric form

$$-2J = -2J_1 \cos^2 \theta - 2J_2 \cos \theta - 2J_3, \quad (32)$$

where J_1 , J_2 and J_3 are determined from the experimental data, the parameters also including the ferromagnetic contribution. Expression (32) correctly describes the angular dependence of superexchange for a broad class of oxide crystals⁷⁶⁻⁷⁸ even without considering J_2 , though the explanation for subtle effects similar to exchange striction in NiO (see Ref. 79) also requires the inclusion of a linear term.

d. Double exchange and heteronuclear complexes

Compounds containing paramagnetic ions of the same metal in close oxidation states can exhibit the so-called double exchange.⁸⁰ Physically, it is due to the fact that the ‘extra’ electron (or hole) migrates between two equivalent centres and alternately interacts

with the localised spins S_i . This causes the formation of spin levels with energies

$$E(S) = \pm bS, \quad (33)$$

$$S = 2S_i + \frac{1}{2}, 2S_i - \frac{1}{2}, \dots, \frac{1}{2},$$

so that the order of the lowest $2S_i$ -levels corresponds to ferromagnetic non-Heisenberg exchange. Using the same notations as above, one gets

$$b \sim \alpha^2 V_1 \cos \theta + \beta^2 V_2.$$

Comparison of this expression with Eqn (31) shows that double exchange can result in strong ferromagnetism even in the case of a large antiferromagnetic contribution. This occurs in, e.g., tetra(μ -1,8-naphthyridine- N,N')bis(bromonickel)tetraphenyl borate.⁸¹ Double exchange in this mixed-valence Ni(II)/Ni(I)-complex with structure similar to that of copper acetate is so significant that only the lowest level ($S = 3/2$) is populated even at $T \approx 400$ K.

There are only a few systems exhibiting double exchange, because in most mixed-valence complexes the 'extra' electron is trapped by one centre and the centres become inequivalent.¹⁴ This is intrinsic in heteronuclear clusters in which the 'extra' electrons are localised on one centre. This causes the appearance of a ferromagnetic contribution due to transfer of the unpaired electron of one centre to the vacant orbital of the other centre and/or one of the electrons of the filled orbital of one centre to the half-filled orbital of the other centre due to direct or indirect interaction.^{10, 11}

An example of the aforesaid is provided by heterobinuclear complex $\text{CuVO}(\text{fsa})_2\text{en} \cdot \text{CH}_3\text{OH}$, where $\text{H}_4(\text{fsa})_2\text{en} = N,N'$ -bis-(2-hydroxy-3-carboxybenzylidene)-1,2-diaminoethane, in which the Cu^{2+} and VO^{2+} ions are linked via an oxygen bridge.⁸² The scheme of interaction between magnetic orbitals in this complex is shown in Fig. 5. The orbitals of the unpaired electrons of Cu(II) and vanadium monoxide ($|x^2 - y^2\rangle$ and $|xy\rangle$), respectively) are orthogonal from symmetry considerations; however, the metal atoms are separated by a monatomic oxygen bridge only. This should result in strong Anderson ferromagnetism. At the same time, the unpaired electron can be transferred from the $|x^2 - y^2\rangle$ orbital of Cu(II) to the vacant orbital $|x^2 - y^2\rangle$ of vanadium monoxide and from the filled orbital $|xy\rangle$ of Cu(II) to the half-filled orbital $|xy\rangle$ of vanadium monoxide. In this case, it is hard to determine which mechanism makes the predominant contribution to the experimental value $-2J = -118 \text{ cm}^{-1}$ (see Ref. 82). The exchange parameters in complexes with a linear magnetic fragment $\text{Cr(III)}-\text{O}-\text{Fe(III)}$ were analysed.⁸³ Such complexes are

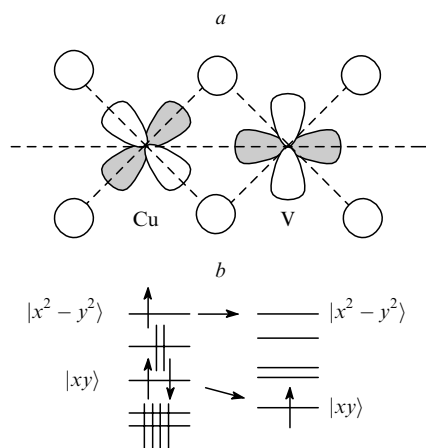


Figure 5. Scheme of interaction between magnetic orbitals in the complex $\text{CuVO}(\text{fsa})_2\text{en} \cdot \text{CH}_3\text{OH}$ (a) and possible types of electron transfer mechanism (b).

characterised by shortened M—O bonds, which must favour the transfer mechanism. Nevertheless, no corresponding anomalies in the $-2J$ values were found.

2. The Hay–Thibault–Hoffmann model

Within the molecular orbital (MO) method, more consistent is the Hay–Thibault–Hoffmann (HTH) model.⁸⁴ According to this model, the parameter $-2J$ of homobinuclear complexes is given by

$$-2J = \frac{-2 \sum_{ij} J_{ij}^f - \sum_{\mu} \Delta^2(\mu)/2K_{ab}}{4S_a S_b}. \quad (34)$$

Here $-2J_{ij}^f$ are the ferromagnetic contributions due to the electrostatic interaction of the unpaired electrons occupying the orbitals $|i\rangle$ and $|j\rangle$ of two centres; the second term is the antiferromagnetic contribution $-2J^{af}$; $2K_{ab} = 5-10 \text{ eV}$ (see Ref. 84) is the metal–metal charge transfer energy, which is stable for the atoms of the same transition-metal row; and S_a and S_b are the spins of the metal ions.²⁰ The parameters $\Delta(\mu)$ are the energy differences between the symmetric (s) and antisymmetric (as) MOs composed of combinations of orbitals of the unpaired electrons of the magnetic sites a and b, $\sim (d_a^a \pm d_b^b)$, and of the ligand orbitals. In Fig. 6, these orbitals and the parameter $\Delta(\mu)$ are shown for the triatomic linear fragment containing three orbitals and four electrons (for simplicity, the non-bridging ligands are not shown).

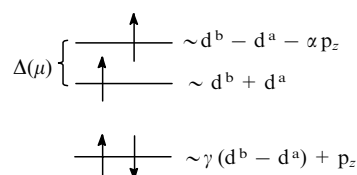


Figure 6. Molecular orbital scheme of the triatomic four-electron fragment.

In the case of a heterobinuclear system, the $-2J^{af}$ values somewhat increase, but the corresponding corrections for the metals of the same row are small.⁸⁵

As shown above, the sign and trends of the changes in the parameter $-2J$ are mainly determined by the antiferromagnetic contribution, which, according to the HTH model, depends on the energy difference between the MOs $d_a^a \pm d_b^b$ (plus the ligand orbitals). This allows the powerful formalism of the MO method to be employed. For instance, it is convenient to calculate the $\Delta(\mu)$ values using the generalised angular overlap model^{21, 86–88} based on the variational perturbation theory.⁸⁹

In the approximation of weak metal–ligand bond covalency, the matrix elements of the effective Hamiltonian for the metal orbitals can be represented as the sum over all k ligands^{21, 86–88}

$$h_{ij} = \sum_k \sum_{mn} H_m H_n U_{mn}^k \langle i|m\rangle_k \langle j|n\rangle_k, \quad (35)$$

where the subscripts i and j label the orbitals of the metal atoms, the subscripts m and n label the ligand orbitals and $H_{m,n}$ are the ligand orbital energies. The matrices, U , of the intraligand interactions can be most conveniently expressed through the inverted matrices

$$U_{mn}^{-1} = \begin{cases} (H_d - H_m - H_n) \langle m|n \rangle, & m \neq n, \\ H_d - H_n, & m = n. \end{cases} \quad (36)$$

Here H_d are the energies of the atomic d-orbitals. No restrictions are imposed on the number of the metal atoms and on the energy of intraligand interactions. Because of this, expression (35) can be applied to mono- and polynuclear complexes with both monatomic and polyatomic ligands that can be either monodentate or polydentate.

a. Polynuclear compounds with OR (XX') bridges

An example of efficient use of the HTH model and the generalised model of angular overlap is provided by the theory of exchange interactions for binuclear copper(II) complexes with OR bridges (Fig. 7).

Often, the O–R bonds in complexes with such a geometry are ignored.¹⁹ In this case, one should expect that the angular dependence of superexchange in such complexes is described by relation-

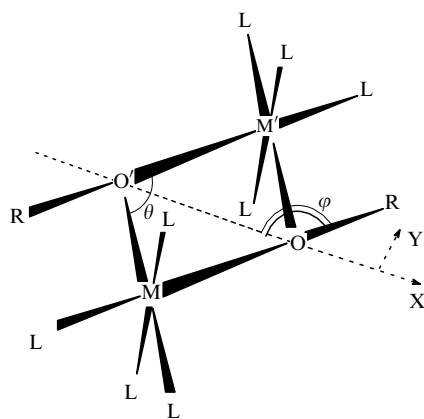


Figure 7. Structure of the central fragment of binuclear complexes with OR bridges (L is any ligand; OR is a carboxylate or alcoholate group).

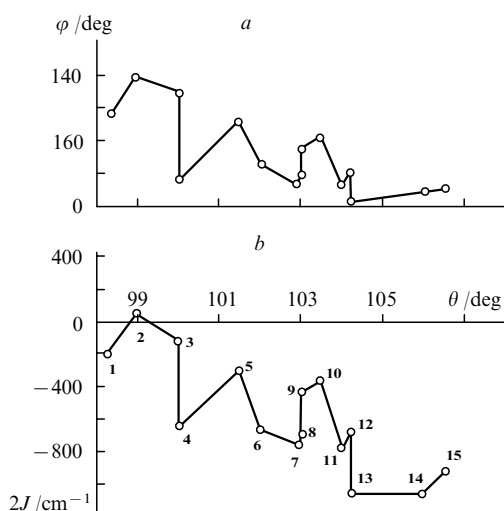


Figure 8. Experimental dependences $\varphi(\theta)$ (a) and $2J(\theta)$ (b) for binuclear Cu(II) complexes with OR bridges.

Compounds: bis[*N*-picolinoyl-3-aminopropoxidoaqua cuprate(II)] (1, see Ref. 90); bis(piperidinium)[di-μ-methoxobis(2,4-dinitrophenolato)-cuprate(II)] (2, see Ref. 91); tetrakisothiocyanatocuprate(I)-bis[μ-[2-(3-aminopropyl)aminoethanolato]-*N,N'*,μ-O]dicopper(II) thiocyanate (3, see Ref. 92); Cu₂(fsa)₂en · CH₃OH (4, see Ref. 93); (2-diethylaminoethanolato)copper(II) thiocyanate (5, see Ref. 94); di-μ-(benzyloxo)-bis[(2,2,6,6-tetramethylheptane-3,5-dionato)copper(II)] (6, see Ref. 95); di-μ-methoxo-bis[(2,4,6-trichlorophenolato)(quinoline)copper(II)] (7, see Ref. 96); bis[heptanetrionato(2)]bispyridinedicopper(II) (8, see Ref. 97); bis[*N,N*-bis(2-diethylaminoethyl)-2-hydroxyethylamino-O]dicopper(II) diperchlorate (9, see Ref. 98); bis[3-(*N,N*-dimethylamino)propyl-2-hydroxyethylamino-O]dimethanoldicopper(II) diperchlorate (10, see Ref. 99); bis[*N*-(3-hydroxypropyl)(pyrrol-2-yl)methylideneiminato]dicopper(II) (11, see Ref. 100); (2-dipropylaminoethanolato)copper(II) isocyanate (12, see Ref. 101); [2-hydroxy-*N*-(3-hydroxypropyl)-α-methylbenzylideneiminato]copper(II) (13, see Ref. 102); [2-hydroxy-*N*-(3-hydroxypropyl)-5-nitrobenzylideneiminato]copper(II) (14, see Ref. 102) and (5-methyl-7-oxo-4-azaoct-4-enolato)copper(II) (15, see Ref. 103).

ship (32). However, this is not the case, as shown by the experimental dependence $2J(\theta)$ presented in Fig. 8. As can be seen, this plot is a broken rather than smooth line and obeys the same pattern as the plot $\varphi(\theta)$, where φ is the angle OOC. Such a shape of the $2J(\theta)$ plot can be explained based on the generalised model of angular overlap.

The complexes in question are comprised of two nearly square mononuclear fragments with the unpaired electrons in the $|x^2 - y^2\rangle$ orbitals. Possible schemes of arrangement of the orbitals of the metal ions, the bridging atom and the substituent are shown in Fig. 9. For simplicity, we will restrict ourselves to analysis of the strongest σ -interactions between these orbitals and the p-orbitals of the bridging O atoms and the σ -bonds O–R.

Figure 9 c presents the projection of the geometry of exchange through one bridging ligand on the *XY* plane. The letters a and b denote the lobes of the $|x^2 - y^2\rangle$ orbitals, directed at the bridging ligand; p₁ and p₂ are the in-plane p-orbitals of the bridging O atom, p₃ (not shown) is the orbital p_z; and σ is the σ -orbital of the carbon atom. From symmetry considerations, for the matrix elements of the effective Hamiltonian (35) constructed in the basis set of the orbitals of copper atoms, |a⟩ and |b⟩, one gets $h_{aa} = h_{bb}$ and $\Delta = 2h_{ab}$. To include the second oxygen bridge, this value should be doubled. Finally, according to expression (34),

$$-2J^{af} = \frac{\Delta^2}{2K_{ab}}.$$

Thus, revealing trends of changes in the $-2J^{af}$ values requires only the parameter h_{ab} to be analysed.

Using relationships (35) and (36) and Figs 7, 9 c, one can easily show that

$$h_{ab} = A \cos \theta + A \frac{x}{1-x} \cos^2 \varphi \cos^2 \frac{\theta}{2}. \quad (37)$$

Here

$$A = \frac{H_p^2 (\langle d|p \rangle^*)^2}{H_d - H_p},$$

$$x = \frac{(H_d - H_p - H_\sigma)^2 (\langle p|\sigma \rangle^*)^2}{(H_d - H_p)(H_d - H_\sigma)};$$

$\langle d|p \rangle^*$ and $\langle p|\sigma \rangle^*$ are the radial components of the overlap integrals for the Cu–O and O–C bonds.

Since $|x| \gg 1$ in the case of interest (strong O–C interaction), one gets

$$h_{ab} \approx A (\cos \theta - \cos^2 \varphi \cos^2 \frac{\theta}{2}). \quad (38)$$

In addition, $\theta \approx 90^\circ$. Then

$$h_{ab} \approx A \cos^2 \varphi \cos^2 \frac{\theta}{2}$$

and

$$-2J^{af} \approx \cos^4 \varphi \cos^4 \frac{\theta}{2}. \quad (39)$$

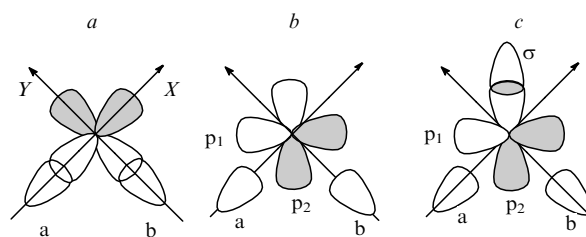


Figure 9. Possible schemes of arrangement of the orbitals of the metal ions (a), bridging atom (b) and the substituent linked to the bridging atom (projection on the *XY* plane) (c).

These relationships point to strong dependence of exchange on the angles $M-O-M$ and $O-O-C$. In real complexes, variations of the angles θ are small (see Fig. 7) because of steric hindrances. Therefore, the $2J^{af}$ values and, hence, the values

$$-2J = -2J^f - 2J^{af},$$

must be primarily determined by the angles $O-O-C$, which can vary over a wide range (from 180° to 90°). A decrease in the angle between the $O-C$ and the Cu_2O_2 plane favours manifestation of the properties of a strong antiferromagnetic, because $\varphi \approx 180^\circ$ corresponds to the maximum $-J^{af}$ value. On the contrary, deviation of the $O-C$ bond from the Cu_2O_2 plane leads to a dramatic decrease in $-2J^{af}$ and, finally, to ferromagnetic properties. Correlations of the experimental dependences shown in Fig. 8 are in good agreement with these conclusions. The fact that $-2J < 0$ already at $\varphi \approx 140^\circ$ can be explained by a very strong dependence of $-2J^{af}$ on φ .

The results obtained have a clear physical meaning. Figure 9a illustrates a 90° exchange through the monatomic bridge while Fig. 9b differs from it only in that the orbitals p_x and p_y are transformed into the equivalent orbitals p_1 and p_2 , respectively (i.e., Fig. 9b corresponds to the same 90° ferromagnetic exchange). This can be understood with ease if one takes into account the fact that the orbital d_a-d_b interacts with the orbital p_1 in exactly the same manner as the orbital d_a+d_b interacts with the orbital p_2 . Because of this, $\Delta = 0$ and the system is ferromagnetic. Consider now Fig. 9c drawn with inclusion of the $O-C$ bond. Here, the orbitals $|p_2\rangle$ and $|\sigma\rangle$ form two combinations (a strongly bonding and a strongly antibonding one), which virtually do not interact with the orbitals of the metal atom. Thus, only the overlap between the d_a-d_b and p_1 orbitals remains, which is strong in the whole range of changes in the angle θ , except for the non-physical range $\theta \approx 0^\circ$. As a consequence, $\Delta \neq 0$, thus providing conditions for antiferromagnetism of all complexes with $\varphi \approx 180^\circ$. At $\varphi \approx 90^\circ$, the in-plane p-orbitals of the O atom are no longer overlapped with the carbon σ -orbital. In this case, the exchange geometry corresponds to the interaction through a monatomic bridge (at $\theta \sim 90^\circ$, this interaction is ferromagnetic; see Fig. 9a, b). Quantitative description of experimental data for some alcohols and related compounds (cubanes) was also reported.⁸⁶

According to Eqn (34), the antiferromagnetic contribution (39) is typical of not only Cu(II) complexes but also any other compounds which contain the unpaired electrons in the $|x^2-y^2\rangle$ orbitals and have appropriate structures (see Fig. 7). In addition, not only the OR bridges but also other $\mu_{1,1}$ -coordinated ligands XX' with strong $X-X'$ bonds can be involved. Therefore, in the case of similar Ni(II), Mn(II), Mn(III), Fe(II), Fe(III) and Co(II) complexes one should expect manifestation of antiferromagnetic properties at $\varphi \approx 180^\circ$ and ferromagnetic properties at $\varphi \approx 90^\circ$. Numerous examples substantiating the correctness of this conclusion have been reported.^{16,20}

General relationships (37) and (38) allow the limiting cases, viz., transition to monatomic ligands ($x = 0$) and to $\theta = 180^\circ$, to be reproduced correctly. In the latter case, the parameter $-2J$ is independent of the position and even the presence of a substituent. If $X-X'$ interactions are weak ($|x| \ll 1$), relations (37) and (38) predict a shift of the minimum $-2J^{af}$ value (strongest ferromagnetic properties) from that corresponding to $\theta \approx 90^\circ$. This can be qualitatively explained with ease using Figs. 9b, c. Indeed, the lobes of the orbitals p_1 and p_2 (Fig. 9b) have the same amplitudes, thus being responsible for $\Delta = 0$. Hence, $-J^{af} = 0$ at $\theta = 90^\circ$. The interaction $|p_2\rangle-|\sigma\rangle$ (Fig. 9c) changes the amplitude and energy of the orbital p_2 . Therefore, to obtain $-2J^{af} = 0$ again, one should change the angle θ . Of course, this can be done if the orbital p_2 is not completely suppressed in the case of strong $|p_2\rangle-|\sigma\rangle$ interaction. This is also in agreement with the experimental data.¹⁰⁴

Relations (37) and (38) also describe more subtle effects, e.g., a linear dependence $-2J(\theta)$ in dimeric hydroxo-bridged complexes

of Cu(II).¹⁰⁵ This required the inclusion of correlation between the angles θ and φ , which was observed experimentally. The reasons for qualitatively different character of the dependences $-2J(\theta)$ in dimeric fragments of oxo- and hydroxo-bridged chromium(III) complexes were established and corresponding quantitative description was obtained using a more complicated theory.¹⁰⁶ Finally, the simple physical nature of the phenomena in question favoured a better insight into the magnetic properties of complexes with more complex ligands.

b. Complexes with bridging ligands N_3^-

Similarly to, e.g., ligands of the OCH_3 type, the bonds in the linear ligands N_3^- are strong. However, high symmetry of the N_3^- ligand leads to quite different structure of energy levels.

The p_y orbitals of this anion are shown in Fig. 10a. As can be seen, the MO $\phi_y(s) \approx p_{y1} + p_{y3}$ is involved in strong π -interaction with the orbital p_{y2} , while the orbital $\phi_y(as) \sim p_{y1} - p_{y3}$ retains its nonbonding character and, hence, can be involved in the interaction with metal atoms. This orbital is schematically shown in Fig. 10b. Clearly, the orbital $\phi_z(as)$ has the same shape. The orbitals p_x are involved in interactions with one another and also with s-orbitals. Therefore, symmetry analysis is insufficient to obtain correct MOs. However, the results of simple calculations using extended Hückel theory⁸⁴ showed that, among all orbitals of this type, only the MO $\phi_x(s)$ shown in Fig. 10c has an energy similar to that of the $\phi_{y,z}(as)$ MO. In addition, the amplitudes of the outer lobes of all the three orbitals $\phi_x(as)$, $\phi_z(as)$ and $\phi_y(s)$ are similar.

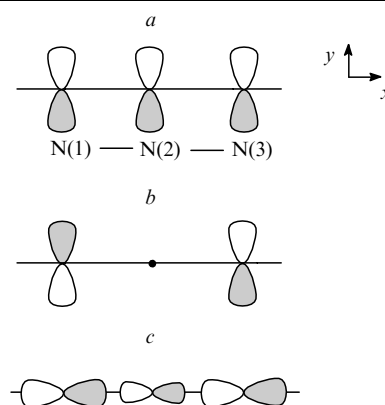


Figure 10. Orbitals of the linear ligand N_3^- ; p_y -orbitals (a), nonbonding orbital $\phi_y(as)$ (b) and nearly nonbonding orbital $\phi_x(s)$ (c).

Let us proceed to interpretation of experimental data. The bridging ligands N_3^- can be coordinated in two fashions. One type of coordination, $\mu_{1,3}-N_3$, is shown in Fig. 11a. The overlap of the orbitals of the $\mu_{1,3}-N_3$ ligand with the lobes of the $|x^2-y^2\rangle$ orbitals of two Cu(II) atoms, a and b, is schematically presented in Fig. 11b. As can be seen, the combination d^a-d^b is involved in effective interaction with both the $\phi_y(as)$ and $\phi_x(s)$ orbitals, while the orbital d^a+d^b remains nonbonding. This must result in large splitting, $\Delta(x^2-y^2)$, between them and in strong antiferromagnetism [see Eqn (34)].

Indeed, all the known Cu(II) complexes with the structure in question possess nearly diamagnetic (or weakly paramagnetic) properties.^{19,107} Similar complexes of nickel(II) and manganese(II) also contain unpaired electrons in the orbitals $|x^2-y^2\rangle$; as a consequence, they also exhibit strong antiferromagnetic properties.¹⁰⁸

The structure of complexes with $\mu_{1,1}-N_3$ bridges is shown in Fig. 12a. The overlap of the orbitals of the $\mu_{1,1}-N_3$ ligand with the



Figure 11. Structure (a) and orbital overlap scheme (b) for binuclear Cu(II) complexes with $\mu_{1,3}$ -bridging ligands N_3^- .

lobes of the orbitals $|x^2 - y^2\rangle$ of two Cu(II) atoms (a and b) is illustrated in Fig 12 b. Visually, this scheme is similar to that of the overlap with orbitals of the monatomic ligand (see Fig. 9 b). They are also similar in essence, because we have shown that the energies and amplitudes of the orbitals $\phi_x(\text{as})$ and $\phi_y(\text{s})$ are also similar (see above). Hence, one should expect that at Cu–N–Cu angles $\approx 90^\circ$ copper(II) complexes with $\mu_{1,1}$ - N_3 bridges manifest strong ferromagnetic properties similarly to the complexes with monatomic ligands.

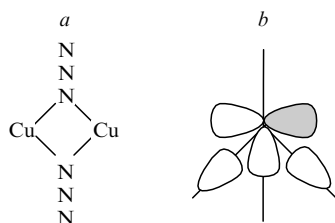


Figure 12. Structure (a) and orbital overlap scheme (b) for binuclear Cu(II) complexes with $\mu_{1,1}$ -bridging ligands N_3^- .

Indeed, all Cu(II) complexes of this type are ferromagnetic (provided there are no significant structural distortions) and the $-2J$ value can be as high as $\sim -200 \text{ cm}^{-1}$ (see Refs 74 and 109).

Similar nickel(II) complexes also possess ferromagnetic properties,¹⁰⁸ because they also contain the unpaired electrons in the $|x^2 - y^2\rangle$ orbitals. Besides, nickel(II) complexes also contain the unpaired electrons in the $|z^2\rangle$ orbitals, for which the conditions for the overlap with the in-plane orbitals of bridging ligands at $\approx 90^\circ$ are much like those for the $|x^2 - y^2\rangle$ orbitals. It should be emphasised that, in addition to the high ground-state spin, these nickel(II) complexes are characterised by large (in absolute value) parameters D (-10 to -20 cm^{-1} , see Refs 110–112). Therefore, such complexes are of particular interest for design of molecular magnets.

Potentially, the N_3^- ligand is a bisbidentate one (see Figs 11 and 12). Therefore, it is convenient for the synthesis of polynuclear complexes and even multidimensional structures. To date, some advances have been achieved in this field.²⁶

It is an easy matter to find out that a symmetric system with an odd number of ligand orbitals always contains a nonbonding orbital which can be involved in efficient interaction with the orbitals of the metal atoms. Because of this, such ligands are rather promising for creating a strong exchange at long metal–metal distances. Indeed, a Cu(II) complex characterised by an exchange parameter, $-2J$, of 26 cm^{-1} at a metal–metal separation of about $7.6 \text{ \AA}$ was synthesised.¹¹³ This is four to five orders of magnitude greater than the value predicted by expression (29). At the same time, it is not surprising because the shortest way of metal–metal exchange is a pentaatomic symmetric chain.¹¹³

c. ‘Parallel’ and ‘antiparallel’ coordination

According to Eqn (35), an increase in the number of identical, symmetrically coordinated bridging ligands must cause the splitting Δ to increase. In the case of heteroligand complexes, the

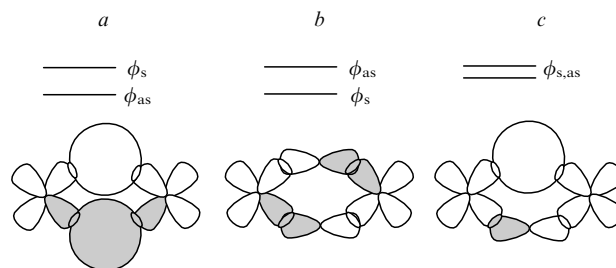


Figure 13. Parallel (a, b) and antiparallel (c) coordination of the bridging ligands.

situation can change. Consider a model system without writing expressions for particular cases.

Figure 13 a,b presents the schemes of the interaction between the bridging ligands through the s- and p-orbitals. In both cases, the ligands contribute to $\Delta(x^2 - y^2)$ in an identical manner (*i.e.*, their action is mutually strengthened):

$$\Delta_s \approx \Delta_{s1} + \Delta_{s2};$$

$$\Delta_p \approx \Delta_{p1} + \Delta_{p2}.$$

Due to different symmetry of the s- and p-orbitals, the high-lying combinations are symmetric (Fig. 13 a) and antisymmetric ones (Fig. 13 b). Both cases must lead to manifestation of strong antiferromagnetic properties, because Eqn (34) contains a term proportional to Δ^2 . However, for a heteroligand complex (Fig. 13 c) the different signs of Δ_s and Δ_p lead to

$$|\Delta_{sp}| \approx |\Delta_{s1}| - |\Delta_{p2}|.$$

Therefore, ‘antiparallelism’ of these contributions should lead to a decrease in Δ even with respect to Δ_{s1} and Δ_{p2} . It is ‘antiparallelism’ of the contributions that provides an explanation for unexpectedly weak antiferromagnetic properties of a large number of heteroligand complexes (see, *e.g.*, Ref. 114).

In principle, Δ_{sp} can be nearly equal to zero. This is the only reason for ferromagnetic properties of Ni(II) complexes of low symmetry, in which the metal atoms are linked through monatomic, triatomic (OH_2) and polyatomic (*e.g.*, OOCMe)^{115, 116} ligands with different node structure of the σ -orbitals.

d. Heterocyclic and other complex bridging ligands

Until now, we have considered complexes with relatively simple ligands that have a clear orbital structure. In complex ligands, the orbital lobes can be oriented in different ways and simple formulae for the angular dependence of superexchange are no longer valid.

Using EHT,⁸⁴ it was shown that in binuclear complexes of Cu(II) with imidazole (Fig. 14 a) the largest contribution to exchange comes from the symmetric and antisymmetric ligand orbitals (Fig. 14 b).¹¹⁷ The strongest ferromagnetic properties should be observed at a Cu–N–N angle of about 158° (see Ref. 117), which nearly corresponds to the bisectrix of the angles between the lobes of the symmetric and antisymmetric ligand orbitals. This is not surprising because of the similar amplitudes and energies of these orbitals.

Expression (35) permits the contributions of these and even more complex ligands to be included by simply inverting the matrices $\|U^{-1}\|$ [see relation (36)]. This allows one to obtain results in the analytical form, which is convenient for revealing various trends. However, in the case of polyatomic ligands of low symmetry, such an inversion will result in complicated multi-parameter expressions, which can hardly be analysed. Therefore, it is more appropriate to analyse complexes with such ligands using a compromise approach, which involves calculations of the electronic structures of the ligands using quantum chemistry methods followed by substitution of the results obtained into expression (35).

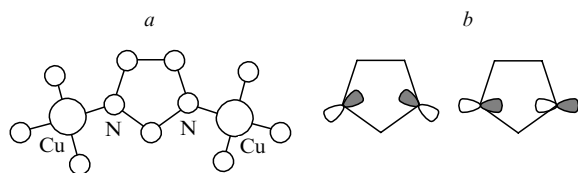


Figure 14. Structure of imidazole-bridged binuclear Cu(II) complexes (a) and the imidazole orbitals involved in effective interaction with the orbitals of unpaired electrons (b).

3. The model of exchange channels

In the case of multielectron metal atoms, the parameter $-2J$ is determined by the sum of the contributions over all pairs of half-filled orbitals [see Eqn (34)]. This strongly complicates analysis and/or the trends in manifestation of exchange interactions, especially if there is no predominant contribution. The model of exchange channels¹¹⁸ allows one to eliminate these problems.

Expression (34) can be re-written in more compact form:

$$-2J = \sum_{ij} \frac{-2J_{ij}}{4S_a S_b} = \frac{-2J_\Sigma}{4S_a S_b}. \quad (40)$$

From relation (34) it can be seen that the parameters $-2J_{ij}$ are independent of the degrees of orbital filling if the orbitals differ from $|i\rangle$ and $|j\rangle$. Therefore, pairs of one-electron orbitals of the sites a and b form specific channels of exchange interaction. The denominator, $4S_a S_b$, is the number of such interaction channels. Among the series of isostructural compounds containing paramagnetic ions of metals of the same row in similar oxidation states, variations of the number of electrons should not cause significant changes in the electronic structure parameters that appear in relationship (34). This suggests transferability of the contributions of the corresponding exchange channels in the series of isostructural systems. Transferability permits the parameters $-2J_{ij}$ to be 'calibrated' against the known experimental data and then used for predicting the magnetic properties of other systems belonging to the given isostructural series.

Let us re-write expression (40) as follows

$$-2J_\Sigma = \sum_{ij} (-2J_{ij}) = -2J 4S_a S_b. \quad (41)$$

The parameter $-2J_\Sigma$ is spin independent. It is determined only by the contributions of the exchange channels. Because of this, physically, this is the exchange energy, which is a convenient parameter for analysing the changes in the mechanisms of exchange interactions upon replacement of paramagnetic ions.¹¹⁹

Consider some binuclear carboxylates $[\text{LM}(\text{COOR})_2]_2$, where $\text{M} = \text{Ti}^{3+}$, V^{3+} , Mn^{2+} , Ni^{2+} and Cu^{2+} (for $\text{M} = \text{Ti}^{3+}$ and V^{3+} , $\text{L} = \text{Cp}^-$ only).^{120–123} These complexes have a rigid structure similar to that of copper acetate monohydrate (Fig. 15) and possess the properties of strong antiferromagnetics due to indirect exchange through OC(O) bridges.

Table 1 lists the half-filled orbitals, the $-2J$ values averaged over a large number of compounds with different R and L as well as the $-2J_\Sigma$ values.

Taking into account the maximum overlap, it is clear that the most effective interaction channels are due to superexchange between the σ -orbitals ($d_{x^2-y^2}$, $-2J_{vv}$) and π -orbitals (d_{xy} , $-2J_{\xi\xi}$) through the OC(O) bridges.

It is an easy matter to find out that pronounced variations of the parameter $-2J$ on going from one metal to another can be explained using the model of exchange channels.

Indeed, among four channels ($d_{xy} - d_{xy}$, $d_{xy} - d_{z^2}$, $d_{z^2} - d_{xy}$ and $d_{z^2} - d_{z^2}$) in the V^{3+} complexes, only the $d_{xy} - d_{xy}$ channel is effective. According to Eqn (41), in this case we get

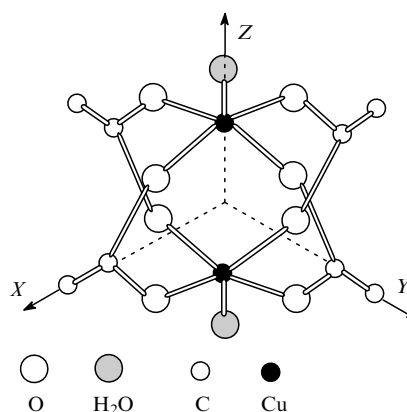


Figure 15. Structure of Cu(II) acetate monohydrate.

Table 1. Magnetic parameters of binuclear carboxylates.

Ion	Half-filled orbitals	$-2J/\text{cm}^{-1}$	$-2J_\Sigma/\text{cm}^{-1}$
Ti^{3+}	d_{xy}	1000 ± 200	1000 ± 200
V^{3+}	d_{xy}, d_{z^2}	280 ± 40	1120 ± 150
Mn^{2+}	$d_{xy}, d_{z^2}, d_{x^2-y^2}, d_{xz}, d_{yz}$	30 ± 4	750 ± 100
Ni^{2+}	$d_{xy}, d_{x^2-y^2}$	300 ± 20	1200 ± 80
Cu^{2+}	$d_{x^2-y^2}$	340 ± 50	340 ± 50

$$-2J_\Sigma = -2J(\text{V}^{3+}) \times 4 \times 1 \times 1 \approx -2J_{\xi\xi} \approx -2J(\text{Ti}^{3+}) = 1000 \text{ cm}^{-1},$$

which is in good agreement with the experimental data. Similarly, for Ni^{2+} dimers one gets

$$-2J_\Sigma \approx -2J_{\xi\xi} - 2J_{vv} \approx -2J(\text{Ti}^{3+}) - 2J(\text{Cu}^{2+}) \approx 1300 \text{ cm}^{-1},$$

which coincides with the experimental value within the limits of experimental error. In the case of Mn(II) complexes, agreement is somewhat worse due to ignoring a total of twenty small ferromagnetic cross-contributions $-2J_{ij}^f$.

Many other examples are also available.^{124–127} Based on the model of interaction channels, the $-2J$ values for ten systems were estimated to a high accuracy using only a set of three calibration parameters.^{125–127}

4. Antiferromagnetics with metal–metal bonds

Until recently, it was accepted that compounds with metal–metal bonds can possess only trivial magnetic properties, viz., be diamagnetic or paramagnetic at an even or odd number of electrons, respectively (see Ref. 128 and references cited therein). However, chromium(III) cyclopentadienylchalcogenates (Fig. 16) have strained structures^{129–131} indicating the presence of metal–metal bonds but possess antiferromagnetic properties ($-2J \sim 400 \text{ cm}^{-1}$, which is typical of the systems with 'through-ligand' exchange).

Using the model of exchange channels, one can also determine the conditions for this class of magnetic materials to exist. Indeed, for the magnetic moment of an antiferromagnetic complex to be temperature dependent at not too high temperatures, at least the first excited state should be populated. This leads to the requirement

$$-2J = \frac{-2J_\Sigma}{4S_a S_b} < 1000 \text{ cm}^{-1}, \quad (42)$$

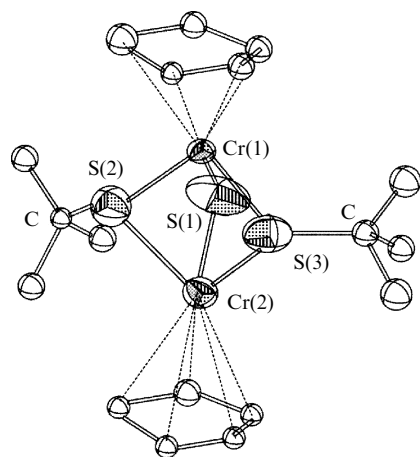


Figure 16. Structure of $(\pi\text{-C}_5\text{H}_5)_2\text{Cr}_2(\mu\text{-S})(\mu\text{-SCMe}_3)_2$.¹²⁹

i.e., $-2J < 1000 \times 4S_a S_b$. From this it follows that the large value of the parameter $-2J_\Sigma$, which is due to the presence of the metal–metal bond, does not necessarily cause diamagnetic properties to be possessed at rather large values of the product $4S_a S_b$. The chromium(III) complexes under consideration ($S_i = 3/2$) meet this condition.

This approach allowed compounds with metal–metal bonds to be found among double chlorides of composition AMCl_3 .¹³²

At the same time, there are strong grounds to believe that if the major contribution to the exchange is due to the formation of the metal–metal bond $d_\eta^a - d_\eta^b$, the largest contribution in expression (34) comes from the second term. Therefore, the energy difference, $\Delta(\eta)$, between the antibonding and bonding MOs is given by¹³³

$$\Delta(\eta) \approx \sqrt{-2J \cdot 4S_a S_b \cdot 2K_{ab}}. \quad (43)$$

This value is a natural measure of the binding energy, which can be estimated with ease, because relationship (43) contains some known or readily measurable parameters. It should be emphasised that attempts to reveal weak metal–metal bonds using other experimental or theoretical methods face great difficulties.

IV. Design of molecular magnets

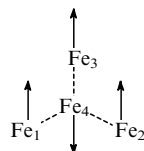
The term ‘design of molecular magnets’ was introduced to denote targeted synthesis and studies of compounds built of molecular blocks and containing unpaired electrons involved in some interactions. This is a very broad field of research. In this review, molecular magnets mean polynuclear complexes which have high spins of the low levels and, hence, high magnetic moments. This bridges the gap between molecular magnets and conventional magnetic materials.

As mentioned above, high magnetic moments due to ferromagnetism can be expected in the case of specific geometry of the bridging groups, different symmetry of the magnetic orbitals and mixed valence of the complex-forming metal. However, the first two cases can hardly be implemented in practice in a predictable manner, while the mixed-valence systems (in addition) tend to be transformed into heterovalent weak ferromagnetic complexes. At the same time, the conditions for occurrence of strong antiferromagnetism are much simpler. This is often employed in various methods of attaining high magnetic moments.

1. Tetranuclear complexes

A typical example of tetranuclear complexes is provided by a trivalent iron complex (Fe_4^{III}), which was synthesised and studied recently.^{64, 134} The structure of this complex is shown in Fig. 1*b*. The interactions between the central and peripheral iron atoms occur through pairs of methoxo bridges and have an antiferro-

magnetic character ($-2J_{1234} = 21.1 \text{ cm}^{-1}$). However, this causes no diamagnetism and the ground-state spin, S , equals five. At first glance, this is a quite unexpected result, but this is not the case [it is sufficient to simply substitute $S_i = 5/2$ and $-2J_{1234} > 0$ ($-2J_{1234} \sim 0$) into relation (21)]. However, there is also a simple qualitative substantiation of this result. Indeed, antiferromagnetic interaction between the central and peripheral Fe atoms leads to antiparallel orientation of the spins of the latter with respect to the spin of the former atom and, hence, their alignment.



Thus, we get $S = 3 \times 5/2 - 5/2 = 5$. The cluster under study is characterised by a rather large D value (-0.2 cm^{-1}) and therefore exhibits a magnetic memory effect (see Section II.4.b), which, however, is observed only at $T \leq 1 \text{ K}$ due to the relatively small S and $|D|$ values.¹³⁴

The magnetic properties of a series of complexes with the $[\text{Mn}_4(\mu_3\text{-O})(\mu_3\text{-X})]^{6+}$ core and a structure similar to that of a distorted cubane, which resembles the structure shown in Fig. 1*b*, were studied.^{135–137} Since the atoms of the magnetic core, $\text{Mn}^{\text{IV}}\text{Mn}_3^{\text{III}}$, are in different oxidation states, antiferromagnetic exchange $\text{Mn}(\text{IV})\text{--Mn}(\text{III})$ results in $S = 9/2$ and a spin alignment similarly to the case of complex Fe_4^{III} . For all complexes of this type the parameter D is negative (more exactly, -0.3 to -0.5 cm^{-1}); therefore, they exhibit a magnetic memory effect at $T \leq 1 \text{ K}$ similarly to Fe_4^{III} .

In a ‘butterfly’-like $\text{Mn}_2^{\text{II}}\text{Mn}_2^{\text{III}}$ complex the central $\text{Mn}(\text{III})$ ions are linked through two O atoms of methanolic groups while their interaction with the terminal $\text{Mn}(\text{II})$ atoms occurs through the same oxygen and bidentate acetate bridges. All the $\text{Mn}\text{--Mn}$ exchange interactions have a ferromagnetic character;¹³⁸ as a consequence, $S = 9$. In combination with the value of the parameter D (-0.32 cm^{-1}) this leads to a relatively high activation energy for relaxation of the magnetisation ($\sim 12 \text{ cm}^{-1}$). In the dehydrated form of the complex $\text{Mn}_2^{\text{II}}\text{Mn}_2^{\text{III}}$, antiferromagnetic exchange through the solvent molecules leads to a decrease in S down to 8, the anisotropic exchange also weakens ($D \approx -0.25 \text{ cm}^{-1}$) and the activation barrier decreases.

A similar complex V_4^{III} is characterised by the $-2J_{12}$ and $-2J_{13}$ values of -31.2 and 27.5 cm^{-1} , respectively (see Ref. 139). The competition between ferromagnetic and antiferromagnetic exchange causes the total spin ($S = 3$) to become smaller than the sum of the spins $S_{\text{max}} = 4$. Because of this, the activation barrier is at most 1.5 cm^{-1} . Complexes of Cr_4^{III} , Mn_4^{III} and Fe_4^{III} (analogues of the vanadium complex in question) also have low ground-state spins.¹³⁹

2. Complex Fe_8

A $\text{Fe}(\text{III})$ complex with the central fragment $[\text{Fe}_8(\mu_3\text{-O})_2(\mu_2\text{-OH})_{12}]^{8+}$ (see Ref. 140) is usually denoted as Fe_8 . It has a D_2 symmetry (Fig. 17), which allows the full matrix of the secular determinant of dimension 1679 616 to be divided into blocks of dimension ≤ 4170 (see Section II.3.b). Exact numerical calculations of the magnetic susceptibility were carried out and the exchange parameters were estimated.⁴⁰ All interactions in the Fe_8 complex have antiferromagnetic character; nevertheless, the ground state has a spin S of 9. The anisotropic exchange parameter D equals -0.19 cm^{-1} (see Refs 141 and 142); therefore, at $T \leq 1 \text{ K}$ the complex exhibits a marked hysteresis of the magnetisation and the activation barrier to relaxation of the magnetisation is rather high ($\sim 17 \text{ cm}^{-1}$, see Ref. 40).

3. Complexes Mn_{12}

A typical representative of Mn_{12} complexes is $[\text{Mn}_{12}\text{O}_{12}(\text{O}_2\text{CR})_{16}(\text{H}_2\text{O})_4] \cdot 2 \text{ MeCOOH} \cdot 4 \text{ H}_2\text{O}$ ($\text{R} = \text{Me}$)¹⁴³

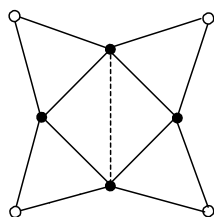


Figure 17. Structure of complex Fe_8 .

with a tetragonal structure (Fig. 18). Even full inclusion of symmetry considerations provides no possibility of division of a total of 10^8 basic states into blocks of admissible size for computer calculations. However, the exchange parameters were estimated by comparing the calculated positions of several low levels with experimental data (see the caption to Fig. 18).¹⁴⁴ This complex is characterised by $S = 10$ and $D = -0.4 \text{ cm}^{-1}$; therefore, the activation barrier to relaxation of the magnetisation reaches a value of 49 cm^{-1} (see Refs 145 and 146). Complex Mn_{12} has a higher symmetry (C_4) than complex Fe_8 so the anisotropic exchange parameters of the type $C(S_+^4 + S_-^4)$ make a much smaller contribution. It is these operators that make the $|S, M\rangle \rightarrow |S', M'\rangle$ transitions allowed; therefore, it is not surprising that at 2 K the Mn_{12} complexes retain their magnetisation for a period of several months.¹⁴⁷

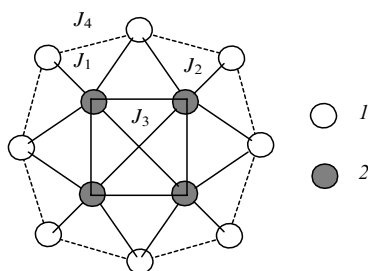


Figure 18. Structure of Mn_{12} complexes.

Mn(III) atoms with a spin of 2 (I) and Mn(IV) atoms with a spin of $3/2$ (2). The exchange parameters are as follows: $-2J_1 = 150 \text{ cm}^{-1}$, $-2J_2 \approx -2J_3 = 60 \text{ cm}^{-1}$ and $-2J_4 = -45 \text{ cm}^{-1}$.

Generally, the outer-sphere ligands have little effect on the magnetic properties of Mn_{12} complexes. However, replacement of bidentate bridging ligands O_2CMe by O_2CEt results in a decrease in S down to 9, while the one-electron reduction of acetate is accompanied by the transformation of $\text{Mn}_8^{\text{III}}\text{Mn}_4^{\text{IV}}$ into $\text{Mn}^{\text{II}}\text{Mn}_7^{\text{III}}\text{Mn}_4^{\text{IV}}$ and by an increase in S to $19/2$.¹⁴⁸ These and a number of other substituted complexes are also characterised by slow relaxation of the magnetisation.¹⁴⁹

4. Complex Fe_{13}

The first thirteen-nuclear complex of trivalent iron is $(\text{C}_5\text{H}_6\text{N}^+)_5[\text{Fe}_{13}(\mu_4\text{-O})_4(\mu_2\text{-OMe})_{12}\text{F}_{24}]\text{MeOH} \cdot 4\text{H}_2\text{O}$.¹⁵⁰ Its structure comprises four triangular $[\text{Fe}_3(\mu_3\text{-O})(\mu_2\text{-OMe})_3]$ subunits linked to the central tetrahedral FeO_4 moiety via monatomic oxygen bridges. The structure of this complex is schematically shown in Fig. 19. Ignoring weak exchange through fluorine bridges, the four triangular subunits can be considered non-interacting. In this case, the theorem (see Section II.3.a) can be applied to this complex. This permits analytical calculations of the energies of all $\sim 1.3 \times 10^{10}$ spin levels of the system and plotting of the theoretical curves of the temperature dependence of the magnetic susceptibility. Interpretation of experimental data (obtained in the temperature range 2–300 K) in the framework

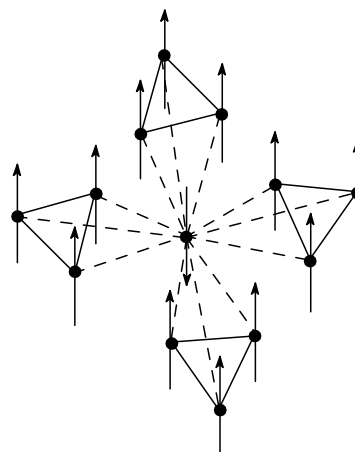


Figure 19. Structure of complex Fe_{13} .

of this theory showed that interactions within the triangular subunits and with the central iron atom are characterised by the exchange parameters $-2J_{12} = 30 \text{ cm}^{-1}$ and $-2J_{13} = 43 \text{ cm}^{-1}$, respectively.¹⁵¹ In spite of the antiferromagnetic character of all interactions, the ground state has a nonzero spin. The high ground-state spin is due to the interaction between the central and peripheral atoms, which tends to align the spins of the latter (see Fig. 19). Unlike the Fe_4 complex, in the compound Fe_{13} due to the competing interactions within the triangular subunits the highest possible spin $S_{\text{max}} = 12 \times 5/2 - 5/2 = 55/2$ is not reached. However, calculations showed that the ground-state spin can increase up to $31/2$ and even more with an increase in the J_{13}/J_{12} ratio from ~ 0.7 to ~ 1 . In practice, this can be attained by, e.g., replacing the $\mu_4\text{-O}$ bridging ligands by some ligands with enhanced electron-donor ability.

5. n -Nuclear complexes with $n > 13$

Currently, the problem of synthesis of polynuclear complexes containing a prescribed number of magnetic metal atoms is still far from being solved. However, methods of synthesis of such complexes are rapidly developing. In particular, crystals containing alternating complexes of trivalent iron $[\text{Fe}_{19}(\mu_3\text{-O})_6(\mu_3\text{-OH})_6 \cdot (\mu_2\text{-OH})_8\text{L}_{10}(\text{H}_2\text{O})_{12}]^+$ (Fe_{19}) and $[\text{Fe}_{17}(\mu_3\text{-O})_4(\mu_3\text{-OH})_6 \cdot (\mu_2\text{-OH})_{10}\text{L}_8(\text{H}_2\text{O})_{12}]^{3+}$ (Fe_{17}), where $\text{H}_3\text{L} = \text{N}(\text{CHRCOOH})_2 \cdot (\text{CH}_2\text{CH}_2\text{OH})$, $\text{R} = \text{H}$, were synthesised and studied.¹⁵² Both complexes have flattened compact structures (Fig. 20) and can be considered as a result of further complication of the structures of complexes Fe_8 and Mn_{12} . Experimental data showed that at least one of the two complexes has a ground-state spin, S , of $33/2$. Complexes of Fe_{19} with $\text{R} = \text{Et}$ and Me characterised by $S = 31/1 - 33/2$ and $S = 33/2$, respectively, were synthesised.¹⁵³ Currently, they have the highest ground-state spins. However, the magnetic memory effects in these complexes are weak because the parameter D of the complex with $\text{R} = \text{Me}$ equals only -0.035 cm^{-1} .

Attainment of large negative D values is likely a common problem to studies of the systems comprising only metal atoms in the S -states. Indeed, in this case the single-ion contribution to D is small⁶⁸ while the exchange is nearly isotropic. Only the dipole–dipole contribution can be large, provided that all the metal–metal bond axes are nearly parallel. Clearly, this is not probable for compact polynuclear molecules. For the same reason, strong magnetic memory effects are also not probable in the high-spin systems containing organic radicals.¹⁵⁴

Experimental data for a large number of other polynuclear complexes and their theoretical interpretation can be found in the literature.^{22–25, 154}

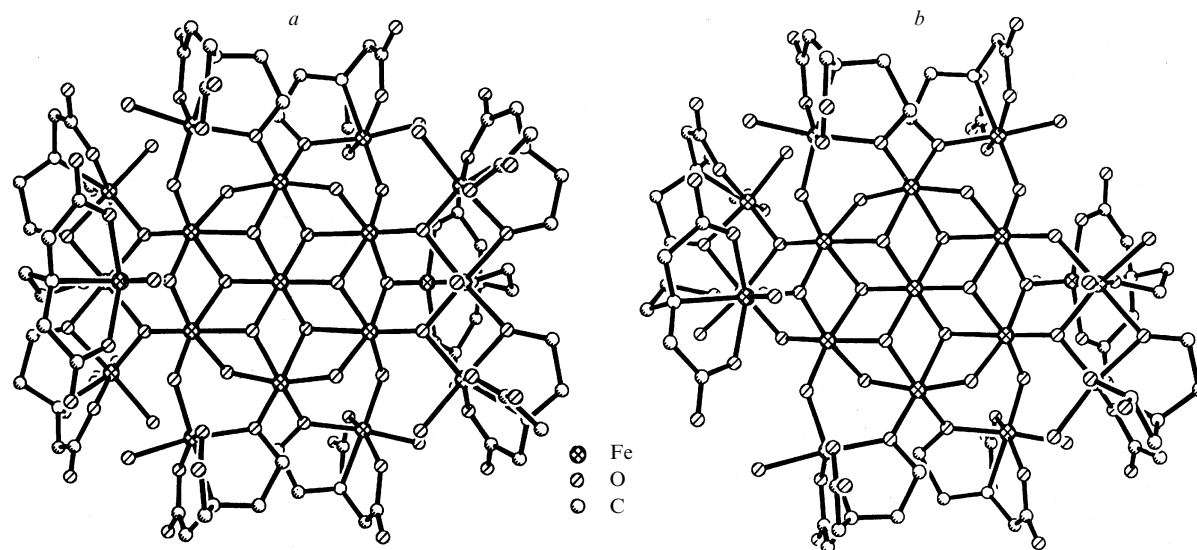


Figure 20. Structures of complexes $[\text{Fe}_{19}(\mu_3\text{-O})_6(\mu_3\text{-OH})_6(\mu_2\text{-OH})_8(\text{L})_{10}(\text{H}_2\text{O})_{12}]^+$ (a) and $[\text{Fe}_{17}(\mu_3\text{-O})_4(\mu_3\text{-OH})_6(\mu_2\text{-OH})_{10}(\text{L})_8(\text{H}_2\text{O})_{12}]^{3+}$ (b).

V. Conclusion

The last five decades have been characterised by rapid development of the chemistry, crystal chemistry and magnetic chemistry of exchange clusters. Analysis of experimental data for several thousands of relatively simple complexes allowed researchers to reveal and theoretically substantiate a variety of correlations between the exchange parameters and the characteristics of the electronic structure and the geometry of both molecular fragments and entire molecules. Taken together with the progress of preparative methods, this serves as a reliable basis for the development of a new research avenue in the field of coordination chemistry, namely, design of molecular magnets. In contrast to colloid chemistry,¹⁵⁵ coordination chemistry concerns polynuclear systems ($N \sim 10-20$) in the form of crystalline substances composed of 'building blocks' (molecules of a particular shape, size and orientation). Hence, such systems possess definite physical properties. At the same time, if magnetic inorganic crystals are usually grown from high-temperature melts, polynuclear complexes can be obtained from solutions at room temperature. This opens up considerable promise for the synthesis of magnets of various composition, structure and properties.¹⁵⁶⁻¹⁵⁸ In particular, the magnetic sites in crystals of polynuclear complexes can comprise molecular and submolecular units possessing nontrivial magnetic properties rather than simple metal ions.

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^b — *Russ. J. Phys. Chem. (Engl. Transl.)*

^c — *Russ. J. Coord. Chem. (Engl. Transl.)*

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^f — *Russ. J. Inorg. Chem. (Engl. Transl.)*

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X-Ray spectra and electronic structure of boron compounds[†]

V D Yumatov, E A Il'inchik, V V Volkov

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Abstract. The state-of-the-art in boron chemistry, the characteristic features of boron compounds and crystalline phases based on them, the chemical bonds in these compounds and their electronic structures are considered. The physical principles of X-ray spectroscopy and the results it provided on the chemical structures of boron compounds and the nature of chemical bonds in them are discussed. Data for X-ray photoelectron and ultraviolet photoelectron spectroscopies for various elemental boron modifications, boron oxide phases, borides, nitrides, halides, derivatives of boron hydrides and carboranes, as well as metalloboranes are compared. The bibliography includes 247 references.

I. Introduction

The chemistry of elemental boron, its compounds and crystalline phases based on them is currently a vast and quite complicated scientific field at the boundary of inorganic and organoelement chemistry. Boron compounds are successfully used in various areas of materials science, in catalysis, inorganic and organic synthesis, biochemistry, agriculture, medicine, *etc.* The fundamental and applied aspects of boron chemistry are covered in sufficient detail in numerous papers, reviews and monographs and in patent literature. The publication of a festschrift on boron chemistry and special journal issues on the subject^{1–3} is evidence of the great scientific and practical value of this field of science.

The study of bond nature in compounds by both theoretical and experimental methods providing information about electronic structure is a task of current interest in modern chemistry. The results of such studies allow explanation of physicochemical properties of compounds and their reactivities and forecast ways for their synthesis. In this review, we generalise the main data of studies on the electronic structures and characteristics of chemical bonds in boron compounds by X-ray emission and X-ray absorption spectroscopies (XES and XAS, respectively). Special attention is focused on the use of these methods in combination with X-ray photoelectron spectroscopy (XPS) and ultraviolet photoelectron spectroscopy (UPS). The role of quantum-chemical calculations in interpreting the spectra is also considered. In

order to systematise data from numerous publications, we first discuss the state-of-the-art of boron chemistry and specific features of chemical bonding and coordination in the most typical classes of boron compounds and then briefly present the principles and experimental fundamentals of XPS, UPS, XES and XAS. The results of X-ray spectral studies are generalised for the main classes of boron compounds; emphasis is made on those classes that have been considered in lesser detail in previous reviews, particularly, on boron hydride compounds. Finally, we discuss the relationship between the discovered features of the electronic structures of boron compounds and their physicochemical characteristics.

II. Characteristics of boron compounds, their structures and chemical bonds

A boron atom ($z = 5$) has the $1s^2 2s^2 2p^1$ electronic configuration. When boron or boron compounds form solid phases, the valence electrons assume a more energetically favourable configuration, *viz.*, $1s^2 2s^1 2p^2$, where the boron atom has four valence atomic orbitals (AO) $2s$, $2p_x$, $2p_y$, $2p_z$ and only three valence electrons.^{4,5} A specific feature of this configuration is that, owing to the small covalent atomic radius of boron (0.80–1.01 Å) and ionic radius of B^{3+} [0.15 Å and 0.25 Å for coordination numbers (CN) 3 and 4, respectively], the electrons of a boron atom and the AOs are localised in the strong field of the nucleus with relatively weak shielding [the first ionisation potential (IP) of a B atom equals 8.3 eV].⁶ This feature imparts unusual chemical properties to boron, which allow this element with a simple electronic structure to form a very complex system of compounds and crystalline phases characterised by numerous types of chemical bonding. In particular, it is noteworthy that a boron atom can form σ -bonds involving AOs in the sp^2 configuration, *e.g.*, in such molecules as BX_3 (where X is a halogen), BR_3 , *etc.* The vacant $2p_z$ -AO predetermines the strong electron-acceptor properties of boron, which interacts with electron donors to give adducts and complexes of the $R_3N \cdot BH_3$, $BX_3 \cdot NH_3$, $Me_2O \cdot BF_3$, $[BF_4]^-$, and $[BPh_4]^-$ types. Multi-centred (mainly three-centred) bonds are formed in cluster-type boron hydrides and their derivatives, certain borides and elementary boron.^{3–5} Such compounds refer to electron-deficient systems. These compounds contain fewer valence electrons than is required to form electron pairs between neighbouring atoms that form chemical bonds. For example, a diborane(6) molecule (B_2H_6) contains 12 valence electrons (six

V D Yumatov, E A Il'inchik, V V Volkov A V Nikolaev Institute of Inorganic Chemistry, Siberian Branch of the Russian Academy of Sciences, Prosp. Akad. Lavrent'eva 3, 630090 Novosibirsk, Russian Federation. Fax (7-383) 234 44 89. Tel. (7-383) 234 39 75 (V V Volkov)

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[†] Dedicated to the 100th anniversary of Academician Anatoly Vasil'evich Nikolaev, the author of many classical works in borate chemistry.

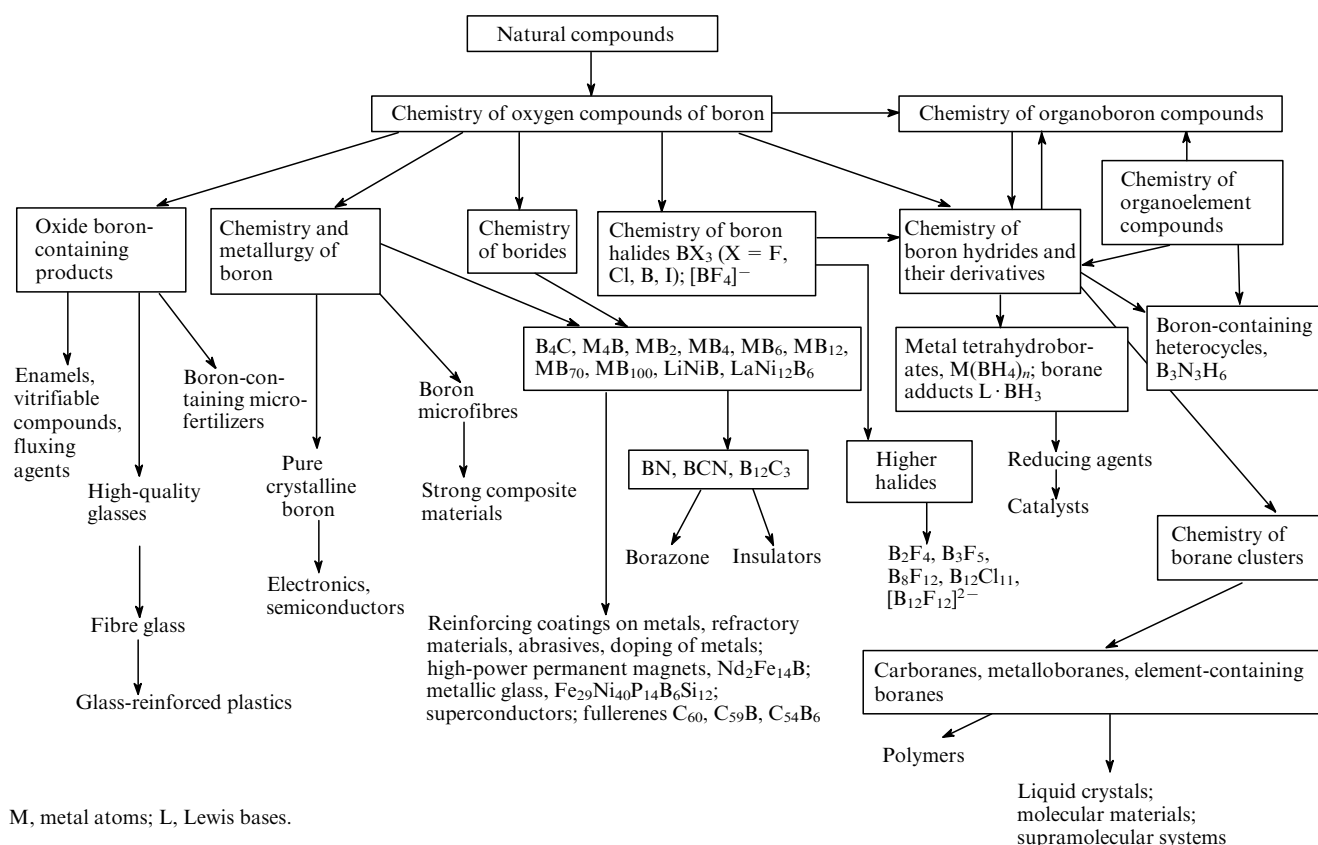


Figure 1. Trends in modern boron chemistry.

pairs), which enable the formation of seven bonds: six B–H bonds and one B–B bond. The electronic structures of this type of molecule are described using the multi-centred two-electron bond concept within the molecular orbital (MO) method. Study of the electronic structures of numerous boron compounds of various types by theoretical (quantum-chemical) and experimental methods is a topical problem.

Figure 1 shows schematically the directions of modern boron chemistry. This is not a comprehensive scheme, but we will use it to determine the order for presenting and discussing experimental data. We will focus the most attention on certain reviews concerning boron chemistry and on experimental methods.

The starting materials for the preparation of boron compounds, boron-containing products and materials based on them include oxide derivatives extracted from ores (boron oxide, boric acid, borates, peroxyborates).^{4, 7–11} The complexity of the crystal structures of B_2O_3 , various modifications of boric acid and structures of borate and polyborate anions in solutions and in crystalline phases has been noted.^{4, 10, 11} Figure 2 shows the structures of a number of oxide boron compounds and their typical fragments. In oxygen compounds, the coordination number of a boron atom can be equal to three (sp^2 -hybridisation and π -bonds) or four (sp^3 -hybridisation and only σ -bonds). The lamellar structure of orthoboric acid¹⁰ consists of triclinic cells, each containing four $B(OH)_3$ molecules, that are held by hydrogen bonds ($=B-O-H \cdots O-B=$) to a considerable extent (their lengths are 2.72 Å if the boron coordination number is equal to three). Each oxygen atom is involved in hydrogen bonds with two hydrogen atoms. Studies of this system are of interest for revealing the effect of hydrogen bonds on the electronic structures of the constituent atoms. The structures of polyborate anions are more complex:^{10, 11} ions containing from 1 to 6 or 9 boron atoms, such as $[B_5O_7(OH)_4]^{3-}$, $\{B_9O_{14}(OH)_4[OB(OH)_2]_2\}^{7-}$, etc., can be present in salts of these anions, both in solutions and in crystals. A six-membered heterocycle boroxol is the main structural fragment of polyborate anions; this can be part of monomeric,

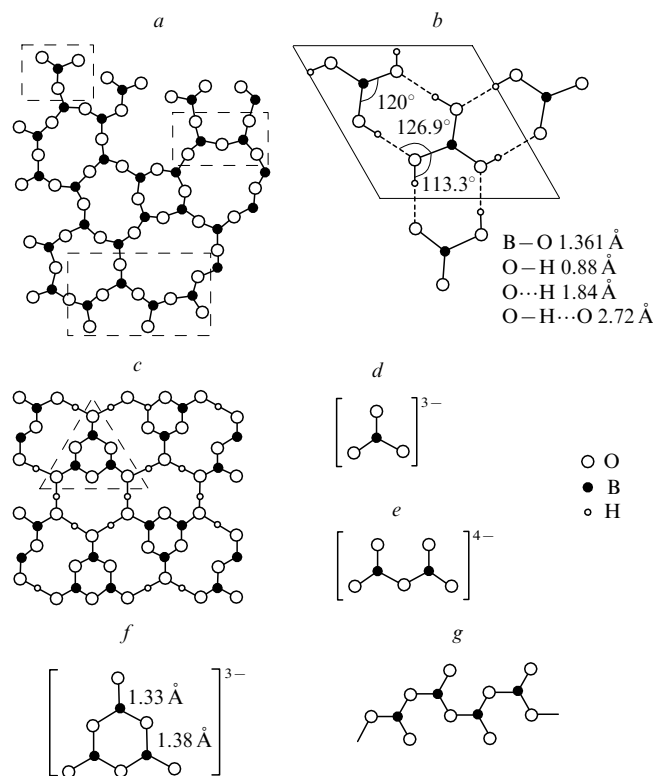


Figure 2. Fragments of structures of some oxygen-containing boron compounds.

(a) Glassy boric anhydride (B_2O_3);⁸ (b) orthoboric acid $[B(OH)_3]$;¹⁰ (c) lamellar structure of orthorhombic metaboric acid (HBO_2);^{4, 8, 10} (d–g) structural fragments of borates (marked by dashed lines in Fig. 2a,c).^{4, 8, 10, 11}

polymeric and 'fused' polycyclic structures containing oxygen atoms with CN = 3.

Numerous publications deal with the preparation of pure boron, study of its structure and properties and technological and applied aspects of its usage (see, *e.g.*, the reviews and monographs^{4, 5, 8, 10, 12–14}). Elementary crystalline boron is an exceptionally 'difficult' subject. Studies of the structures of its crystalline phases and the respective physical properties are complicated by the fact that over ten polymorphic modifications of boron are known.^{5, 12} The three most stable polymorphic modifications of fused boron have been characterised reliably: the α -rhombohedral (B_{12}), α -tetragonal (B_{50}) and β -rhombohedral modifications (B_{105}). Figure 3 shows fragments of certain crystal structures of boron. The β -rhombohedral form is thermodynamically most favourable.^{10, 12, 14} Amorphous boron phases are also known; they are generally formed at relatively low temperatures. Difficulties in the preparation of chemically pure samples of individual boron phases are caused by its high melting point (2450 K), its considerable chemical reactivity (*i.e.*, high probability of contamination by admixtures from the gaseous environment and from the equipment) and the large number of crystal modifications with slow phase transitions between them. All these facts should be taken into consideration in studies and interpretation of the data on boron properties. An icosahedron with I_h symmetry is the structure-forming element of crystalline boron phases, 12 boron atoms with coordination numbers 5 occupy its vertices (B_{12}) (the coordination number is 6 in the formation of bonds between the B_{12} clusters), the B–B interatomic distances are equal to 1.73–1.79 Å (see Fig. 3*a*).^{2, 10} Owing to the electron deficiency and the relatively high ionisation energy of boron atoms (8.298 eV¹⁵), the B–B bond has substantially covalent rather than metallic character.¹⁰ Polymorphic modifications differ in the spatial arrangements of the B_{12}

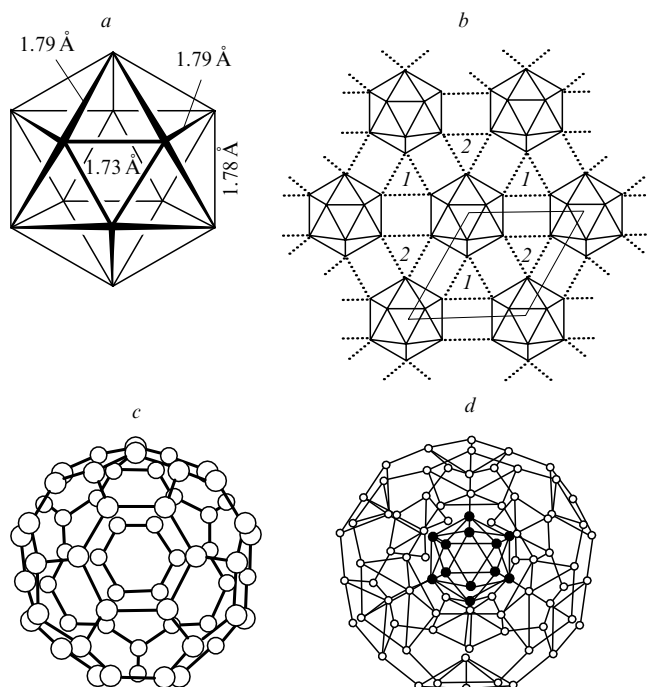


Figure 3. Fragments of structures of elementary boron crystal modifications.^{4, 5, 8, 10, 12, 14}

(*a*) B_{12} icosahedron; (*b*) basis layer of B_{12} icosahedra in the structure of α -rhombohedral boron; the numbers 1 and 2 indicate that the triangles are located in different levels (1, upper, 2, lower); (*c*, *d*) structural fragments of β -rhombohedral boron based on a 'giant icosahedron' B_{84} (to provide a better picture, the B_{12} icosahedron existing in the structure is drawn in black circles).

icosahedra, the nature of bonds between them and the coordination numbers of boron atoms. Figure 3*b* shows an example of the mutual arrangement of the B_{12} icosahedra in crystalline structures. Furthermore, this polyhedron or its fragments are incorporated in many boron compounds belonging to various types. Amorphous boron can contain discrete groups containing from 2 to 6 bound B_{12} clusters together with structural units of about 100 atoms built of species involving more than 12 boron atoms (with a size of ~ 15 Å), as well as undeveloped icosahedra and sole atoms in pores.^{13, 16–18} Such structure variations affect boron properties, including electronic properties.

Borides, *i.e.*, compounds and phases in which boron atoms are bound with more electropositive elements (mainly with metals, M), represent a vast class of compounds with diverse compositions and structural types.^{4, 5, 8, 10, 12, 19–22} Many of them have a set of valuable physicochemical properties (including mechanical, thermal, corrosion, electrophysical and magnetic properties); a number of phases were found to be superconductors. The crystal-chemical aspects of boride chemistry are generalised in a monograph.²⁰ The compositions and structure types of binary borides M_mB_n are greatly diverse (Fig. 4). The existence of about 200 such borides were reported.¹⁰ Twenty-four boride compositions have been studied reliably, *viz.*, from M_5B (the metal-rich boride range) to MB_{100} (the boron-rich boride range); however, six variants of the following stoichiometric compositions, the M_2B , MB , MB_2 , MB_4 , MB_6 and MB_{12} are the most abundant. Moreover, numerous variable-composition phases and solid solutions are known. There are at least six possible configurations of boron atoms in boride structures^{10, 22} in which M–B, B–B and M–M bonds are combined in different ways, while boron can be present as single atoms or pairs of atoms, or form zigzag linear structures, branched chains, planar one-dimensional and two-dimensional hexagonal networks, and 3D cluster fragments (see Fig. 4). In a number of works,^{10, 20, 23} binary borides were classified according to the position of the metal in the Periodic table; however, no correlation of boride compositions and structures with the position of the metal could be revealed. For example, hexaborides MB_6 are typical of both alkaline-earth metals and lanthanides and actinides that are quite different from the former; however, these borides have similar structures. Diborides MB_2 are formed by metals of different groups, *viz.*, Mg, Al, Gd, Zr, V, U, *etc.*^{4, 10, 20} The nature of chemical bonding in borides is complex. Various combinations of covalent, ionic and metallic bonds exist. Numerous ternary and more complex borides and other compounds, including boron-containing fullerenes and nanostructures, have been obtained and studied.^{8, 10, 12, 20, 22, 24} The results of quantum-chemical studies on electronic structures and chemical bond nature in borides were generalised by Ivanovskii and Shveikin.^{12, 22}

At least 2500 publications (apart from patents) dealt with problems of chemistry and technology of boron nitride (BN), its crystalline modifications and most important applied properties; Refs 12 and 25–32 are the most interesting. Four crystal modifications of boron nitride are known: two graphite-like modifications, *viz.*, hexagonal (hBN) and rhombohedral (rBN), and two dense diamond-like ones, *viz.*, cubic, or sphalerite-like (cBN) and wurtzite-like (wBN), are present in the phase diagram.^{33–35} In lamellar graphite-like modifications, the B and N atoms form σ -bonds with each other; moreover, π -bonding also occurs in the layer planes due to interaction of vacant AOs of the boron atom with the lone electron pair of the nitrogen atom. Bonding between the layers in the hBN structure is also largely determined by the van der Waals and electrostatic interactions of oppositely charged boron and nitrogen atoms in layers located one above another (see Fig. 4*f*). The bonding of the boron and nitrogen atoms with the tetrahedral coordination in cBN occurs due to the interaction of sp^3 -hybrid states. The electronic structure of boron nitride was studied comprehensively; see, *e.g.*, Refs 12 and 36–39.

The fundamentals of the chemistry of boron halides are described in a number of reviews.^{10, 40, 41} Covalent trihalides

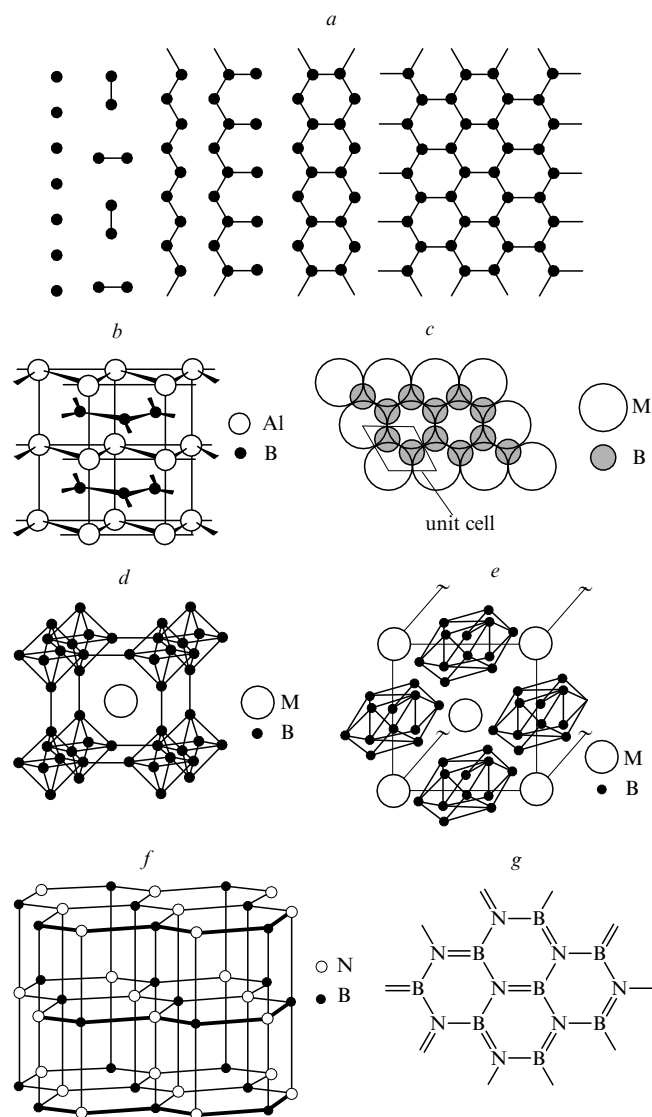


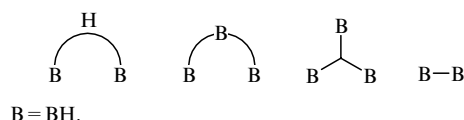
Figure 4. The main structural motives of certain metal borides and hexagonal boron nitride (hBN).

(a) shapes of ideal boron atom bonding in metal-rich borides;^{10,20,22} (b) the AlB₂ crystal structure characteristic of many other diborides;^{10,20} (c) hexagonal layers of B and M atoms in MB₂ structures; (d) cubic structure of metal hexaborides MB₆ containing octahedral clusters of boron atoms;^{4,10,22} (e) cuboctahedral B₁₂ clusters in the structures of dodecaborides MB₁₂;¹⁰ (f, g) lamellar structure of hBN and bonding of B and N atoms in layers.^{4,10}

BF₃, BCl₃, BBr₃ and BI₃ are the most typical. Their molecules are characterised by planar trigonal structures with *D*_{3h} symmetry; sp²-hybridisation of the 2s-, 2p_x- and 2p_y-AOs of the boron atom occurs in these molecules, whereas the 2p_z-AO remains vacant.^{10,40} Therefore, boron trihalides are strong Lewis acids (electron acceptors) that form adducts of the type L·BF₃ with Lewis bases (L) (see Refs 42–44). Higher boron halides are also of interest for scientists;^{45,46} these include, *e.g.*, B₂F₄ and B₃F₅, clusters such as B₈Cl₈ and B₈F₁₂ and the icosahedral *closo*-B₁₂F₁₂²⁻ anion.

The chemistry of boron hydrides and their derivatives is currently matter of intense development. Its fundamentals were established in 1912 in the classical studies by Stock, which he generalised in a monograph.⁴⁷ In 1920–1940s, boranes were considered as some kind of ‘chemical exotics’, as their stoichiometry and the nature of chemical bonds in them could not be rationalised in terms of the classical electronic valence theory. It is

of note that the chemistry of boranes and the principles of the valence theory (Lewis’ octet theory of bonding electron pairs) appeared almost simultaneously; however, the former turned out to be an opposite of the latter. A rapid development of boron hydride chemistry began in the 1950s. Of note are two types of structures and compositions of the borane systems. The first one includes the simplest systems, such as borane (BH₃), BH₃·L, the tetrahydroborate anion (BH₄⁻) and its derivatives, *e.g.*, diborane(6) (B₂H₆). The second type, which is extraordinarily abundant, includes higher boron hydrides and their cluster derivatives, *e.g.*, B₅H₉ and B₁₀H₁₄; substituted decaboranes B₁₀H₁₂L₂; *closo*-borate anions B₁₀H₁₀²⁻, B₁₂H₁₂²⁻ (of the B_nH_n²⁻ type); carboranes B_{n-2}C₂H_n, including *ortho*-, *meta*- and *para*-carboranes(12) (B₁₀C₂H₁₂) and their anionic derivatives B₉C₂H₁₂⁻; ‘sandwich’-like complexes of transition metals with the composition [M^{III}(η⁵-B₉C₂H₁₁)₂]⁻; metalloboranes and metallocarboranes, *e.g.*, Sn^{II}B₉C₂H₁₁; skeletal isomers of the heteroatomic cluster (C₅H₅)₂Co^{III}B₈C₂H₁₀; thia-*nido*-borane clusters B₉SH₁₁, B₉SH₁₂, B₉SH₁₁·L; borane polymers, and many other compounds.^{4,10,46–63} Figures 5 and 6 show schematically the main bond types and examples of structures typical of borane systems. The structures of such compounds (see Fig. 5) are mainly formed with involvement of such bonds as B–H (two-centred terminal σ-bond), B–B (two-centred bond, *e.g.*, in B₅H₈–B₅H₈), B–H–B (three-centred bridging bond in B₂H₆ and other boranes), B–B–B (three-centred triangular bond, deltahedron in clusters), BBB (three-centred central bond), M–H–B–H (three-centred bridging heteroatomic bond, *e.g.*, in Zr[BH₄]₄).



It is impossible to describe borane clusters in terms of two-centred bonds due to electron deficiency. The concept of a two-electron three-centred bond in boranes was introduced by Longuet-Higgins⁶⁴ and developed in the Lipscomb topological system,^{65–67} which resulted in the formulation of the Wade ‘2*n* + 2’ rule for the calculation of ‘skeletal’ electrons that perform bonding in a cluster polyhedron. If one knows the number of ‘skeletal’ electrons, it is possible to explain and predict the structures of cluster systems in terms of the topology of polyhedra and to systematise such systems.^{56,68–70} These concepts serve as a base for classifying cluster structures into *closo*, *nido*, *arachno* and *hypho* types; they are also taken into consideration in the prediction of ways for synthesising new compounds. Yet another, exceptionally important feature of deltahedral borane clusters is that many of them are three-dimensional aromatic systems. The concept of three-dimensional aromaticity and even superaromaticity was introduced by Hoffmann and Lipscomb back in 1962⁷¹ and was subsequently developed in a number of publications.^{4,46,52,57,72–75} Such properties of borane clusters as delocalisation of electrons over MOs,⁷⁶ chemical stability and specific reactivity⁷⁷ are related to aromaticity. Like benzenoid cyclic aromatic systems, different types of three-dimensional borane cluster structures are characterised by high exaltation values[‡] of diamagnetic susceptibility^{75,78,79} and polarisability. The nature of bonds formed by M atoms in metalloboranes is a matter of discussion, as electron density can be distributed between a metal and aromatic clusters in different ways.^{56,58,80} It is undoubtedly interesting to use experimental methods that reveal electronic structures in studies of the nature of bonds in boron hydrides. Until now, the available reviews have covered this subject insufficiently.

[‡] Exaltation of diamagnetic atomic susceptibility is the increase in the absolute diamagnetic susceptibility upon inclusion of the atom in an aromatic system.

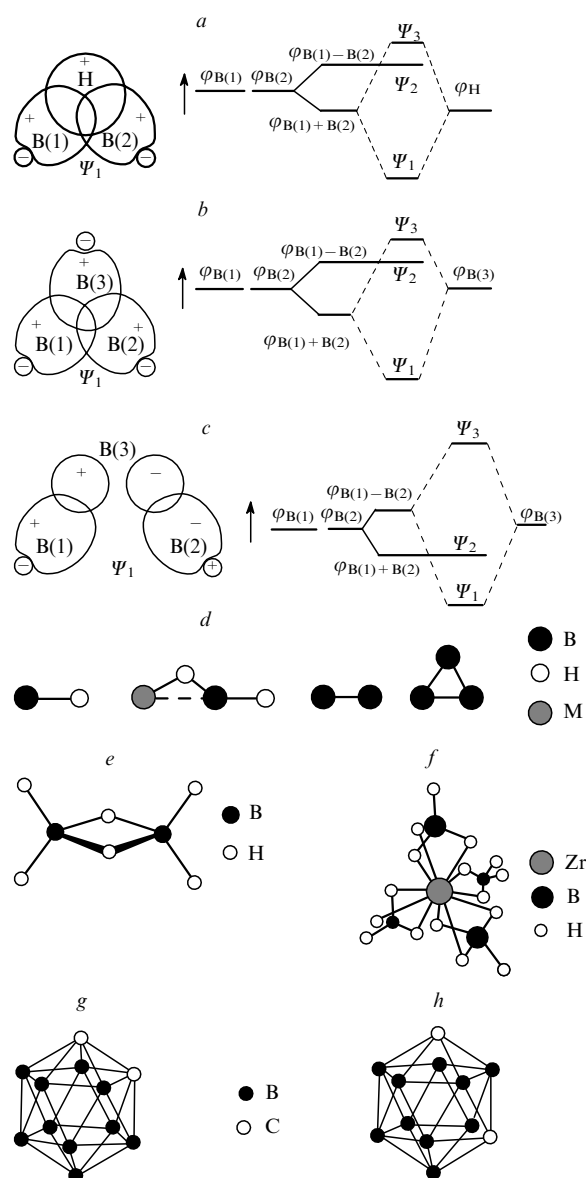
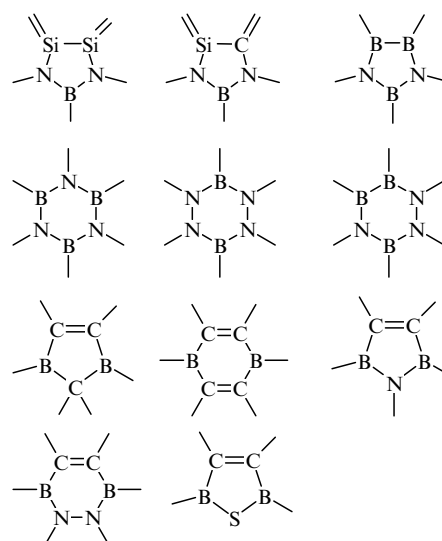


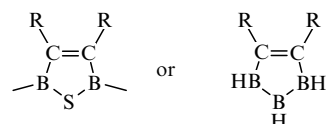
Figure 5. Bond type characteristics of boranes and their derivatives.^{4, 10, 58, 64–67}

(a) Formation of a B–H–B three-centre bridging bond and schematic representation of the relative energies of three MOs; (b) same for central BBB bonds; (c) same for open B–B–B bonds; (d) types of bonds and structure fragments, including the heteroatomic M–H–B–H bridging bond and a triangular element of a BBB deltahedron; (e) structure of diborane(6) molecule incorporating B–H bonds and a B–H–B bridging bond; (f) structure of zirconium tetrahydroborate $[\text{Zr}(\text{BH}_4)_4]$ molecule with heteroatomic $\equiv\text{Zr}-\text{H}-\text{B}-\text{H}$ bridging bonds; (g, h) closed deltahedral clusters consisting of B and C atoms in *ortho*- and *meta*-carboranes(12), respectively.

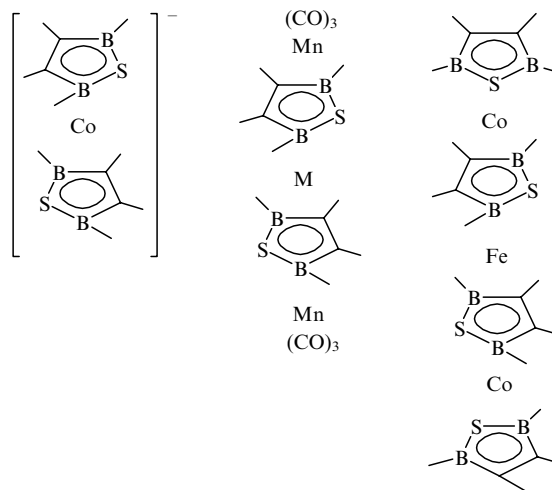
The chemistry of heterocyclic boron compounds is vast. These compounds are characterised by heteroatomic structures containing mainly from 4 to 6 atoms in a ring, systems of fused boron heterocycles and polymers.^{10, 81–87} However, no molecular cyclic systems consisting exclusively of boron atoms (similar to cyclohexane, benzene and naphthalene molecules) are known. Along with B atoms, the rings can contain C, O, N, P, Si and S atoms in various combinations. A scheme of MOs upon interaction of B and N atoms in heterocycles is shown in Fig. 7.



Ligands at the ring-forming atoms mainly include organic substituents (alkyls, aryls) and halogens that also stabilise the system. Certain five-membered heterocycles, e.g.,



are aromatic and form mononuclear and polynuclear mono- and polymetallic ‘multi-decker’ ‘sandwich’-type complexes with transition metals (Fe, Co, Ni, Cr, Ru) in which planar B_2SC_2 , B_3C_2 and other rings serve as bidentate ligands.^{61, 86, 88}



M = Fe, Co, Ni.

The nature of chemical bonding in cyclic structures, especially in boron complexes, is rather complex. This involves vacant $2p_z$ -AOs of boron, which interact with lone electron pairs belonging to the AOs of other atoms in rings (N, P, S, etc.) with partial π -bonding.

By now, the chemistry of organoboron compounds has evolved into an extensive field of science that studies the laws of formation, reactivities, structures and properties of compounds and systems containing $=\text{B}-\text{CR}=$ bonds with consideration of modern concepts on the electronic nature of bonds.^{84, 85, 89, 90}

To a certain extent, the data considered above reflect the complex structure of boron compounds and the diversity of chemical bond types therein. Therefore, the use of experimental methods, such as X-ray emission spectroscopy, X-ray photoelectron spectroscopy and UV photoelectron spectroscopy, com-

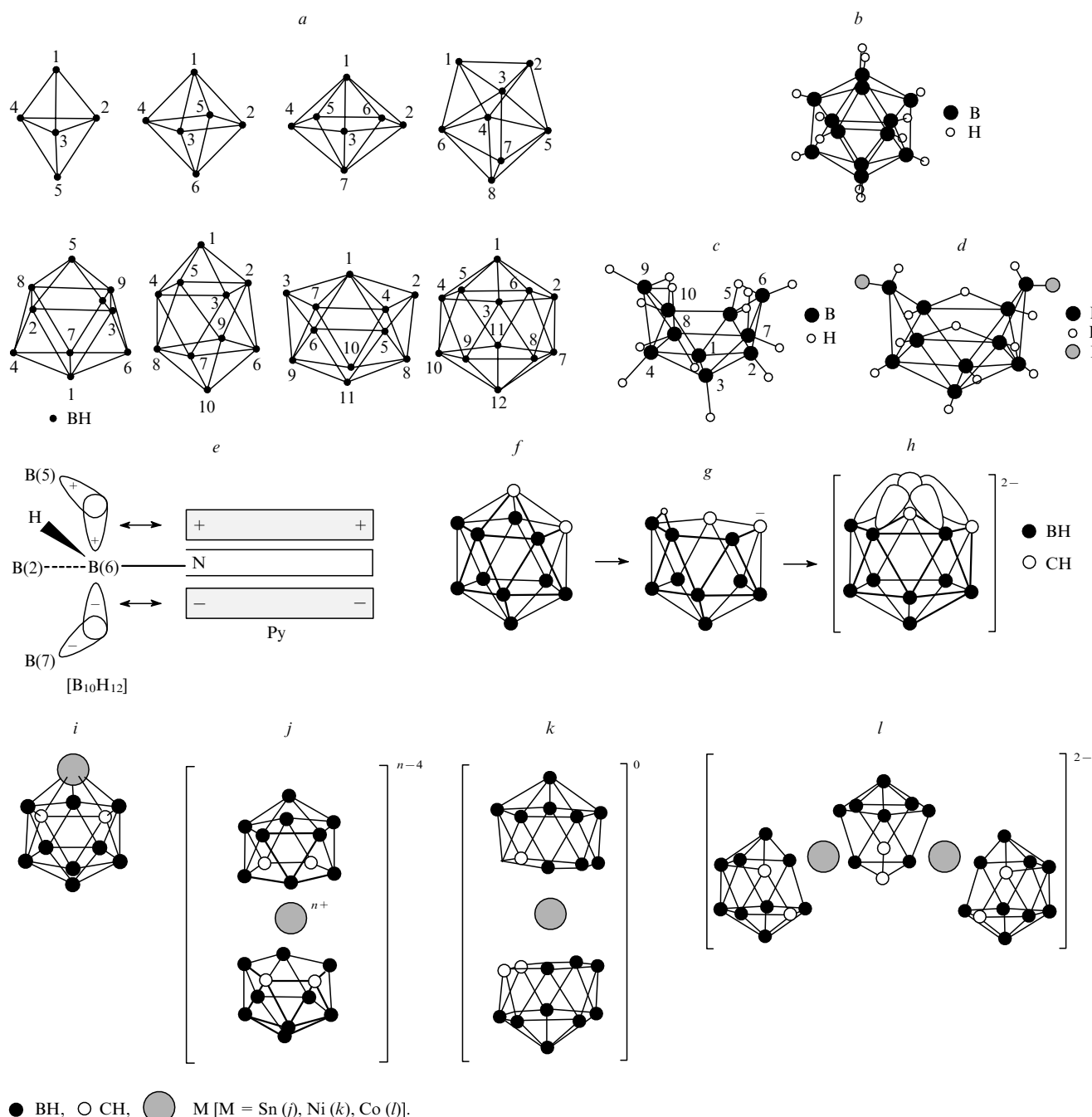


Figure 6. Schematic structures of borane clusters and their derivatives.^{4, 10, 46, 52, 54, 56, 68}

(a) Cluster-type *closo*-anions $B_nH_n^{2-}$ ($n = 5-12$); (b) a $B_{12}H_{12}^{2-}$ anion; (c) a decaborane(14) ($B_{10}H_{14}$) molecule; (d) a molecule of the 6,9- $B_{10}H_{12}L_2$ adduct; (e) interaction of the MOs of boron atoms in the $[B_{10}H_{12}]$ cluster with those of nitrogen atoms in $B_{10}H_{12}Py_2$; (f, g, h) *ortho*-carborane(12) and its anionic derivatives $B_9C_2H_{12}^-$, $B_9C_2H_{11}^{2-}$, respectively; (i) $SnB_9C_2H_{11}$ metallocarborane; (j) 'sandwich' structure of tin bisdicarbollyl anionic complex; (k) structure of the $[Ni^{IV}(B_9C_2H_{11})_2]^0$ complex; (l) structure of the $[(1,2-B_9C_2H_{11})Co^{III}(B_8C_2H_{10})Co^{III}(1,2-B_9C_2H_{11})]^{2-}$ complex.

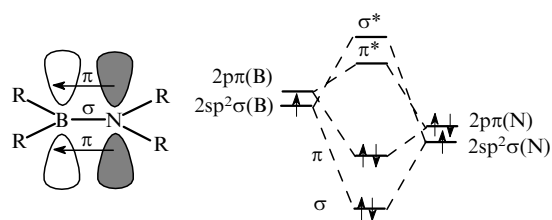


Figure 7. Scheme of AO interaction and qualitative scheme of MOs for the interaction of boron and nitrogen atoms in heterocycles with partial π -bonding.⁸³

bined with modern quantum-chemical methods for calculation of electronic structures, allows a deeper insight into the nature of chemical bonds in boron compounds.

III. The physical bases of X-ray spectroscopy

The principles of the XPS, UPS, XES and XAS methods and their experimental bases have been covered in numerous publications, starting from the classical monographs by Blokhin⁹¹ and Siegbahn *et al.*⁹² These principles and the experimental techniques for their implementation have subsequently been developed in detail and used to study various compounds.^{42, 93-103} It should be noted

that the majority of works on this subject have been carried out in the 1970s and in the early 1980s, when these methods were being implemented intensely. The basic theoretical principles of these methods have not changed considerably since that time. Great advances in the hardware implementation of these research methods have been achieved in recent years due to the development of synchrotron radiation (SR) sources.

1. The bases of X-ray photoelectron spectroscopy and UV photoelectron spectroscopy

Let us start our consideration of the physical bases of X-ray spectroscopy from the XPS and UPS methods, since these methods are used to study the process of 'preparation' for a secondary electron transition in an atom, namely, electron photoemission upon impact of ultraviolet (UV) or X-ray photons and formation of a vacancy on one level of an atom or a molecule. The probability of vacancy formation as a function of the excitation irradiation energy is studied using X-ray absorption spectroscopy. In turn, X-ray emission spectroscopy is used to study the decay of such a vacancy; in particular, the latter can be located on an inner atomic shell.

The XPS and UPS methods are based on the Einstein equation for photoeffect:

$$h\nu = IP + E,$$

where $h\nu$ is the energy of a photon (excitation radiation) impacting an atom; IP is the ionisation energy (potential) or the binding energy (E_b) of a valence or an inner electron level of an atomic-molecular system, which is coordinated with the calculated orbital energy; E is the kinetic energy of a photoelectron, which can be measured by an electron speed analyser. UPS employs ultraviolet irradiation for the excitation, whereas XPS employs soft X-ray irradiation. The most common UV sources include the He(I), He(II) and Ne(I) resonance lines (21.2, 40.8 and 16.8 eV, respectively), which allows the energies of outer electrons of atomic-molecular systems to be determined.^{42, 94, 96, 98} The sources used in XPS mainly include the MgK_{α} - (1253.6 eV) and AlK_{α} -radiation (1486.6 eV).^{42, 93, 96, 97, 99, 100} A photoelectron spectrum is the dependence of the number of emitted photoelectrons per unit time, *i.e.*, the line intensity (I), on the ionisation potential (IP) or binding energy (E_b) (the magnitudes of IP and E_b are usually expressed in eV). The measured values of IP or E_b make it possible to reveal the order of energy levels in a molecule, their symmetry, the bonding or antibonding character of separate MOs, and the relative contributions of different AOs of adjacent atoms when a MO is formed (these data are important for understanding various physical and chemical properties of a compound). In order to interpret UPS and XPS spectra of various compounds, it was suggested (with a considerable degree of approximation) to allocate three spectral regions, depending on the electron binding energy.¹⁰³ The first region ($E_b \approx 0-15$ eV) characterises structures formed with involvement of electrons from outer valence MOs, which are mainly formed by incompletely filled electrons of valence AOs. The second region ($E_b \approx 15-50$ eV) covers the structures formed by electrons of inner valence MOs (IVMOs). Finally, the third region ($E_b \gtrsim 50$ eV) contains lines reflecting the positions of deep inner (core) AOs. At present, a concept is being developed that IVMOs are considerably involved in chemical bonding along with valence MOs.¹⁰³ X-Ray spectroscopy confirms some statements of this concept by shedding light on the very complex actual electronic nature of chemical bonds. It should also be noted that the UPS method is used to study valence shells, whereas XPS is often used to study inner (atomic) shells, though it is used rather extensively to study outer shells as well.

2. X-Ray emission and absorption spectroscopies and their specific features

X-Ray emission and absorption methods provide information about the energy, composition and symmetry of molecular

orbitals. The use of these methods for the study of chemical bonds is covered in a number of monographs.^{42, 96, 99, 101}

Let us consider the physical principles of the XES and XAS methods. X-Ray emission radiation appears to be due to transitions of electrons from outer occupied levels of a molecule to inner atom-like levels that contain vacancies, which, in turn, are formed due to interaction of the molecules with a beam of high-energy electrons or upon irradiation by X-ray photons. X-Ray absorption spectra reflect transitions of electrons from an inner level to outer vacant levels of a molecule caused by incidence X-ray radiation. The main distinctive feature of these processes is that these are involved in both emission and absorption electron transitions of an inner level; the electrons on this level contribute only slightly to the chemical bond and have an almost atomic character. On the other hand, outer MOs form a system of orbitals common to the entire molecule. One can find the ionisation potential of a valence MO (IP_i) by determining the energy of an X-ray photon, which is equal to the energy of electron transition between two levels, *viz.*, an outer valence level (i) and an inner level (k), $h\nu = E_{ik}$, and given the ionisation potential of the inner MO (IP_k) (which is obtained by XPS):

$$IP_i(\text{MO}) = IP_k(\text{AO}) - E_{ik}.$$

Experimental values of $IP_i(\text{MO})$ are also provided by UPS. Hence, using the above relationship as the base, one can compare the X-ray and photoelectron spectra in a single energy scale of ionisation potentials (this operation was called matching).⁹⁶ Such a combined use of XES, UPS and XPS allows much more precise identification of specific spectral lines. However, X-ray emission spectra of different elements of a chemical compound under study can provide not only the values of MO energies but also data on the contributions of separate AOs of these elements to these values. X-Ray absorption spectra provide similar data about vacant MOs. As noted above, XES and XAS spectra can be used not only to study the energy spectrum of a molecule but also to analyse the composition of molecular orbitals, namely, to determine the squares of the coefficients at the atomic wave functions constituting an MO. To illustrate this, Fig. 8 shows a qualitative scheme of X-ray transitions from two MOs, i and j , to inner 1s-levels of boron and carbon atoms (taken as examples) within a polyatomic molecule. (It should be remembered that the short notation of X-ray spectra includes the element symbol, the level to which the electron transition occurs, and — for emission spectra — a Greek letter indicating the particular transition. In the case of absorption spectra, no Greek letter is specified.) As one can see from Fig. 8, transitions from valence MOs i and j to the same inner level, *e.g.*, B1s, give X-ray BK_{α} -spectral lines whose intensity ratio is equal to the ratio of squares of the contributions of the 2p-AOs of boron ($I_i/I_j = c_{iB2p}^2/c_{jB2p}^2$). CK_{α} -Spectral lines can be analysed in

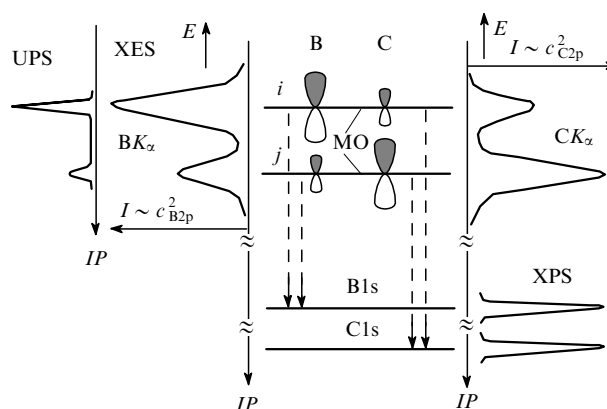


Figure 8. Scheme of X-ray transitions in the molecule and their identification. See the text for explanations.

a similar way; furthermore, more valence and inner levels can be taken as examples. A detailed analysis of this method for the determination of energy positions of MOs and their compositions is presented in a number of publications^{42,96,101} where its scope and limitations are discussed. It should be noted that the K_{α} -spectra of B, C, N, O and F atoms considered in this review allow one to determine the contributions of 2p-AOs of these atoms to MOs of chemical compounds; the K_{β} -spectra of P, S and Cl atoms allow the determination of the contributions of 3p-AOs to MOs, the $L_{2,3}$ -spectra of these atoms provide the contributions of 3s- and 3d-AOs, and finally, the L_{α} -, L_{β} -spectra of Fe, Co and Ni atoms provide the contributions of the 3d-AOs.

The instruments and procedures used to obtain X-ray emission and absorption spectra have been described in detail in a number of monographs.^{42,91,95,96,99,101,104} The scheme of an X-ray spectrometer is shown in Fig. 9. The X-ray emission radiation of a compound under study, that can be either in a solid or gaseous state, is excited by electrons or photons. The induced radiation passes through a number of diaphragms and falls on the dispersing element and, after reflection from the latter, on the detector. Expansion of the X-ray radiation from the compound into a spectrum by the dispersing element followed by recording of the spectrum can give the dependence of the radiation intensity on the wavelength or photon energy (in eV). X-Ray absorption spectra are obtained as follows. A sample to be studied is placed in the way of X-ray radiation and the attenuation/absorption factor (defined as the logarithm of the ratio of the beam intensity that has passed through the sample to the initial beam intensity) is determined as a function of the energy of the monochromatic exciting radiation. In the case of samples non-transparent to soft X-ray irradiation, X-ray absorption spectra are recorded in the electron yield mode (complete or partial yield, or yield of Auger electrons as a function of energy discrimination of detected electrons).¹⁰⁴ Synchrotron radiation, whose intensity is many orders of magnitude higher than that from X-ray tubes, is increasingly used at present to excite X-ray transitions in chemical systems.^{105–107}

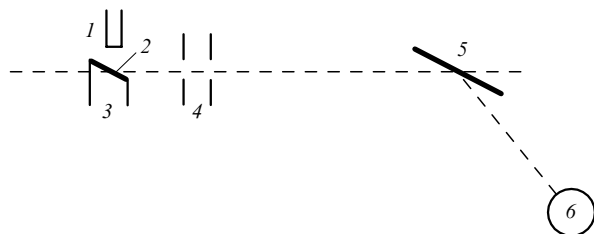


Figure 9. Schematic diagram of an X-ray spectrometer.

(1) Electron gun or primary radiation (photon) source; (2) compound under study; (3) sample holder (secondary anode); (4) system of apertures; (5) dispersing element (analyser crystal or diffraction lattice); (6) detector.

The information provided by X-ray absorption spectra can also be obtained from electron energy loss spectra (EELS).¹⁰⁸ The essence of this spectral method is as follows: as a result of inelastic collision of monochromatic electrons with molecules under study, one of their inner electrons passes to one of the available vacant levels, whereas the loss of the energy of the incidence electron is equal to the energy of this transition. Having determined the electron energy before the collision and that after the collision using an energy analyser, one can plot the energy spectrum of transitions from different inner molecular levels to vacant orbitals.^{108,109} Inelastic scattering of hard X-ray irradiation (X-ray Raman scattering) can be used in a similar way.

A specific feature of chemical bonding in many boron-containing compounds is that it involves donor–acceptor interactions. The formation of a donor–acceptor bond between two molecules (e.g., $NX_3 \cdot BY_3$, where X, Y = H, Hal, Alk etc.) occurs

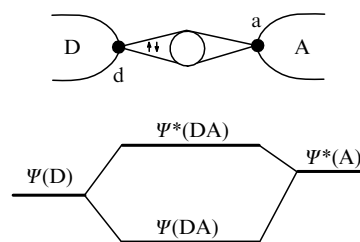


Figure 10. Scheme of donor–acceptor interaction in the two-level model approximation. See the text for explanations.

due to the electron density transfer from the highest-energy occupied orbital of the donor to the lowest-energy vacant orbital of the acceptor (for more details, see Refs 110–112).

Donor–acceptor interaction in the two-level model approximation is demonstrated in Fig. 10. A system under study contains two valence-saturated molecules, viz., a donor (D) and an acceptor (A). The highest occupied MO (HOMO) of the donor contains a lone electron pair localised on the ‘d’ atom (see Fig. 10). The wave function of this orbital, $\Psi(D)$, consists of one wave function of the ‘d’ atom, $\psi(d)$. The lowest unoccupied MO (LUMO) of the acceptor is localised on the ‘a’ atom. Its wave function $\Psi^*(A)$ (here and below, vacant orbitals are marked with asterisks) also consists of one wave function of the ‘a’ atom of the acceptor molecule, i.e., $\psi^*(a)$. It is sometimes called a lone hole pair. Thus, the HOMO of the ‘D’ molecule and the LUMO of the ‘A’ molecule are similar to the AOs of the ‘d’ and ‘a’ atoms, respectively. Interaction of the ‘D’ and ‘A’ molecules through the ‘d’ and ‘a’ atoms results in an occupied bonding orbital with the wave function $\Psi(DA)$ and a vacant antibonding orbital with the wave function $\Psi^*(DA)$:

$$\Psi(DA) = c_d \Psi(D) + c_a \Psi^*(A) = c_d \psi(d) + c_a \psi^*(a),$$

$$\Psi^*(DA) = c_d^* \Psi(D) - c_a^* \Psi^*(A) = c_d^* \psi(d) - c_a^* \psi^*(a),$$

where c_d , c_a , c_d^* and c_a^* are expansion coefficients of the MOs over the AOs. The degree of electron density transfer from the donor to the acceptor, in both the main and excited states, depends on the values of the squares of these coefficients.

Let us consider how the donor–acceptor interaction manifests itself in X-ray spectra. The HOMO of the donor molecule (lone electron pair) is described by the wave function of the highest occupied AO of the donor atom. The expansion coefficient of the AO in the MO is equal to unity ($c_{ij} = 1$). The donor molecule does not have any other orbital with such a high contribution of this AO. Naturally, inasmuch as $I \sim c_{ij}^2$ (see Fig. 8), the electron transfer from the HOMO gives the most intense line in the X-ray spectrum. In the two-level model approximation, the HOMO of the new compound DA resulting from the formation of a donor–acceptor bond is described by a wave function consisting of two AOs, viz., that of the ‘d’ atom of the ‘D’ molecule and that of the ‘a’ atom of the ‘A’ molecule. Accordingly, the participation coefficient of the AO of the ‘d’ atom of the donor molecule ‘B’ becomes less than unity. Hence, the relative intensity of the X-ray line originating from the electron transfer from the MO of the DA molecule to the inner level of the ‘d’ atom of the same molecule also decreases. It is assumed that deeper MOs of both the donor and acceptor do not change, that is, the bond formed between the molecules does not introduce considerable disturbance, and their electrons are not involved in the formation of the chemical bond. As a result, the structure and intensity of the rest of the X-ray spectrum change quite insignificantly. In such a case, filling of the LUMO under consideration changes the intensities in the X-ray absorption spectra of the acceptor molecule within the DA adduct. It should be noted that the approach described above is

rather approximate and that it is useful for illustration purposes only.

IV. X-Ray spectroscopy and electronic structure of boron compounds

Fundamental X-ray spectral studies of boron compounds were carried mostly in the 1960–1970s by a group of physicists from the Leningrad University.¹⁰⁴ The X-ray spectra recorded in the 1930–1940s when the ultra-mild X-ray spectroscopy was in its infancy were limited by the low resolution of equipment and were only descriptive (see the references in the monograph by Maisel *et al.*⁹⁹).

1. Oxide systems

X-Ray studies have been conducted for only a few oxygen-containing boron compounds. The majority of studies dealt with the electronic structure of boric anhydride (B_2O_3). The following spectra were recorded and discussed: emission BK_α -spectra,^{39, 93, 104, 113–127} OK_α -spectra^{116, 117} and absorption BK -spectra.^{39, 104, 115, 122, 123, 128–132}

Extensive application of synchrotron radiation as a source for the excitation of X-ray fluorescence in studies of the electronic structure of B_2O_3 began in the 1990s.^{121–125} It was used in a number of studies^{122, 123, 128–131} of X-ray absorption spectra of boron. O'Brien *et al.*¹²¹ and Muramatsu *et al.*^{122–124} studied the BK_α -emission spectra of boron (Fig. 11) using monochromatic synchrotron radiation. It was found that changes in the energy (or wavelength) of excitation radiation change both the energy positions of single lines and their intensities, and hence the shape of the entire spectrum. The behaviour of the highest-energy

structure (the region of ~ 190 – 210 eV in the transition energy scale) is characterised by the greatest differences. Having related the energies of emission lines to the values of the energy maxima in the X-ray absorption spectrum (see Fig. 11 *a*), one can say that vacant orbitals (excited state) specifically manifest themselves in the emission spectrum due to reemission transitions. Reemission transitions have first been studied by Fomichev *et al.*³⁹ The reemission process involves two steps, *viz.*, transition of an electron occurs in the first step, *e.g.*, from an occupied K -shell to a vacant orbital to form a line in the absorption spectrum and reverse transition of the electron to the original level K occurs in the second step, which results in a line in the emission spectrum. Generally, these lines have the same energies if both spectra are compared (see, *e.g.*, Ref. 104). Studies of the behaviour dynamics of reemission lines as a function of the exciting radiation energy revealed the existence of some kind of resonance: if the excitation energy coincides with the energy of electron transition from the K -shell of the boron atom to a vacant orbital, the intensity of the reemission line increases.^{123, 124} The theory of resonance excitation was considered in a series of fundamental studies (see, *e.g.*, the monograph by Mazalov *et al.*⁹⁶ and references cited therein). It should be noted that a version of X-ray emission spectroscopy which uses resonance excitation is called resonant inelastic X-ray scattering (RIXS) in current literature.

A combined analysis of the K_α -spectra of boron and oxygen and the XPS spectrum of B_2O_3 in the valence band was carried out.¹³³ All the spectra were reduced to a common energy scale using XPS data. The structure of a particular cluster was considered. Based on X-ray spectra, conclusions on the contributions of the 2p-AOs of oxygen and boron to different levels of the valence band were drawn.

One of the first interpretations concerning boron X-ray emission and absorption spectra was based on quantum-chemical calculations in the CNDO approximation.¹³⁴ It was assumed that the symmetry point group of the boron atom's nearest environment in the planar network is D_{3h} . The calculation was first performed for the BO_3^{3-} cluster, *i.e.*, only the first coordination sphere was taken into account; after that, for better fit with experimental X-ray emission and absorption spectra, the BO_3B_3 cluster was calculated, *i.e.*, the second coordination sphere was also taken into account. This is likely to be the only study where X-ray emission and absorption spectral lines of boric anhydride, B_2O_3 , are compared with the symmetry and energy parameters of levels calculated by quantum-chemical methods. The $X\alpha$ -DV (discrete variation) approximation was used to simulate the X-ray BK_α -emission spectrum,¹²⁴ though Muramatsu *et al.*¹²² reported only the overall spectrum shape but not the energies of the spectrum-forming MOs calculated by the quantum-chemical method. A more detailed approach was used by Kawai *et al.*¹³⁵ who reported the energies of the MOs forming the theoretical spectrum and their symmetries; in the case of boric anhydride B_2O_3 , they considered the $B_2O_5^{4-}$ cluster (point symmetry group D_{2d}) in which each boron atom is surrounded by three oxygen atoms. However, Kawai *et al.*¹³⁵ only studied the X-ray OK_α -emission spectrum.

The X-ray emission and absorption spectra of B_2O_3 reduced to a common energy scale using the binding energies of inner electrons¹⁰⁰ are presented in Fig. 12, which shows XPS spectra in the valence band. The zero of the binding energy scale corresponds to the Fermi level (E_F) of the X-ray photoelectron spectrometer (see Refs 92 and 133). Different spectra were compared using XPS data in the energy region corresponding to inner layers.¹⁰⁰ To identify the structures of these spectra, let us compare different spectra, as has been done by Nakhmanson and Baranovskii,¹³⁴ based on data on the electronic structure of the BO_3^{3-} cluster with D_{3h} symmetry. X-Ray OK_α - and BK_α -emission spectra provide data on the contributions of the 2p-AOs of oxygen and boron to the occupied MOs, while the corresponding absorption spectra reflect the structures of vacant orbitals. The low-energy (henceforth, the transition energy scale is implied) $e'(\sigma)$ -

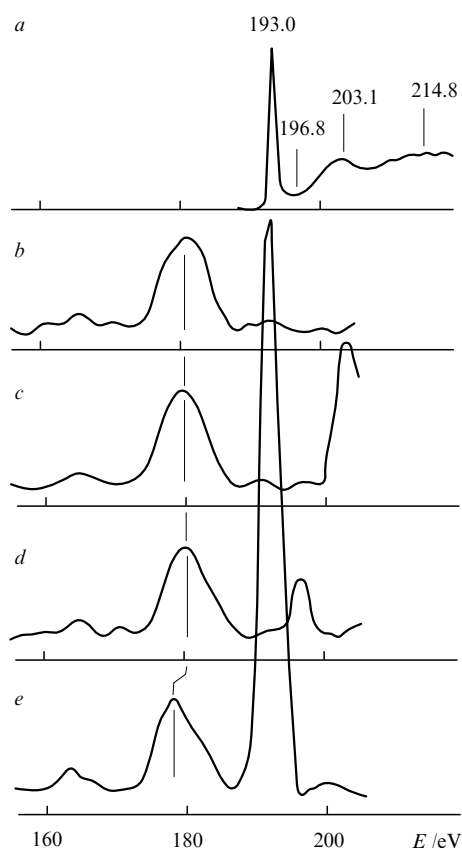


Figure 11. X-Ray absorption spectrum of boron (*a*) and X-ray BK_α -emission spectra of boric anhydride B_2O_3 (*b*–*e*) obtained at different synchrotron excitation energies (E_{hv}).¹²³ $E_{hv} = 214.8$ (*b*), 203.1 (*c*), 196.8 (*d*), 193.0 eV (*e*).

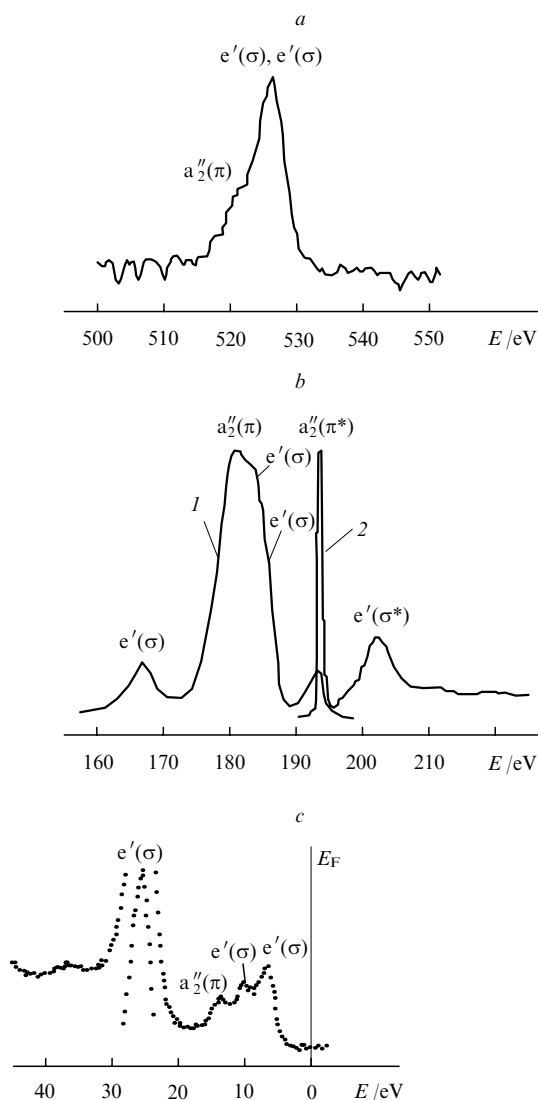


Figure 12. X-Ray OK_{α} -emission spectrum (a),¹¹⁶ X-ray BK_{α} -emission spectrum (b, spectrum 1),¹¹⁵ X-ray spectrum near the radiation BK -absorption edge (b, spectrum 2)¹³¹ and X-ray photoelectron spectrum in the B_2O_3 valence band (c).¹³³

line of the X-ray BK_{α} -emission spectrum, which coincides with an intense line in the XPS spectrum (see Fig. 12), matches the MO with e' symmetry mainly formed from oxygen and boron 2s-AOs. In the X-ray BK_{α} -emission spectrum, this is manifested due to a small admixture of the $B2p$ -AO. Electrons of this orbital form σ -bonds between boron and oxygen atoms. They are followed by one orbital with a'' symmetry (π -bond) and two MOs with e' symmetry (σ -bond) mainly consisting of boron and oxygen 2p-AOs. They manifest themselves as a low-energy shoulder on the dominant line and as this line of its own in the X-ray OK_{α} -emission spectrum, and also as a broad intense band in the X-ray BK_{α} -emission spectrum (see Fig. 12). There is a corresponding broad band consisting of three lines in the X-ray photoelectron spectrum. The first line of the X-ray spectrum near the BK -absorption edge of boron, which is identified as a vacant $a''(\pi^*)$ -MO, matches the highest-energy maximum of the X-ray BK_{α} -emission spectrum. This provides reasons to assign the latter to a reemission transition line, *i.e.*, electron transition from the excited $a''(\pi^*)$ -level to a vacancy in the boron K -shell. Finally, the last broad line in the absorption spectrum is matched with the antibonding unoccupied $e'(\sigma^*)$ -MO.

The X-ray OK_{α} -emission spectrum of boron suboxide B_6O was studied.^{135, 136} Quantum-chemical calculations of the B_6O structure and of this spectrum were performed in the $X\alpha$ -DV approximation using a cluster of two triangles, which contained boron atoms in the vertices and oxygen atoms in the centres (B_6O_2). The electronic structures were calculated and the X-ray OK_{α} -emission spectra were constructed as a function of the distance between the oxygen atoms and hence between the planes in which these triangles are located. Kawai *et al.*^{135, 136} chose this distance in such a way that the theoretical and experimental spectra matched most closely and compared it with data on the B_6O structure. An experimental X-ray BK_{α} -emission spectrum was published earlier,¹³⁷ with the spectrum structure studied at different energies of the excitation SI.

The X-ray BK_{α} -emission spectrum^{113, 120} and X-ray OK_{α} -emission spectrum of H_3BO_3 were obtained.¹³⁸ The BK -absorption spectra of this compound were recorded in a number of studies,^{128, 129, 132, 139} the first of which employed SI. The X-ray absorption spectrum was also reported.¹³⁹ The spectra of H_3BO_3 and B_2O_3 are very much alike because the boron and oxygen atoms have the same nearest environment. The identification of maxima in the structures of X-ray BK_{α} -emission and BK -absorption spectra of H_3BO_3 was performed on the basis of calculation of these spectra in the CNDO approximation.¹³⁴

The electronic structures of other oxide compounds of boron were also studied.^{113, 120, 128} For example, X-ray emission spectra of boron were recorded and described for $Na_2B_4O_7$,¹¹³ $AlBO_3$, $Be_2(BO_3)OH$, $Mg[(OH)_3BOB(OH)_3]$, $CaB_2Si_2O_8$ and BPO_4 .¹²⁰ The X-ray absorption spectra of boron for $Na_2B_4O_7 \cdot 10H_2O$, $NaBO_3 \cdot 4H_2O$, $Zn[B_2O(OCOME)_5]_2$ and BPO_4 were obtained using SI.¹²⁸

2. Elementary boron, borides and boron carbide

Numerous studies deal with X-ray emission (Refs 93, 104, 113–117, 122, 126 and 140–145) and X-ray absorption spectra of elementary boron.^{104, 115, 122, 129, 130, 140, 143, 144} Although several modifications of crystalline and amorphous boron exist, their X-ray spectra differ insignificantly. The most considerable 'chemical' effects are observed in the BK_{α} -spectra on transition from elementary boron to its oxide and nitride (see Sections IV.1 and IV.3). The spectra of B, B_2O_3 and BN show noticeable differences: a considerable low-energy shift of the main band is observed for B_2O_3 and BN (by 2.72 and 2.45 eV, respectively, with respect to B); in addition, the spectra of B_2O_3 and BN contain new lines in comparison with the spectra of elementary boron. These include a low-energy line (165.4 eV in the spectrum of B_2O_3 and 169.0 eV in the spectrum of BN), which originate probably from electron transitions from the MO mainly containing the $B2s$ -AO (with a small contribution of the $B2p$ -state) to the K -shell of the boron atom containing a vacancy, as well as the maxima which appear due to reemission transitions (191.4 and 190.0 eV for B_2O_3 and BN, respectively).⁹³ These features may be related to changes in both the chemical environment of the boron atom and the character of binding (see, *e.g.*, Ref. 93). A comparison of X-ray emission and X-ray absorption spectra of amorphous boron allowed the band gap width to be evaluated.¹⁴⁰ Sobczak and Persy¹⁴⁴ reduced the BK_{α} -emission and BK -absorption spectra, as well as the photoelectron spectrum in the valence band, to a common energy scale using the energies of inner $B1s$ -electrons. They also presented an X-ray isochromate¹⁴⁴ of elementary boron whose structure compares with that of the XAS spectrum (the method to obtain isochromates was described, *e.g.*, by Maisel *et al.*,⁹⁹ who also gave references to early X-ray spectroscopic studies). Results of studies on the electronic structures of different modifications of elementary boron were generalised in the monograph by Ivanovskii and Shveikin.¹²

The monograph by Zhurakovskii¹⁴⁶ should be considered among the first works on the electronic structures of borides M_nB_m (where M is a metal) studied by X-ray spectroscopy. He presented a large number of X-ray spectra and related them to

parameters that characterise the electronic structures of compounds (the energies and relative intensities of spectral lines). The results of more recent studies on the electronic structures of metal borides were generalised in the monograph by Ivanovskii and Shveikin.¹²

Studies on medium-temperature superconductivity carried out in the past decade showed that this property is inherent in MgB_2 as well.¹⁴⁷ Its electronic structure was studied by various physical methods, including XES and XAS.¹⁴⁸

The X-ray BK_α -emission spectra,^{104, 113–116, 118, 120, 126, 149, 150} CK_α -emission spectra¹¹⁶ and X-ray absorption spectra^{104, 115, 130, 149, 150} of boron carbide B_4C were recorded and described. The X-ray BK_α -emission and BK -absorption spectra of B_{10}C and B_{11}C were studied,¹⁵⁰ and the X-ray BK_α -emission spectrum of B_{12}C_3 was published.¹¹⁷ Unfortunately, traditional analysis of these spectra based on calculation results was not carried out in these studies, hence identification of spectral lines was not performed either.

3. Boron nitrides and other binary compounds

The X-ray BK_α -emission spectra of boron nitrides (Refs 39, 93, 104, 113–118, 120, 121, 124–126, 133, 136, 140, 151–155) their X-ray BK -absorption spectra,^{39, 104, 115, 122, 130, 140, 151–153, 156, 157} NK_α -emission spectra^{93, 104, 116–118, 126, 133, 140, 151–154} and NK -absorption spectra were studied.^{104, 131, 151–153, 156} Considerable attention was given to the study of the structures of these spectra. For example, it was shown that admixtures of elementary boron or a boron oxide film affect the X-ray BK_α -emission spectrum of hBN.³⁹ Furthermore, the existence of several modifications of crystalline boron nitride gave grounds for studying the composition of a BN sample in order to find out whether it contained only one or several modifications.¹⁵⁴ The X-ray spectra of boron nitride modifications, cBN and hBN, differ markedly. Joyner and Hercules¹³³ studied X-ray emission spectra along with the photoelectron spectrum in the valence band of hBN.¹³³

As noted above (see Section III.2), SI is currently being used ever more often to obtain X-ray spectra. This irradiation source was also used to study the emission and absorption X-ray spectra of boron nitride.^{121, 122, 124, 125, 130, 131, 158–170} In a number of experiments, emission spectra of boron nitride were recorded with excitation of X-ray fluorescence by monochromatic (or quasi-monochromatic) SI. The X-ray fluorescence spectra obtained in this way differ in the energy positions of separate lines and their relative intensities depending on the wavelength of the excitation line. This effect was observed for X-ray lines of both BK_α - and NK_α -emission.^{121, 122, 124, 158–165} In some works,^{124, 159, 161} monochromatic radiation was used to study the high-energy structures of spectra or lines of reemission transitions (*cf.* Section IV.1, analysis of the X-ray spectra of B_2O_3). The intensity of a line corresponding to reemission transition increases abruptly at a certain energy of the excitation photon.

The polarisation character of X-ray emission spectra of hBN single crystals and changes in the bands of these spectra (their positions and intensities) for different directions of the radiation exit from single crystals with respect to particular crystallographic orientations were studied.^{171–174} Synchrotron radiation was used as the irradiation source in many studies.^{37, 158, 167, 175–180} The orientation emission effect was also used to determine the symmetry of vacant orbitals that manifest themselves in absorption spectra.^{167, 177–180} Electron energy loss spectroscopy was used to study the orientation effects in hBN crystals.^{181, 182} The dependence of the reflection factor of ultrasoft X-ray irradiation by hBN near the K -edge of boron absorption on the grazing incidence angle was studied.^{183, 184} In this study, reflections from two crystal faces cut in parallel and normally to its main symmetry axis were measured successively. These spectra agree satisfactorily with those obtained in the electron yield mode (see Section III.2).

One of the first calculations of boron nitride was carried out for hBN using the CNDO method with the first (the BN_3^{6-} cluster) and second (BN_3B_6) coordination spheres taken into account.¹³⁴

As expected, the results are similar to X-ray spectroscopic experimental data provided that the effect of the second coordination sphere is taken into account. The main specific features of X-ray emission and absorption spectra are related to the structure of the nearest environment of an excited atom, which explains the differences between the X-ray spectra of different BN modifications. Based on calculations of the electronic structure in the $X\alpha$ -DV approximation, a theoretical X-ray BK_α -emission spectrum of boron nitride was obtained.¹²² Data on calculations on the electronic structure of boron nitride were summarised and compared to experimental spectra in certain monographs.^{12, 185} The most recent achievements in this field are reported in Refs 186–192.

This was the general survey of X-ray studies on the electronic structure of boron nitride. Let us consider some of its aspects more specifically and see how chemical bond features manifest themselves in the X-ray spectra. Figure 13 *a, b* shows the X-ray spectra of the hexagonal and cubic modifications of boron nitride, respectively. The X-ray BK_α - and NK_α -emission spectra were taken from Refs 151 and 152, while the BK - and NK -absorption spectra were taken from Ref. 131. All the spectra refer to a common energy scale relative to the Fermi level, taking into account the binding energies of inner B1s- and N1s-electrons obtained by XPS;¹⁰⁰ they are compared with photoelectron spectra of boron nitride in the valence band.^{193, 194} The X-ray spectra of hexagonal boron nitride are interpreted on the basis of results of CNDO calculations¹³⁴ for the BN_3^{6-} cluster (symmetry point group D_{3h}) and MNDO calculations (MOPAC-60 software) for a hypothetical isolated BN molecule (symmetry group $C_{\infty v}$). The results of the latter are shown in Fig. 14. MNDO calculations for such a molecule give quite a moderate qualitative picture of the electronic structure of boron nitride as a polyatomic system that has different modifications, but maintains its main features. Passage from an isolated BN molecule to a polyatomic system results in dithering of the MO into a band whose description requires calculations within the zone theory of solids or quantum-chemical calculations of polyatomic clusters. If hBN is considered with the nearest environment taken into account, then the e' -MO is the orbital whose electrons form the σ -bond in the layer plane (hBN is considered as a lamellar structure). Molecular orbitals of this symmetry are built of $2p_x$ - and $2p_y$ -AOs of boron and nitrogen; the MOs with the a_2'' symmetry are built of $2p_z$ -AOs and are responsible for the π -type chemical bond in the layer normal to the network plane. The deepest valence level is comparable with the low-energy line of X-ray BK_α -emission spectrum of low intensity (see Fig. 13); no similar line was found in X-ray NK_α -emission spectra presented in Refs 151 and 152. Only Hayasi¹¹⁶ succeeded in obtaining a low-intensity maximum with a transition energy of ~ 377 eV. A comparison of both of these low-energy lines in the X-ray BK_α - and NK_α -emission spectra show that their energies match each other and the energy of the most intense line in the XPS spectrum.¹⁹³ According to quantum-chemical calculations, these lines can be related to the level corresponding to the σ -bond and mainly consisting of the $2s$ -AOs of boron and nitrogen. They appear in X-ray BK_α - and NK_α -emission spectra because the $e'(\sigma)$ -MOs contain an admixture of $2p$ -AOs of the same atoms (see Fig. 13). An increase in the transition energy produces intense maxima with fine structure in X-ray BK_α - and NK_α -emission spectra; these maxima coincide if the spectra are superimposed. It is suggested to match the intense BK_α -band with the a_2'' -MO and to match the high-energy shoulder successively with two orbitals with e' symmetry.¹³⁴ However, the results of MNDO calculation (see Fig. 14) and data of studies on polarisation effects in X-ray emission spectra³⁷ (see Fig. 13) suggest that a somewhat different order of these orbitals should be assumed: as the transition energy increases, two MOs with e' symmetry are followed by a MO with a_2'' symmetry (see Fig. 13). The fact that the maxima in X-ray BK_α - and NK_α -emission spectra and XPS spectra coincide in the valence band if a comparison is made using the energy positions of inner orbitals allows these

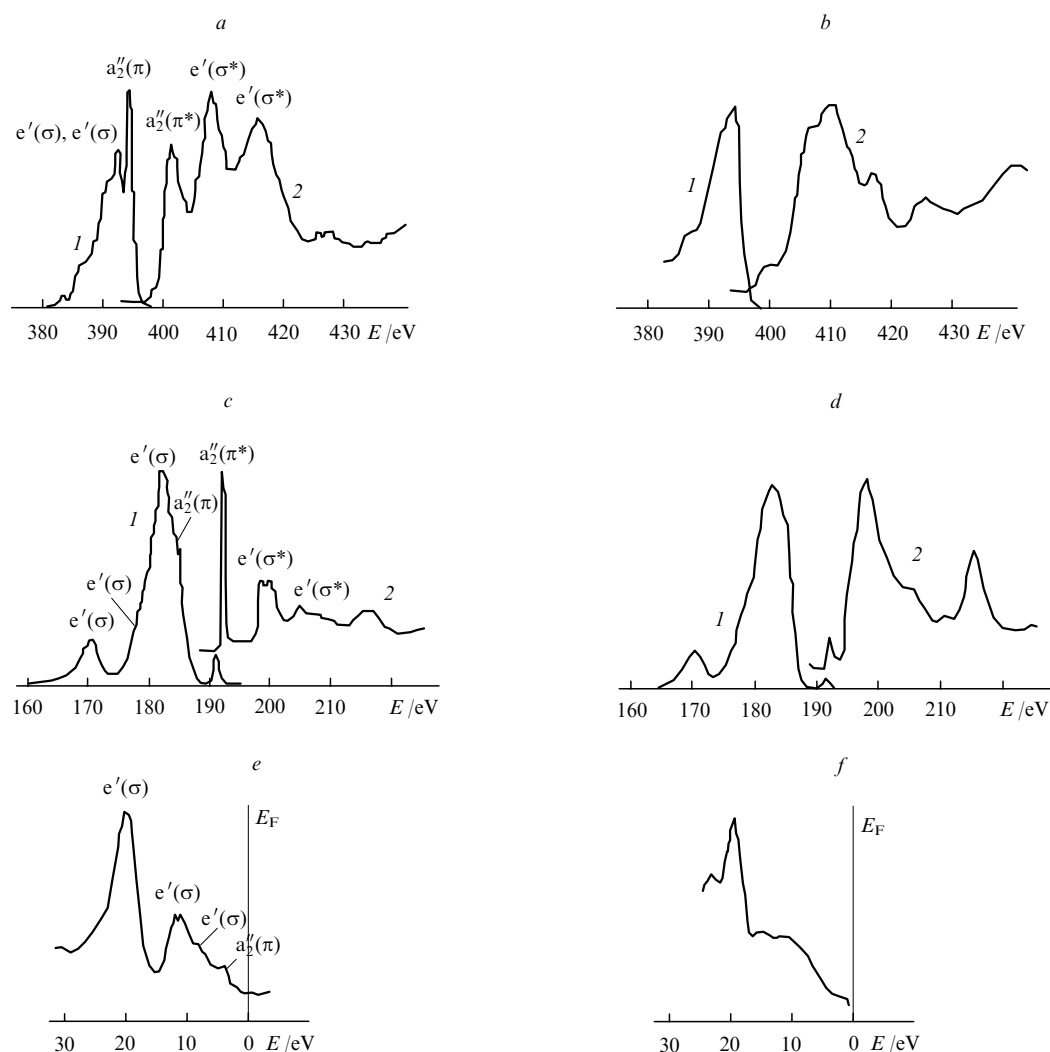


Figure 13. X-Ray NK_{α} - (a, b) and BK_{α} -emission spectra (c, d) (spectra 1)^{151, 152} and NK- (a, b) and BK-absorption spectra (c, d) (spectra 2)¹³¹ and photoelectron spectra (e, f)^{193, 194} in the valence band of hexagonal (a, c, e) and cubic (b, d, f) boron nitride.

X-ray spectra to be interpreted as well (see Fig. 13). According to CNDO calculations, the first vacant orbital¹³⁴ has a_2'' symmetry and corresponds to a narrow line in the X-ray BK-absorption spectrum (see Fig. 13) and to a distinct line in the X-ray NK-absorption spectrum.¹³¹ The same conclusion can be drawn based on the fact that the line positions coincide when the X-ray BK- and NK-spectra are superimposed. It is also evident from Fig. 13 that

the first low-energy line in X-ray absorption spectra coincides with the reemission line in the X-ray BK_{α} -emission spectrum, which thus can be related to the lowest vacant $a_2''(\pi^*)$ level. The two next vacant MOs with the e' symmetry manifest themselves in X-ray absorption spectra as two distinct lines¹³¹ (see Fig. 13).

As noted above, studies of orientation (polarisation) effects have played an important role in the interpretation of boron

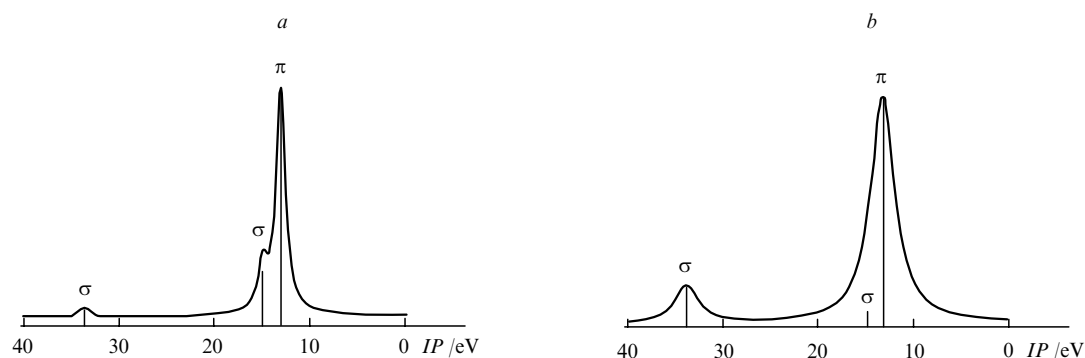


Figure 14. Theoretical X-ray NK_{α} - (a) and BK_{α} -emission spectra (b) of boron nitride (MNDO calculation). The vertical bars show the contributions of atomic N2p (a) and B2p orbitals (b) to the MO.

nitride spectra (see Refs 37, 158, 167 and 171–180). In fact, for a one-dimensional layer of crystalline hBN (assuming weak interaction between the layers), band electron states can be subdivided according to σ - and π -symmetry corresponding to σ - and π -bonding between atoms. The electric-field vector of the electromagnetic wave (polarisation plane) appearing due to the transition, *e.g.*, from the π -state to a $1s$ -vacancy, is parallel to the $2p_z$ -orbital. If one varies the orientation of the analyser crystal (which expands the emission radiation into a spectrum) relative to the boron nitride single crystal, it is possible to record changes in the intensity of the band related to the π -state and even its disappearance.^{42, 171, 172} The use of SI for studying this effect provides yet another advantage. The point is that such radiation becomes plane-polarised. By changing the angle between the incidence radiation and the plane of the boron nitride crystal (grazing incidence angle), one can also observe changes in the intensity of the π -band in the spectrum. The emission spectra of hBN obtained with the use of SI at different grazing incidence angles³⁷ are presented in Fig. 15.

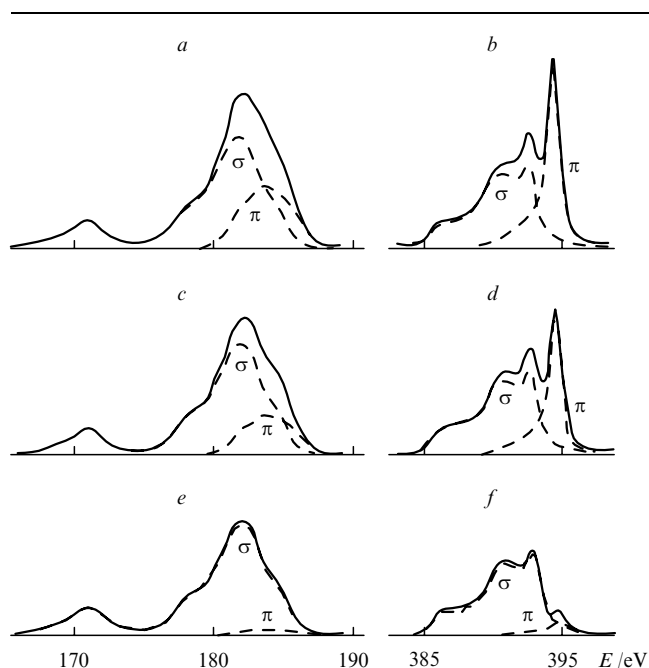


Figure 15. Orientation effects in X-ray BK_{α} - (a, c, e) and NK_{α} -emission spectra (b, d, f) of hexagonal boron. Dependence of the relative intensities of the lines corresponding to σ - and π -bonds on the angle between the incident polarised radiation and the crystal surface (grazing incidence angle θ).³⁷

$\theta = 10^\circ$ (a, b), 30° (c, d), 80° (e, f).

The X-ray spectra of boron phosphide were studied.^{104, 114, 117, 137, 151, 195–197} A comprehensive X-ray spectral study of this compound was carried out; its BK_{α} -, PK_{β} - and $PL_{2,3}$ -emission spectra, as well as BK_{α} -, PK_{β} - and $PL_{2,3}$ -absorption spectra were obtained.^{104, 151, 195, 196} The dependence of BK_{α} -spectrum on the excitation radiation length was studied.^{137, 197} Interpretation of boron phosphide spectra was carried out.¹⁹⁸ Studies reporting X-ray emission spectra of boron and phosphorus in $B_{13}P_2$ and $B_{13}As_2$ are also of note.^{117, 136}

4. Boron halides and their derivatives

X-Ray BK_{α} - and FK_{α} -emission spectra of boron trifluoride (D_{3h} symmetry group) in solid¹³⁸ and gaseous¹⁹⁹ states were published. Studies of X-ray absorption by BF_3 are more numerous. For example, X-ray BK_{α} -absorption spectra^{104, 115, 129, 200–205} and FK_{α} -absorption spectra^{204–206} were described. In some studies,^{201–203, 206} SI was used to obtain X-ray spectra of boron

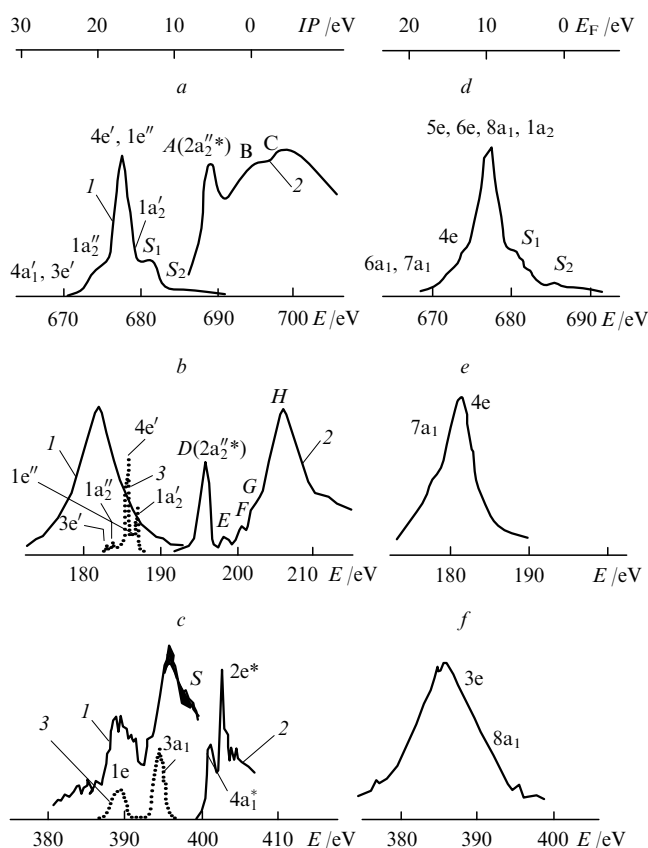


Figure 16. Experimental X-ray and photoelectron [He(I)] spectra of NH_3 and BF_3 (a–c) and X-ray emission spectra of $NH_3 \cdot BF_3$ (d–f).

(a) FK_{α} - (1)¹⁹⁹ and FK_{α} -spectra (2);²⁰⁴ (b) BK_{α} - (1),¹⁹⁹ BK_{α} -spectra (2)¹¹⁵ and photoelectron spectrum of BF_3 (3);²²³ (c) NK_{α} - (1),¹⁹⁹ NK_{α} -spectra (2) and photoelectron spectrum of NH_3 (3);²²⁷ (d) FK_{α} -spectrum; (e) BK_{α} -spectrum; (f) NK_{α} -spectrum.¹⁹⁹ (IP is the ionisation potential relative to the vacuum for the gas phase, E_F is the ionisation potential relative to the Fermi level for the solid phase, E is the X-ray transition energy. See the text for the designations of the lines.)

trifluoride. Electron energy loss spectra were recorded for BF_3 ;²⁰⁷ moreover, vibration excitation upon inelastic scattering of electrons on this molecule was studied.²⁰⁸ The spectra of boron trifluoride were also discussed elsewhere.^{209–218} Experimental emission spectra were compared with theoretical spectra obtained by *ab initio* calculations on the electronic structure of BF_3 .¹⁹⁹ The X-ray BK_{α} -emission spectrum of BF_3 was calculated by the $X\alpha$ -DV method.¹²² X-Ray absorption spectra of the BF_3 molecule were analysed by quantum-chemical methods.^{219–222} The X-ray emission BK_{α} - and FK_{α} -spectra of boron trifluoride¹⁹⁹ are presented in Fig. 16a. It also shows the X-ray BK_{α} - and FK_{α} -absorption spectra^{115, 204} and the photoelectron spectrum of boron trifluoride.²²³ (XPS data for BF_3 were taken from Ref. 224.) Figure 17 presents theoretical X-ray emission spectra.¹⁹⁹ In the boron trifluoride molecule, the $2a_2''$ π -type orbital acts as the LUMO. This vacant (acceptor) orbital interacts with the orbital of the lone electron pair of the donor molecule resulting in the formation of a donor–acceptor bond. This orbital manifests itself as rather distinct lines A and D in X-ray BK_{α} - and FK_{α} -absorption spectra (see Fig. 16a,b). The interpretation of other lines in BK_{α} - and FK_{α} -spectra (B, C, E, F, G and H) and the dissension that appeared in this connection were discussed.^{207, 208} The assignment of lines in the X-ray emission spectra of boron trifluoride (occupied orbitals) is demonstrated in Fig. 16. Studies showed that the MOs whose electron density is located on fluorine atoms are the highest occupied orbitals. They are followed by MOs with predominant population on the boron atom. The S , S_1 and S_2

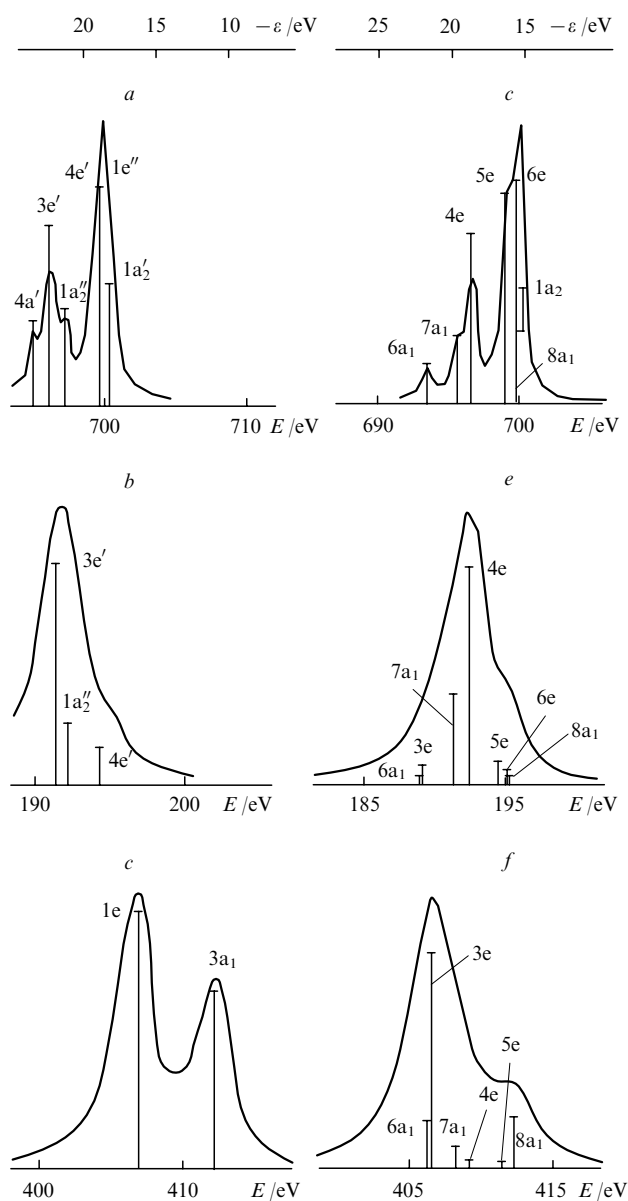


Figure 17. Theoretical X-ray emission spectra of NH_3 and BF_3 (a–c) and $\text{NH}_3 \cdot \text{BF}_3$ (d–f) obtained by *ab initio* calculations.¹⁹⁹

(a, d) $\text{FK}\alpha$ -spectra; (b, e) $\text{BK}\alpha$ -spectra; (c, f) $\text{NK}\alpha$ -spectra (ϵ is orbital energy). The vertical bars show the contributions of atomic orbitals to the MOs.

maxima are caused by electron transitions in double-ionised molecules; they are generally not considered in interpretations of X-ray spectra in the context of chemical bond studies (see, e.g., Ref. 99).

Boron trichloride has only been studied by X-ray absorption spectroscopy. The X-ray BK- and $\text{ClL}_{2,3}$ -absorption spectra of BCl_3 ^{104, 200, 202, 218, 225, 226} almost coincide. The spectra were interpreted based on *ab initio*²⁰² and CNDO/2²¹⁹ calculations. Identification of separate lines in the X-ray absorption spectrum of boron trichloride was reported.^{225, 226} It was noted²⁰⁰ that the BK-absorption spectrum of BCl_3 is less shifted towards high energies than the similar spectrum of BF_3 . This results from the fact that the effective positive charge on the B atom in boron trichloride is lower. The X-ray BK-absorption spectrum of BBr_3 was obtained and its interpretation based on *ab initio* calculations was carried out.²⁰²

Let us consider in more detail the $\text{NH}_3 \cdot \text{BF}_3$ complex (symmetry group C_{3v}), which is formed upon donor–acceptor inter-

action of NH_3 and BF_3 molecules. This complex was studied by X-ray spectral methods.¹⁹⁹ The ammonia and boron trifluoride molecules were first considered separately, then changes observed in the spectra during complexing were noted. The experimental and theoretical X-ray spectra¹⁹⁹ and the photoelectron spectra of ammonia²²⁷ and boron trifluoride²²³ are shown in Figs 16 and 17. The spectra were compared using the energy positions of inner-shell electrons.²²⁴ The absorption spectrum of $\text{NH}_3 \cdot \text{BF}_3$ was obtained by Akimov *et al.*²²⁸ The spectrum structure was identified using calculations in the *ab initio* and MNDO approximations.¹⁹⁹

The scheme of MOs of ammonia, boron trifluoride and the $\text{NH}_3 \cdot \text{BF}_3$ complex composed using the results of MNDO calculations¹⁹⁹ is shown in Fig. 18. It also presents results of fragment analysis (expansion of a molecule's MOs into the constituent fragment orbitals).²²⁹ It should be expected within the framework of donor–acceptor bonding that the main interacting orbitals include the $3a_1$ HOMO of ammonia and the $2a_2^{**}$ LUMO of boron trifluoride (or $6a_1^*$ in pyramidal configuration, symmetry group C_{3v} , for BF_3 in the complex with ammonia). It is evident from Figs 16–18 that these are orbitals ($3a_1$ and $2a_2^{**}$) with high contributions of the 2p-AOs of nitrogen and boron, respectively. It follows from calculations (see Fig. 18) that the nitrogen–boron bond in $\text{NH}_3 \cdot \text{BF}_3$ mainly involves electrons of three MOs, *viz.*, $8a_1$, $7a_1$ and $6a_1$; the properties of the wave functions of remaining occupied MOs are similar to those of the original molecules (NH_3 and BF_3). Orbitals with a_1 symmetry are bonding and appear due to interaction of the $3a_1$ -MO of ammonia with $6a_1^*$, $5a_1$ - and $4a_1$ -MOs of boron trifluoride. It should be noted that only the formation of the $8a_1$ orbital predominantly involves the vacant $6a_1^*$ -MO of boron trifluoride (see Fig. 18). Hence, the $8a_1$ -MO can be related (to a certain approximation) to the bonding orbital of

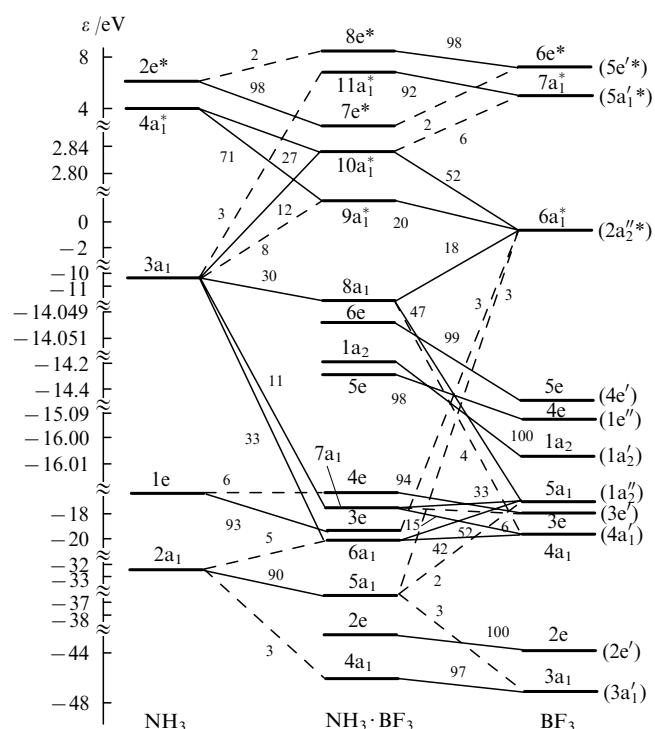


Figure 18. Correlation diagram of MOs for the $\text{NH}_3 \cdot \text{BF}_3$ complex and its fragments, NH_3 and BF_3 . Results of MNDO calculation.¹⁹⁹

The calculation was carried out for the pyramidal BF_3 molecule (C_{3v} symmetry); designations of the corresponding MO of the planar BF_3 molecule (D_{3h} symmetry) are given in parentheses. The numbers near the connecting lines correspond to the contributions (in percent) of the orbitals of the NH_3 and BF_3 fragments to the MOs of the $\text{NH}_3 \cdot \text{BF}_3$ molecule. Dashed lines indicate contributions smaller than 10%.

the two-level donor–acceptor bond model (see Section III.2), though it involves rather a large contribution ($\sim 47\%$) of the occupied $5a_1$ orbital of the acceptor. The changes in the electronic structure on passage from isolated NH_3 and BF_3 molecules to the $\text{NH}_3 \cdot \text{BF}_3$ complex are reflected in X-ray NK_α -emission spectra (see Figs 16 and 17). The intensity ratio of lines $I(8a_1)/I(3e)$ in the spectrum of the complex is much lower than the $I(3a_1)/I(1e)$ ratio in the spectrum of pure NH_3 . Since it follows from calculations that the $1e$ -MO of ammonia and the $3e$ -MO of the $\text{NH}_3 \cdot \text{BF}_3$ complex are similar, the relative intensities of their corresponding X-ray lines almost do not change, hence one can state that the contribution of the $\text{N}2p$ -AO to the $8a_1$ HOMO of the complex is smaller than that of the similar $3a_1$ -MO of ammonia. This can serve as a confirmation of electron density transfer from the ammonia molecule to the boron trifluoride molecule, which mainly involves the highest valence MOs. The complex in question contains two vacant orbitals, *viz.*, $9a_1^*$ and $10a_1^*$ (see Fig. 18), which can be matched with the vacant MO in the two-level model (see Section III.2). Data of experimental and theoretical studies¹⁹⁹ of the $\text{NH}_3 \cdot \text{BF}_3$ complex (see Figs 16–18) allow the character of electron density distribution in it to be understood. For example, the highest occupied orbitals are mainly populated by $\text{F}2p$ electrons. At higher binding energies, predominant contribution to the orbitals is made by boron $2p$ -AOs. The deepest valence MOs are mostly composed of nitrogen $2p$ -AOs. It should also be noted that the overlapping of bands in the NK_α - and BK_α -spectra evident when they are compared can suggest that the nature of the $\text{B} - \text{N}$ bond is largely covalent.

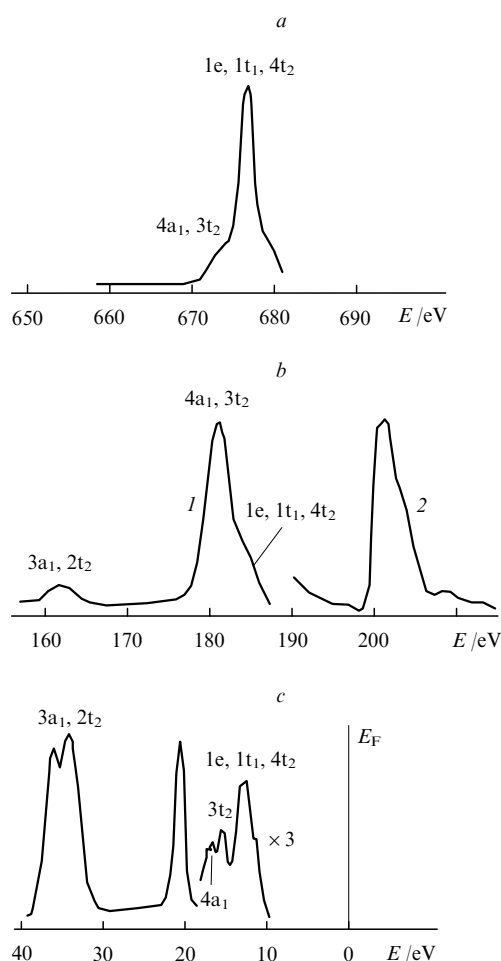


Figure 19. X-Ray emission FK_α - (a) and BK_α -spectra (b, spectrum 1),²³¹ BK -absorption spectrum (b, spectrum 2)¹²⁸ and X-ray photoelectron spectrum in the valence band of BF_4^- (c).²³¹

X-Ray emission spectra of boron and fluorine were obtained for $\text{BF}_3 \cdot \text{C}_6\text{H}_5\text{CH}=\text{NC}_6\text{H}_4\text{Me-}p$.¹³⁸

Compounds KBF_4 and NH_4BF_4 (the point symmetry group of the BF_4^- anion is T_d) were studied by X-ray emission spectroscopy, and K_α -emission spectra of boron^{230, 231} and fluorine²³¹ were obtained. X-Ray BK -absorption spectra were studied^{128, 129} using SI as the excitation source. Figure 19 presents X-ray emission spectra and X-ray photoelectron spectra in the valence band for the BF_4^- anion²³¹ and its X-ray absorption spectra.¹²⁸ Identification of spectral lines was carried out elsewhere.²³¹

5. Boron hydrides and their derivatives

a. Simplest systems

Experimental X-ray spectral data for borane (BH_3) are unavailable. This results from the fact that BH_3 molecules do not exist as monomers under ordinary conditions; they occur as B_2H_6 bridge dimers (see Fig. 5e). The X-ray absorption spectrum of diborane was obtained by Zimkina and Vinogradov.²⁰⁴

Analysis of the electronic structure of $\text{Me}_3\text{N} \cdot \text{BH}_3$ based on X-ray emission spectroscopy data was carried out.²³⁰ X-Ray BK_α - and NK_α -emission spectra were obtained. A comparison of X-ray NK_α -emission spectra of Me_3N and its adduct with BH_3 showed that the relative intensity of the line in the X-ray emission spectrum of trimethylamine associated with the lone electron pair decreases abruptly in the $\text{Me}_3\text{N} \cdot \text{BH}_3$ spectrum.^{230, 232} As with the $\text{NH}_3 \cdot \text{BF}_3$ complex discussed above (see Section IV.4), this results from electron density transfer from the trimethylamine nitrogen atom to the vacant orbital of the borane molecule with formation of a donor–acceptor bond.

The anions BH_4^- with tetrahedral symmetry in the KBH_4 and NaBH_4 molecules were studied;²³⁰ X-ray emission²³⁰ and absorption¹²⁸ spectra were obtained.

b. $\text{B}_n\text{H}_n^{2-}$ anions and boron clusters

The *closo*-borane anions $\text{B}_{10}\text{H}_{10}^{2-}$ and $\text{B}_{12}\text{H}_{12}^{2-}$ (symmetry groups D_{4d} and I_h , respectively, see Fig. 6a), the electronic structures of which were studied by X-ray spectroscopy,^{230, 233} are characterised by considerable electron density delocalisation over the entire cluster, which determines their aromatic properties and unusually high resistance to decomposition in different chemical reactions (see the references in Ref. 230). The geometric structure of the $\text{B}_{10}\text{H}_{10}^{2-}$ anion is such (see Fig. 6a) that two groups of equivalent boron atoms exist, *viz.*, vertex atoms $\text{B}(1)$ and $\text{B}(10)$ and equatorial atoms (all the rest). Their coordination numbers are 5 and 6, respectively; a greater negative charge is localised on atoms with the smaller coordination number, *i.e.*, $\text{B}(1)$ and $\text{B}(10)$, in the cluster.^{230, 233}

Figure 20 demonstrates the X-ray BK_α - and $\text{CuL}_{\alpha 1,2}$ -emission spectra of $\text{Cu}_2\text{B}_{10}\text{H}_{10}$ and the X-ray BK_α -emission spectrum of $\text{Cs}_2\text{B}_{10}\text{H}_{10}$. These spectra show that the distribution maximum of copper $3d$ -electron density is located in the upper part of the valence band (~ 3.3 eV below the Fermi level), whereas the distribution maximum of boron $2p$ -electron density corresponds to its lower part (~ 6.7 eV below the Fermi level). The observed overlapping of the BK_α - and $\text{CuL}_{\alpha 1,2}$ -bands allows one to assume that the interaction of the copper $3d$ -orbitals with the hydroborate anion is of covalent nature.^{230, 233}

The shape of the BK_α -emission spectrum of ionic $\text{Cs}_2\text{B}_{10}\text{H}_{10}$ and the energy positions of lines in it (Fig. 20) remain almost unchanged, which results most likely from delocalisation of valence electrons in the $\text{B}_{10}\text{H}_{10}^{2-}$ anion stabilising the system of its valence MOs.

X-Ray emission BK_α - and CK_α -spectra of *ortho*- and *meta*-carboranes(12) 1,2- and 1,7- $\text{C}_2\text{B}_{10}\text{H}_{12}$ were studied²³⁴ (see Fig. 5g,h); the electronic structures of these compounds were calculated by the *ab initio* method in the 6-31G* basis set and the corresponding simulated spectra were obtained (Fig. 21). Correlation and fragment analysis of the MOs of these compounds and the $\text{B}_{12}\text{H}_{12}^{2-}$ boron cluster were carried out (Fig. 22).

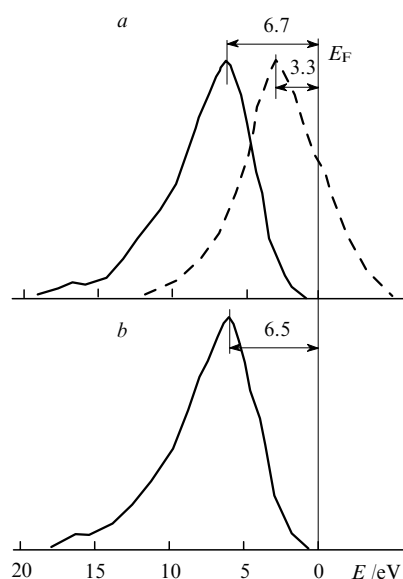


Figure 20. X-Ray emission BK_{α} -spectra (solid lines) of $\text{Cu}_2\text{B}_{10}\text{H}_{10}$ (a) and $\text{Cs}_2\text{B}_{10}\text{H}_{10}$ (b).²³⁰ The dashed line shows the X-ray $\text{CuL}_{\alpha 1,2}$ emission spectrum.

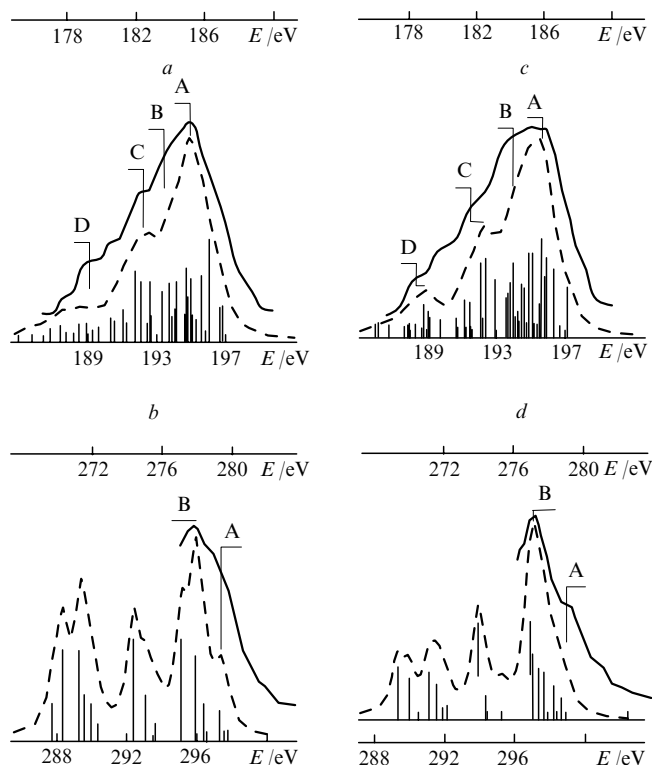


Figure 21. Experimental (solid lines, upper scales of transition energies) and theoretical (dashed lines, lower scales) X-ray emission spectra of 1,2- $\text{C}_2\text{B}_{10}\text{H}_{12}$ (a, b) and 1,7- $\text{C}_2\text{B}_{10}\text{H}_{12}$ (c, d).²³⁴ (a, c) BK_{α} -spectra; (b, d) CK_{α} -spectra.

Electron energy loss spectra (see Section III.2) were obtained for a series of boranes and carboranes, viz., *nido*-pentaborane(9) (B_5H_9), *nido*-2,3-diethyl-2,3-dicarbaheptaborane(8) ($\text{Et}_2\text{C}_2\text{B}_4\text{H}_6$), *nido*-decaborane(14) ($\text{B}_{10}\text{H}_{14}$), *closo-o*-carborane ($\text{C}_2\text{B}_{10}\text{H}_{12}$), and 1,2-dicarbaundecaborane(11) ($\text{C}_2\text{B}_9\text{H}_{11}$).^{235, 236} Quantum-chemical calculations of the electronic structures of these compounds

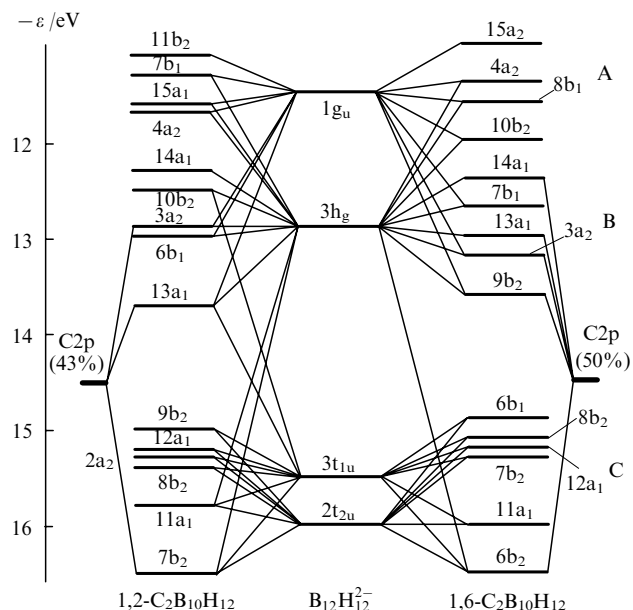


Figure 22. Correlation diagram (MNDO calculation) of energy levels in the $\text{B}_{12}\text{H}_{12}^{2-}$ anion, 1,2- $\text{C}_2\text{B}_{10}\text{H}_{12}$ and 1,7- $\text{C}_2\text{B}_{10}\text{H}_{12}$.²³⁴ The capital letters A, B and C designate the MOs which appear as the corresponding maxima in the X-ray spectra; the numbers in parentheses indicate the total contributions of the carbon 2p-AOs to the MOs.

were carried out in the MNDO and EHMO approximations (extended Hückel method); this served as a basis for composing theoretical spectra and interpreting experimental spectra.^{235, 236}

c. Borane clusters with Lewis bases ($\text{B}_{10}\text{H}_{12}\text{L}_2$)

The electronic structure of borane clusters $\text{B}_{10}\text{H}_{12}\text{L}_2$ (where L is a Lewis base) was considered in terms of X-ray emission transitions for three compounds, viz., $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$, $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ and $\text{B}_{10}\text{H}_{12}(\text{PPh}_3)_2$.

X-Ray studies of 6,9-bis(ammonia)-*arachno*-decaborane(12) [$\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$] have been carried out.^{230, 237, 238} The structure of this cluster (point symmetry group C_{2v}) and the atom numbering in it are shown in Fig. 6d. When considering the electronic structure of $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$ it was assumed that its molecule consists of two fragments, viz., the borane cluster ($\text{B}_{10}\text{H}_{12}$) and the ammonia molecule.^{237, 238} The chemical bond between these fragments is assumed to be of donor–acceptor nature; the NH_3 molecule acts as a donor, while the borane fragment is an acceptor. Quantum-chemical calculations of the electronic structure of the $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$ cluster and its fragments, i.e., $\text{B}_{10}\text{H}_{12}$ and NH_3 , were carried out using the MNDO method.^{238, 239} Figure 23a shows the correlation diagram built on this basis and the results of fragment analysis of the composition of the $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$ molecular orbitals formed by the MOs of the fragments, i.e., the $\text{B}_{10}\text{H}_{12}$ borane cluster and the NH_3 molecule. Among the highest occupied orbitals of the $\text{B}_{10}\text{H}_{12}$ cluster, one can note a group of MOs, e.g., $3a_2$, $8a_1$ and $5b_1$, which become orbitals of the complex and almost do not change their symmetry upon coordination of ammonia. In this case, they are shifted upwards in parallel with a decrease in the binding energy (see Fig. 23a). Similar behaviour is observed for deeper MOs. For example, the $5b_2$ orbital of the $\text{B}_{10}\text{H}_{12}$ cluster contributes noticeably to the $8b_2$ -MO of the complex. The electrons of this orbital are localised in the cluster and are not involved in the formation of the chemical bond with ammonia. The formation of the orbitals of the complex responsible for the interaction of ammonia with the borane fragment involves not only the vacant MOs of the $\text{B}_{10}\text{H}_{12}$ cluster as an acceptor but also its occupied orbitals, which play an important role in the process. While only electrons of the $3a_1$

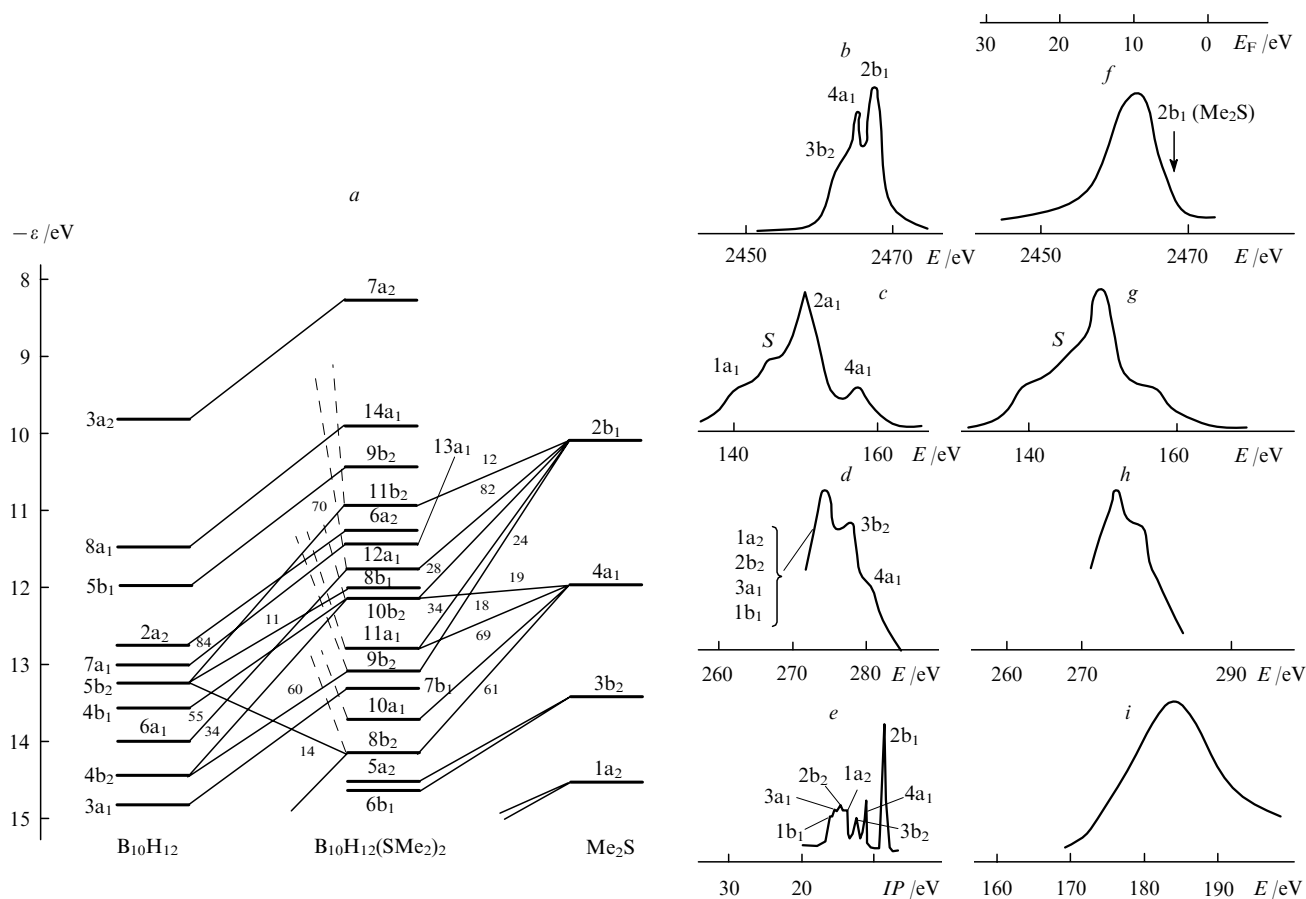


Figure 25. Scheme of MOs of the $B_{10}H_{12}(SMe_2)_2$ cluster and its fragments (a), experimental X-ray and UV [He(I)] photoelectron spectra of Me_2S (b–e) and experimental X-ray spectra of $B_{10}H_{12}(SMe_2)_2$ (f–i).²⁴⁰ (b, f) SK_{β} -spectra; (c, g) $SL_{1,2}$ -spectra; (d, h) CK_{α} -spectra, (e) UPS spectrum; (i) BK_{α} -spectrum. Dashed lines indicate the contributions of vacant orbitals.

diagram of MOs of the $B_{10}H_{12}(SMe_2)_2$ cluster and of its fragments ($B_{10}H_{12}$ and Me_2S); the results of fragment analysis of this cluster (MNDO calculation); the X-ray and UV [He(I)]²²⁷ photoelectron spectra of Me_2S reduced to a common energy scale (with the use of XPS data²²⁴); and X-ray spectra of $B_{10}H_{12}(SMe_2)_2$. The point symmetry group of both compounds is C_{2v} . As one can see from Fig. 25 b, f, the most noticeable changes on transition from dimethyl sulfide to its adduct with borane are observed in the X-ray SK_{β} -emission spectrum. They are similar to the changes observed in X-ray spectra upon coordination of the ammonia molecule to the borane cluster. The maxima in all emission spectra of free dimethyl sulfide are also identified in this figure.^{96, 241} For example, the $2b_1$ HOMO is formed by a lone electron pair or, more accurately, it is an orbital with high S3p-population. Interaction of the $2b_1$ HOMO of Me_2S with the $5b_2$, $6a_1$ and $4b_2$ orbitals of $B_{10}H_{12}$ upon coordination of a dimethyl sulfide molecule to the borane cluster (see Fig. 25 a) results in a series of new MOs, viz., $11b_2$, $12a_1$, $10b_2$ and $11b_2$ (see Fig. 25 a); the contribution of the 3p-AO of the sulfur atom to these orbitals is much lower than the contribution to the $2b_1$ HOMO of the free dimethyl sulfide molecule. Hence, the X-ray SK_{β} -emission spectrum will contain a low intensity line instead of the intense line corresponding to the lone electron pair (see Fig. 25 b, f). On the other hand, the structure of deeper MOs changes insignificantly. Thus, it can be concluded that the chemical bond between dimethyl sulfide and the borane cluster is of donor–acceptor nature and that it is formed by the lone electron pair of Me_2S and the 2p-orbitals of boron. The correlation diagram shows that the structure of the wave functions of the three occupied MOs, viz., $7a_2$, $14a_1$ and $9b_1$, of the $B_{10}H_{12}(SMe_2)_2$ cluster almost coincides with the structure of the three orbitals of the borane cluster in a

free state (see Fig. 25 a). The only difference is that the bond energy in the $B_{10}H_{12}(SMe_2)_2$ cluster is lower. The electron densities of the MOs of the above adduct are localised on boron atoms (and are absent from the ligands). This electron density distribution is clearly seen in the X-ray spectra. In fact, as one can see in Fig. 25 f–i, as the binding energy increases, the boron line with a maximum at ~ 5 eV with respect to the Fermi level (transition energy ~ 184 eV) characterising the contributions of the boron 2p-AO to the MO is the first line to appear; it is followed by lines characterising the contributions from the AOs of the ligands starting from the first line of the $SL_{2,3}$ -spectrum with a maximum of ~ 7 eV with respect to the Fermi level. It can be concluded from a comparison of spectra arranged in this way that the electron density of the highest MOs is predominantly localised on borane cluster atoms. In the dimethyl sulfide molecule, lone electron pairs ($2b_1$ -MO) are involved actively in the chemical bond with the borane cluster, including the B(6) and B(9) atoms (see Fig. 6 c). It was shown²⁴⁰ that in this case one can speak of preferential formation of an S–B donor–acceptor σ -bond. Finally, deeper MOs of the borane– Me_2S adduct are mainly composed of dimethyl sulfide's MOs. The formation of the chemical bond between the borane cluster and dimethyl sulfide molecules with involvement of vacant orbitals has certain specific features. Their contribution is spread along the series of the $B_{10}H_{12}(SMe_2)_2$ MOs and does not exceed 8% for any single orbital, although the total contribution of the vacant boron 2p-AOs amounts to 30%. The same situation is observed for the $B_{10}H_{12}(NH_3)_2$ cluster. It follows from quantum-chemical studies (MNDO calculations)²³⁹ that a bond of predominantly σ -type is formed between the B(6), B(9) and L atoms (see Fig. 6 d). However, a contribution of the π -component is also possible in

some cases, *e.g.*, with $L = \text{MeCN}$ and $\text{C}_2\text{H}_5\text{N}$. This interaction is very weak in the $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$ cluster.

Changes in the valence of a sulfur atom with different coordinations on transition from such non-cluster compounds as H_2S and Me_2S (with a coordination number of 2) to $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ and, finally, to the $\text{B}_9\text{SH}_{12}^-$ anion, in which the sulfur atom is directly introduced in the borane cluster,²⁴⁰ with a coordination number of 3, were studied. The changes in the chemical bond nature between the sulfur and boron atoms on passing from the $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ cluster to the $\text{B}_9\text{SH}_{12}^-$ anion are no less interesting. The geometric structure of this anion and its X-ray SK_β -emission spectrum obtained by Yumatov *et al.*²⁴⁰ are presented in Fig. 26. The sulfur atom in the H_2S molecule forms two σ -bonds with hydrogen atoms, whereas the dimethyl sulfide molecule contains two similar $\text{S}-\text{C}$ σ -bonds along with a weak π -bond resulting from interaction of a lone electron pair of the sulfur atom with the 2p-electrons of the carbon atoms. This interaction does not affect considerably the structure of the X-ray SK_β -emission spectrum on transition from H_2S to Me_2S (see Figs 25 and 26): just a small decrease of the relative intensity of the line corresponding to the lone electron pair of the sulfur atom (b_1 -MO) is observed. As noted previously, the sulfur atom in the $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ molecule forms a σ -type chemical bond (donor-acceptor bond) with a boron atom and two σ -bonds with carbon atoms of the methyl groups. In the $\text{B}_9\text{SH}_{12}^-$ thiaborane cluster (see Fig. 26), the sulfur atom forms two σ -bonds with the B(5) and B(7) atoms. By analogy with the dimethyl sulfide molecule, one can assume that there is weak π -interaction between these sulfur and boron atoms. The conjugation of the S atom with the B(2) cluster atom possibly involves a lone electron pair of the sulfur atom. Similar interaction manifests itself in X-ray SK_β -emission spectra on transition from the Me_2S molecule to the $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ cluster. The line in the X-ray SK_β -emission spectrum of $\text{CsB}_9\text{SH}_{12}$, which was associated with a lone electron pair on the sulfur atoms in the spectra of H_2S and Me_2S (see Fig. 26), has very low intensity. The identity of X-ray SK_β -emission spectra of $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ and $\text{CsB}_9\text{SH}_{12}$ confirms the assumption that the electronic states of the sulfur atom coordinated by three boron atoms in these clusters are similar. Hence, it can be assumed that noticeable conjugation of the lone electron pair of the sulfur atom with the 2p-electrons of the boron atoms occurs in the $\text{CsB}_9\text{SH}_{12}$ cluster, but it appears impossible to determine the type of the

$\text{S}-\text{B}(2)$ interaction based on X-ray spectral data only. Most likely, mixing of σ - and π -bonding occurs in this case, and it is the reason for the strong decrease in the electron-donor properties of the sulfur atom incorporated in the borane cluster.

Thus, the $\text{S}-\text{B}$ chemical bond in $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ results from σ -interaction of the HOMO of dimethyl sulfide, which predominantly consists of the 3p-AO of the sulfur atom (lone electron pair), with orbitals of the borane cluster. The interaction of similar orbitals of B and S atoms probably occurs in the $\text{CsB}_9\text{SH}_{12}$ molecule as well. The results considered above reflect the substantial differences in the electronic state of sulfur atoms in non-cluster systems and in borane clusters with various coordination numbers. These differences can manifest themselves as differences in the reactivity of the systems in question.

Interaction of a ligand with the borane cluster in the molecule $\text{B}_{10}\text{H}_{12}(\text{PPh}_3)_2$ is no less complex.²⁴² The point is that the lone electron pair of the phosphorus atom in the free triphenylphosphine molecule interacts with electrons of the phenyl groups.^{110, 241} This affects markedly the structure of the X-ray PK_β -emission spectrum (Fig. 27). In fact, transition from triethylphosphine, in which this kind of interaction is absent, to triphenylphosphine is accompanied by a decrease in the relative intensity of the high-energy line caused by the lone electron pair of the phosphorus atom. One would think that the addition of a Ph_3P molecule to the $\text{B}_{10}\text{H}_{12}$ borane cluster would decrease the relative intensity of this line even more, as it was observed in the X-ray NK_α -emission spectrum on transition from NH_3 to $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$ and in the SK_β -spectrum on transition from Me_2S to $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$. However, such an effect is not observed in this case. Possibly, the AO of the lone electron pair of the phosphorus atom in the complex is strongly bound to the MO of the borane cluster and cannot participate in π -conjugation with benzene rings.²⁴²

In this review, XPS results are considered only in combination with data from X-ray spectroscopy, although the former method is of great value on its own. In particular, this allows one to determine the charge characteristics of atoms in a molecule.^{92, 100} Let us provide a few examples. As noted above in the discussion of the X-ray absorption spectra of BF_3 and BCl_3 , the electron density on the boron atom is higher in the boron trichloride molecule than

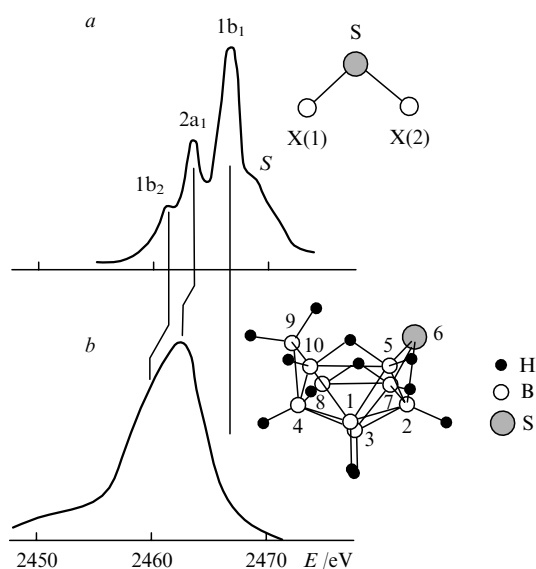


Figure 26. X-Ray SK_β emission spectra of H_2S (a) and $\text{B}_9\text{SH}_{12}^-$ (b) and geometric structure of X_2S (a) and $\text{B}_9\text{SH}_{12}^-$ molecules (b).²⁴⁰ X = H, Me; S is a satellite peak.

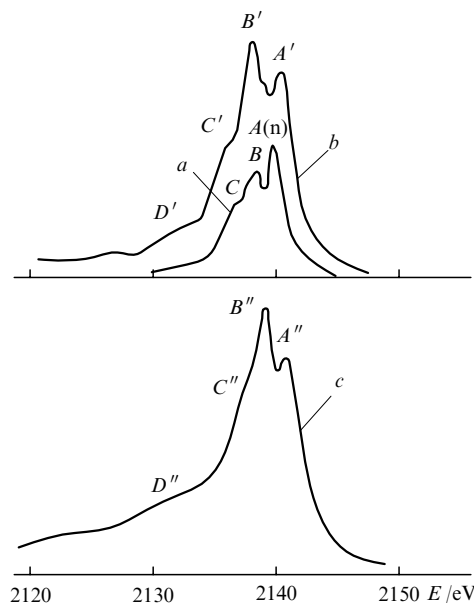


Figure 27. X-Ray PK_β emission spectra of Et_3P (a), Ph_3P (b) and $\text{B}_{10}\text{H}_{12}(\text{PPh}_3)_2$ (c).²⁴² Matching spectral lines are designated by the same letters ('n' indicates a lone electron pair).

in the boron trifluoride molecule. According to XPS data, the energy of the B1s level decreases from 202.8 to 200.5 eV on transition from BF_3 to BCl_3 (mean values out of the values available in the database).²²⁴ This also suggests that the electron density on the boron atom is higher in the BCl_3 molecule than in BF_3 .⁹² The donor–acceptor interaction in $\text{NH}_3 \cdot \text{BF}_3$ and $\text{B}_{10}\text{H}_{12}\text{L}_2$ ($\text{L} = \text{NH}_3, \text{Me}_2\text{S}$) is accompanied by electron density transfer from the donor molecule to the acceptor molecule. Naturally, this decreases the electron density on the donor atom involved in the coordination. For example, transition from NH_3 to $\text{NH}_3 \cdot \text{BF}_3$ changes the energy of the N1s level from 398.8 to 402.1 eV,¹⁰⁰ suggesting an increase in the positive charge on the nitrogen atom.⁹² Similar behaviour is observed on passage from NH_3 to $\text{B}_{10}\text{H}_{12}(\text{NH}_3)_2$: the energy of the N1s level increases from 398.8 (see Ref. 100) to 402.4 eV,²³⁰ while transition from Me_2S to $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$ changes the energy of the S2p_{3/2}-level from 163.0 (see Ref. 100) to 164.4 eV.²⁴³ In these cases, a positive charge also appears on the donor atom involved in the coordination upon the formation of $\text{B}_{10}\text{H}_{12}(\text{SMe}_2)_2$. More detailed XPS studies of boron-containing compounds are covered by reviews.^{244, 245}

d. Metalloborane and metallocarborane derivatives

X-Ray spectral studies of Fe^{III} , Co^{III} , Ni^{III} and Ni^{IV} dicarbollyl ‘sandwich’ complexes were carried out.^{230, 246} These compounds include anionic complexes $[\text{M}(\text{B}_9\text{C}_2\text{H}_{11})_2]^-$ ($\text{M} = \text{Fe}^{\text{III}}, \text{Co}^{\text{III}}, \text{Ni}^{\text{III}}$) and a molecular complex $[\text{Ni}^{\text{IV}}(\text{B}_9\text{C}_2\text{H}_{11})_2]^0$. Their ligands include cluster anionic derivatives of *ortho*-carborane(12), $(\text{B}_9\text{C}_2\text{H}_{11})^{2-}$ (see Fig. 6*j–l*). The M atom in such compounds is located between pentagonal planes $-\text{B}-\text{C}-\text{C}-\text{B}-\text{B}-$ formed by two $(\text{B}_9\text{C}_2\text{H}_{11})^{2-}$ anions; a ‘sandwich’ structure is formed as a result. In $[\text{M}(\text{B}_9\text{C}_2\text{H}_{11})_2]^{2-}$ complexes, the $-\text{C}-\text{C}-$ atom pairs in conjugated π -ligands $(\text{B}_9\text{C}_2\text{H}_{11})^{2-}$ can be located *trans* to the M^{III} atom for $\text{M} = \text{Ni}, \text{Fe}$, etc. (see Fig. 6*j*) or *cis* for $\text{M} = \text{Co}^{\text{III}}$, as in the $[\text{Ni}^{\text{IV}}(\text{B}_9\text{C}_2\text{H}_{11})_2]^0$ structure (see Fig. 6*k*, rotational isomerism). The configuration of ligands affects intermolecular interactions. The nature of the $(\text{B}_9\text{C}_2\text{H}_{11})-\text{M}-(\text{B}_9\text{C}_2\text{H}_{11})$ ‘sandwich’ bond is a matter of discussion. In early studies, this bond was considered as an analogue of the $\text{M}-\text{C}_5\text{H}_5$ π -bond in $\text{M}(\pi-\text{C}_5\text{H}_5)_2$

metallocenes. This assumption was based on the similarity of the geometric structure of $\text{M}-(\text{B}_9\text{C}_2\text{H}_{11})^-$ with the ‘sandwich’-type structure formed by the M atom and the cyclopentadienyl anion. Later, the concept regarding the nature of the $\text{M}-(\text{B}_9\text{C}_2\text{H}_{11})^{2-}$ bond changed: it is now believed that more considerable σ -bonding (σ -delocalisation) occurs in these complexes in comparison with the interaction of the delocalised π -electronic system of C_5H_5^- with the metal atom in $\text{M}(\pi-\text{C}_5\text{H}_5)_2$ (see Refs 230 and 246 and references therein). Therefore, dicarbollyl complexes are ‘sandwich’ cluster systems to a considerable extent. In most cases, charge transfer from the ligand to the metal atom occurs in these compounds.

X-Ray BK_α -emission spectra of dicarbollyl complexes²³⁰ are presented in Fig. 28 along with L_α -spectra of the central atoms. It was shown that an increase in the number of electrons in a metal 3d-shell results in a decrease in the energy band occupied by the HOMOs mainly formed with participation of electrons of that shell. In fact, the half-width of the $\text{Fe}L_\alpha$ -line is ~ 6.0 eV, that of $\text{Co}L_\alpha$ is ~ 4.0 eV and that of $\text{Ni}L_\alpha$ is ~ 3.0 eV. On the other hand, the binding energy of electrons of this group of orbitals increases in the same order. In fact, the energy of ML_α -lines for metals in dicarbollyl complexes relative to the Fermi level is ~ 2.5 eV for $\text{Fe}L_\alpha$, ~ 3.2 eV for $\text{Co}L_\alpha$ and ~ 4.2 eV for $\text{Ni}L_\alpha$. Thus, metal 3d-AOs make the main contribution to the HOMOs, whereas the MOs composed with participation of the boron 2p-AO lie deeper. Their energy is ~ 6.5 eV relative to the Fermi level. The strong overlapping of the BK_α - and L_α -bands may be evidence of efficient interaction of ligands with the central metal atom. Transition from the Ni^{III} complex to the Ni^{IV} complex stabilises the MOs composed with involvement of 3d-AOs even more and enhances the B2p–Ni3d interaction. Let us note the high stability of the energy position of the MO with a considerable contribution of the 2p-AO of the boron atom, which is probably caused by the aromatic character of closed three-dimensional systems.

6. Heterocyclic boron compounds

To our knowledge, heterocyclic boron compounds have only been studied by Doering *et al.*²⁴⁷ They studied the electron energy loss spectra of borazine (point symmetry group D_{3h}) (Fig. 29), which were noted (see Section III.2) to be similar to X-ray absorption spectra. According to the results of these studies, the π -system orbital (ϵ'') is the LUMO in the $\text{B}_3\text{N}_3\text{H}_6$ molecule; it manifests itself as an intense low-energy maximum in the spectra. It should

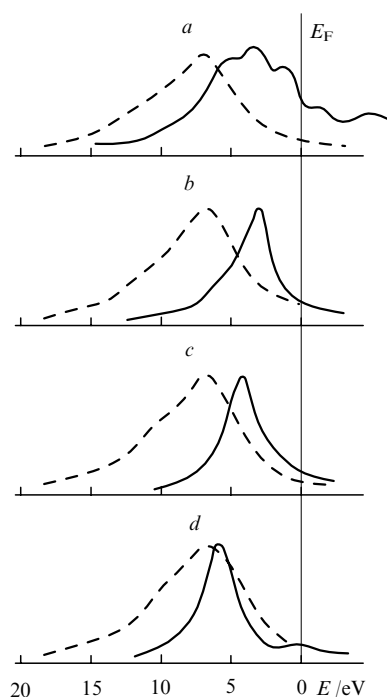


Figure 28. X-Ray BK_α and ML_α emission spectra (dashed and solid lines, respectively) of $\text{Cs}[(1,2-\text{B}_9\text{C}_2\text{H}_{11})_2\text{M}]$ dicarbollyl complexes.²³⁰ $\text{M} = \text{Fe}$ (a), Co (b), Ni (c), $(1,2-\text{B}_9\text{C}_2\text{H}_{11})_2\text{Ni}$ (d).

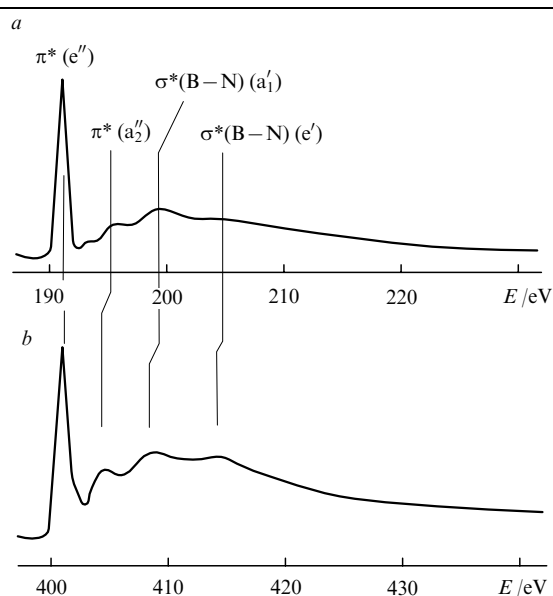


Figure 29. Electron energy loss spectra of borazine.²⁴⁷ (a) BK spectra; (b) NK spectra.

be added that certain details of electronic structures of a number of five- and six-membered boron-containing heterocycles were studied rather thoroughly by UPS and NMR spectroscopies.⁸³ Figure 7 shows a scheme of interaction of nitrogen and boron AOs and a qualitative scheme of MOs in some heterocyclic boron compounds. These systems involve π -bonding.^{83, 87}

V. Conclusion

In this review, it was shown for boron-containing systems as an example that X-ray spectral studies provide vast information about the electronic structures of chemical compounds. A specific feature of X-ray spectroscopy is that it provides information on the energy positions and structures of MOs which is comparable with results of quantum-chemical calculations. Although detailed information about the properties of occupied and vacant orbitals can be extracted from X-ray emission and absorption spectra, it seems most efficient to use these methods in combination with UV and X-ray photoelectron spectra reduced to a common energy scale. The use of absorption spectra, quantum yield spectra and energy loss spectra is especially beneficial for studies of boron compounds that possess acceptor properties. However, because of problems associated with the methods and instruments used, comprehensive X-ray spectral studies with involvement of UPS and XPS have as yet been carried out for a rather limited number of compounds.

A distinctive feature of studies on the electronic structures of chemical compounds of boron is associated with donor–acceptor interactions. In fact, clear detection of a lone electron pair of a donor molecule (HOMO) in X-ray emission spectra and a lone hole pair of an acceptor molecule (LUMO) (with a boron compound as an acceptor) in the absorption spectra, as well as changes in the electronic structures of these molecules upon adduct formation that are observable in X-ray spectra, made this a promising method for studies on the nature of donor–acceptor interaction. Studies of this interaction are based on the two-level model, according to which the formation of a bond only involves the HOMO of the donor and the LUMO of the acceptor; however, this is only an approximate model. The formation of this type of chemical bonds also involves deeper valence MOs of the donor and the acceptor. It is possible that this mechanism can be expanded for the donor–acceptor ligand–metal interaction in complex compounds; the results of its X-ray spectral studies are generalised in the monograph by Mazalov and Yumatov.²⁴¹

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^a — *Crystallogr. Rep. (Engl. Transl.)*

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^f — *Physics-Uspekhi (Engl. Transl.)*

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^j — *Theor. Exp. Chem. (Engl. Transl.)*

^k — *Russ. J. Phys. Chem. (Engl. Transl.)*

Use of cyclodextrins for separation of enantiomers

O A Shpigun, I A Ananieva, N Yu Budanova, E N Shapovalova

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Abstract. The review surveys data on the use of cyclodextrins as chiral selectors in high-performance liquid chromatography and capillary electrophoresis. The mechanisms of enantiomer separation and the factors influencing the selectivity and efficiency of separation in various methods of chromatography and capillary electrophoresis are considered. Numerous examples of the practical application of cyclodextrins in separation of optical isomers are given. The bibliography includes 325 references.

I. Introduction

The necessity of separating stereoisomers (in particular, enantiomers) is, to a large extent, associated with their various biological activities.^{1–4} This problem arises in different fields of chemistry, biochemistry, pharmacology and agrochemical industry. The enantiomeric compositions of chiral compounds are generally determined by chromatographic methods and capillary electrophoresis (CE).

Enantiomers can be separated only with the use of systems containing a chiral selector, which should recognise the three-dimensional configurations of two isomers identical in chemical and physical properties.⁵ Two modes of separation are possible. In one mode, a chiral stationary phase (SP) and an achiral mobile phase (MP) are used. By contrast, another mode employs achiral stationary and chiral mobile phases. Chromatography more often employs the former mode of separation, whereas the latter mode is more commonly used in capillary electrophoresis.

Enantioselectivity of a chiral selector is based on the difference in its interactions with a pair of enantiomers. Two types of enantioselectivity, *viz.*, kinetic and thermodynamic, are considered. Kinetic enantioselectivity reflects the difference in the rate of interaction of a chiral selector with two enantiomers, whereas thermodynamic enantioselectivity reflects the difference in stabil-

ity of two possible diastereomeric adducts formed in the course of interaction. The mechanisms of separation of optical isomers are explained using models of chiral recognition, which are often based on a model of a 'three-point interaction' proposed by Dalgliesh.^{6,7} Interactions between a chiral selector and enantiomers are determined by a combination of various attractive and repulsive forces. Repulsive interactions occur generally due to steric hindrance and, more rarely, to dipole–dipole repulsions, whereas attractive interactions may be of diversified nature and include hydrogen bonds, Coulombic or dipole–dipole attractions, the formation of charge-transfer complexes (CTC), hydrophobic interactions (in aqueous systems), *etc.*

The formation of charge-transfer and inclusion complexes is of most importance in enantioselective sorption. The presence of π -electron systems in interacting compounds is necessary for the formation of CTC. Aromatic systems acting as both donating and withdrawing components often form stable CTC. Such π – π interactions together with Coulombic interactions and hydrogen bonds provide high activity of chiral selectors. Inclusion complexes are formed by compounds with specific structural features (the presence of a cavity), due to which their molecules can trap and hold suitable guest molecules. Rigid requirements providing the possibility of the formation of host–guest complexes assume stereoselectivity of this process, *i.e.*, enantiomeric guest molecules can be completely separated with the use of chiral host molecules. Cyclodextrins and crown ethers belong to a class of chiral selectors whose action is based on the inclusion effect.

Finally, in some cases chiral recognition can be performed based only on steric compatibility. The idea of 'molecular fingerprints' consists of creating a rigid chiral cavity in a polymer network such that it is suitable only for one of two enantiomers.²

Of a large number of known chiral selectors, polysaccharides⁸ and cyclodextrins (CD)^{9–12} find extensive application in chromatography and capillary electrophoresis. Cyclodextrins are particularly versatile because their modifications allow one to prepare selectors possessing new properties. Cyclodextrins modified with polar groups have not been adequately explored as selectors in HPLC. Aminated β -CD remains virtually unstudied. The use of this chiral selector in HPLC was first described by us.^{13,14}

The wide application of CD in liquid chromatography is favoured by the preparation of CD-based stable chiral sorbents by chemical modifications of silica gels. A sorbent of this type was first prepared by Fujimura *et al.*¹⁵ by the reaction of tosylated CD with aminopropylated silica gel, but this sorbent was readily subjected to hydrolysis. Armstrong and Mond¹⁶ used spacers containing from 2 to 20 carbon atoms and prepared cyclodextrin-modified silica gels possessing high hydrolytic stability by remov-

O A Shpigun, I A Ananieva, N Yu Budanova, E N Shapovalova Department of Chemistry, M V Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax (7-095) 939 46 75. Tel. (7-095) 939 13 82. E-mail: shpigun@analyt.chem.msu.ru (O A Shpigun). Tel. (7-095) 939 54 64. E-mail: ananieva@analyt.chem.msu.ru (I A Ananieva), shapovalova@analyt.chem.msu.ru (E N Shapovalova). Tel. (7-095) 939 15 68. E-mail: natasha_budanova@mail.ru (N Yu Budanova)

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ing non-selective polar adsorption centres. This gave impetus to the rapid development of chiral liquid chromatography. Recently, Crini *et al.*¹⁷ synthesised chiral phases by treating silica gel with cyclodextrin-containing polymers. However, sorbents of this type are insufficiently selective and their further improvement is required.

Cyclodextrins find application as chiral selectors in gas^{18–20} and liquid chromatography and capillary electrophoresis. The use of CD in enantiomer separation was examined in a large number of studies and surveyed in a number of reviews^{10, 12, 21–35} devoted to the discussion of both the principal theoretical problems and practical application of chiral separations on CD. However, Russian publications on chiral separations are scarce (many of these studies were carried out by Davankov and co-workers and were devoted to chiral ligand-exchange chromatography^{21, 36–38}). Reviews of cyclodextrin chiral selectors are lacking.

The aim of the present review is to close this gap. We consider the mechanisms of enantiomer separation and factors responsible for enantioselectivity of cyclodextrins with different structures. A large number of examples of the practical application of CD in separation of optical isomers are given. Taking into account a huge number of studies in this field, we focus our attention on the results of studies by high-performance liquid chromatography, capillary electrophoresis and electrocapillary chromatography published in 2000–2001. In the review, chiral separations on CD by gas and liquid chromatography and capillary electrophoresis are compared.

II. Cyclodextrins and their derivatives

Cyclodextrins are cyclic oligosaccharides similar in shape to crown ethers. Cyclodextrins are produced under the action of *Bacillus macerans* amylase on starch and consist of 6–12 D-glucose residues linked to each other by α -(1,4) bonds. Cyclodextrins containing 6–8 glucose residues are called α -, β - and γ -CD, respectively (Fig. 1).

The physical and chemical characteristics of CD are given in Table 1. As can be seen from this table, solubility of β -CD in water is very low compared to that of other oligosaccharides. However, its solubility increases substantially in aqueous organic solutions (methanol or ethanol, < 30%), at high pH, with the use of a supporting electrolyte and also on going to various β -CD derivatives.

The hydroxy groups of CD can be rather readily modified by chemical reactions giving rise to CD derivatives with various degrees of substitution. The chemical compositions of the products are determined by a number of factors, such as reaction conditions, properties of the reagents used, their ratio, *etc.*

Table 1. Selected chemical and physical characteristics of cyclodextrins.^{10, 39}

Parameter	Cyclodextrin		
	α	β	γ
Number of glucose residues	6	7	8
Molecular mass	972	1135	1297
Inner diameter /nm	0.57	0.78	0.95
Depth of the cavity /nm	0.78	0.78	0.78
Specific rotation (25 °C) /deg	150.5	162.5	177.4
Solubility (25 °C) /g/100 ml of H ₂ O	14.5	1.85	23.2
pK _a	12.33	12.20	12.08

Depending on the substituents introduced into CD, either uncharged or charged modified CD are produced. Methylated, acylated, hydroxyethylated and hydroxypropylated cyclodextrins belong to the former group, whereas aminated, methylaminated, carboxymethylated, sulfated, phosphorylated, *etc.* cyclodextrins belong to the latter group.^{10, 13, 14, 23, 39}

It should be noted that the preparation of cyclodextrin derivatives is a rather complicated process in the course of which either all hydroxy groups or only some of them are replaced. In some cases, the structures of the selectors thus formed were not studied in detail. In original publications, the names of selectors were often not detailed and only the types of substituents were reported. As a result, a large number of trivial names exist, which hinders a comparison of the results of investigations and their interpretation. In the present review, we give names of selectors which were used by authors of the cited studies.

The properties of modified CD differ from those of non-modified CD. The selectivity of enantiomer separation can be improved by increasing solubility, using the ability of CD derivatives to form secondary bonds or controlling the degree of hydrophobicity of the CD cavity.¹⁰ For example, dimethyl- β -CD (DM- β -CD) has a higher solubility and possesses a larger interaction surface compared to β -CD. The hydroxy groups of a substituent in β -CD, which are either charged or can be charged, may be very useful for optimisation of separation by HPLC and CE.

β -Cyclodextrin bearing hydroxypropyl substituents is of interest for separation of enantiomers containing one aromatic or heterocyclic ring and a two–four-membered carbon chain with substituents, which can form hydrogen bonds or serve as proton acceptors.²³ The presence of hydroxy groups in substituents modifying CD provides additional centres for hydrogen bonding. It should be noted that acylated β -CD and β -CD containing hydroxypropyl groups act both in reversed-phase and ‘polar

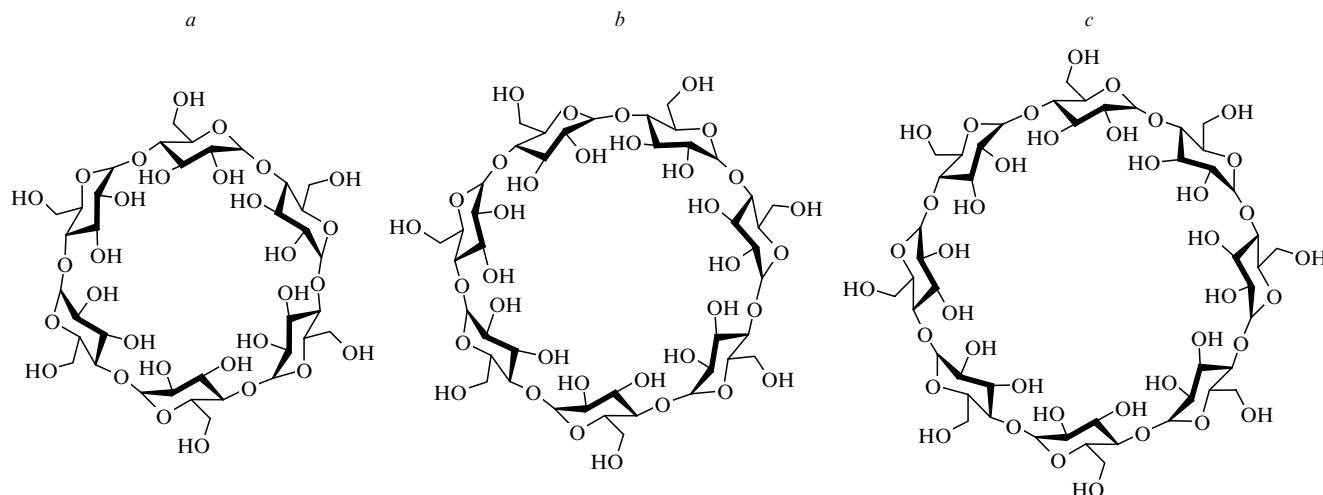


Figure 1. Molecular structures of cyclodextrins: α -cyclodextrin (a); β -cyclodextrin (b); γ -cyclodextrin (c).

organic' HPLC as well as CE, whereas methylated β -CD is used only in reversed-phase HPLC.

β -Cyclodextrins with bulky substituents, for example, (*S*)- and (*R*)-naphthylethylcarbamates and 3,5-dimethylphenylcarbamates, are commonly used for separation of enantiomers by HPLC.¹⁰

III. Cyclodextrins as chiral selectors in high-performance liquid chromatography

Enantiomer separation is most often carried out by high-performance liquid chromatography. In the last decade, this method has been extensively developed. Considerable progress in this area was made due to thorough investigations of the processes of chiral recognition of enantiomers and factors influencing this process. The use of cyclodextrins in HPLC provided a deeper insight into the characteristic features of enantiomeric recognition and extended the field of its application.

1. Mechanisms of separation on cyclodextrin chiral phases

In aqueous media, cyclodextrins adopt a toroidal conformation with a hydrophobic inner surface, because all hydroxy groups are located outside the cavity of the molecule. For this reason, hydrocarbon fragments of many organic compounds readily occupy the inner cavity to form inclusion compounds with CD. Cyclodextrins can be involved in both hydrophobic and polar interactions as well as in hydrogen bonding with sorbed molecules due to which this chiral selector has a broad spectrum of action. The main prerequisite for enantioselectivity of separation on CD is a particular size of the sorbate molecule, because the formation of an inclusion complex of the sorbate with CD plays a decisive role.

Stability of an inclusion complex depends substantially on the degree of hydrophobicity and steric compatibility between the guest and host (CD) molecules. Evidently, an inclusion complex cannot be formed if the diameter of the molecule is larger than the size of the CD cavity. If the diameter of the molecule is smaller than the size of the CD cavity, the complex can be formed, but the constant of its formation is much smaller than that for a molecule, which can be rigidly fixed in the cavity. It was experimentally found that compounds bearing one aromatic ring (for example, benzene) have a size suitable for α -CD, compounds with two aromatic rings (for example, naphthalene) are suited to the separation on β -CD, and compounds such as substituted pyrenes are suitable for the separation on γ -CD. The presence of one or several polar groups in the sorbate molecule is favourable for hydrogen bonding with the hydroxy groups of CD.

The selectivity of complex formation is determined by the energy difference between inclusion complexes of CD with enantiomers. In most cases, enantiomers contain an aromatic ring (often more than one ring). It was found^{40,41} that separation depends on the position of the chiral centre and its environment. The enantiomeric resolution is higher if a chiral centre is involved in the ring and is bound to two or three sp^2 -hybridised carbon atoms. Complexes with a chiral centre enclosed in a sandwich consisting of two π systems, one of which is an aromatic ring and the other one is either a carbonyl group or the second aromatic ring, are best suited to the enantiomer separation. Successful separation is associated with the high rigidity of the molecule, the chiral centre serving as a point about which fragments of the molecule can rotate.

Most of the published experimental data demonstrate that the size of the β -CD cavity is optimum for the separation of a broad spectrum of optically active compounds, including those used in the pharmaceutical industry.²³ It should be emphasised that the sorbate molecule does not need to be completely located inside the CD cavity. Numerous examples of separation on β -CD of enantiomers containing three or four aromatic rings have been given.¹⁰ It appeared that it is quite sufficient if the sorbate

molecule is only partially located in the cavity and forms an inclusion complex.

The overwhelming majority of enantiomer separations were carried out with the use of β -CD and its various derivatives.¹⁰ To reveal the reasons for this advantage in separation of various compounds, let us consider the structure of the CD molecule (Fig. 2). Hydrophobic molecules analogous to benzene can enter into and leave the CD cavity and are reversibly sorbed on this surface. However, in the absence of hydrophobic sorbates, any other particles, including ions, can penetrate into the cavity. In addition, sorbate molecules can form hydrogen bonds with the hydroxy groups of the CD surface and/or interact with substituents located outside the cavity (in modified CD) and the residual silanol groups of silica gel.

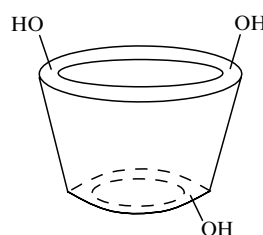


Figure 2. Shape of the β -cyclodextrin molecule in aqueous solutions.²³

To extend the field of application and enhance the selectivity of chiral stationary CD phases, substituted CD with various functional groups are used.^{10,23} The presence of such groups provides additional interactions between the sorbate and the surface, which allows one to extend substantially the spectrum of racemates separated. Extensive investigations in this area are being continued. We proposed a new chiral selector, viz., aminated β -CD. Silica gel modified with aminated β -CD serves as an efficient sorbent for separation of amino acid derivatives and its application made it possible to extend substantially the spectrum of amino acid derivatives which can be separated. For example, separations of *N-tert*-butoxycarbonyl derivatives of amino acids were carried out. Earlier, the latter derivatives had been separated only with the use of hydroxypropyl derivatives of β -cyclodextrin.^{13,14}

In the case of modified β -CD with hydrophobic substituents, for example, with (*S*)-naphthylethylcarbamate or 3,5-dimethylphenylcarbamate, interactions on the surface occur through another mechanism. Depending on the type of the mobile phase, the following interactions between the sorbate and the surface prevail on these chiral stationary phases: the formation of π complexes in a normal phase, hydrogen bonding in a polar organic phase, and the formation of inclusion complexes in a reversed phase.¹⁰

The above-described chiral selectors are multimodal, because they are successfully used for separation of a large amount of various enantiomers and interact with the latter according to different mechanisms. The choice of a mobile phase is governed by the structure of the compound analysed, its stability and solubility in the mobile phase. The normal-phase method is most preferable, the 'polar organic' method ranks next, and the reversed-phase method occupies the last place because of its low resolution, relatively short lifetime of such chromatographic columns and small capacity factors.

Cyclodextrins find wide application as chiral additives to a mobile phase in enantiomer separations. In this case, recognition of enantiomers occurs due to the distribution of the sorbate between the stationary phase and the inclusion complex in the mobile phase. The resolution and selectivity in these systems depend on the type and concentration of the CD, the nature of the mobile and stationary phases and temperature. In some cases,

CD can be sorbed on the surface of a mobile phase and form a pseudostationary phase.⁴²

2. Separation of enantiomers in reversed-phase high-performance liquid chromatography

Most separations on CD-based chiral stationary phases are carried out by reversed-phase liquid chromatography, because inclusion complexes can be formed only in aqueous or aqueous–organic solutions. The stability constants of complexes are generally larger in water and decrease as the fraction of an organic solvent increases. It is known that the addition of various organic solvents to an eluent can change the selectivity of enantiomer separation. This effect is observed also for CD-based stationary phases.¹⁰

a. Choice of a mobile phase

Methanol and acetonitrile are used as organic additives to mobile phases. Ethanol, propanol, dioxane, dimethylformamide and tetrahydrofuran are used much more rarely. Water has the smallest eluting ability. For alcohols, the polarity increases in the series methanol < ethanol < propanol. Tetrahydrofuran and acetonitrile are similar in polarity to propanol. Solvents which are less polar than water and whose molecular sizes correspond to the sizes of the CD cavities are prone to be retained on stationary CD phases. Therefore, the capacity factors of sorbates depend on how rapidly the solvent molecules displace the compound to be determined from the CD cavity. For example, it is necessary to use a larger percentage of methanol than that of propanol to obtain comparable retention times in both cases.

Different ways of optimising the concentration of an organic solvent in a mobile phase are available. There are three possible types of chromatographic behaviour of compounds on the surface of the stationary CD phase. The corresponding dependences of the retention on the concentration of an organic solvent in a mobile phase are shown in Fig. 3.⁴³ The most general dependence is represented by curve 1, which shows that the retention decreases as the concentration of an organic component in the mobile phase increases. The curve reaches a minimum, *i.e.*, the 'dead time', and the further addition of the organic solvent has no effect on retention. This chromatographic behaviour is typical of compounds soluble in organic solvents (phenols, anilines and other aromatic and heterocyclic compounds).

Curve 2 illustrates the unique properties of stationary CD phases, which enable one to extend substantially the range of the compounds separated due to the application of 'polar organic' liquid chromatography. A decrease in the buffer/organic solvent ratio in the mobile phase leads to a decrease in retention (and

resolution). The retention minimum is achieved in the range of 50%–80% of an organic solvent in the mobile phase.⁴³ A further increase in the percentage of an organic solvent increases retention. Therefore, it can be assumed that the mechanism of recognition on stationary CD phases in elution of sorbates with mobile phases with a dominant concentration of an organic solvent differs substantially from that taking place in reversed-phase chromatography.

The third type of chromatographic behaviour is described by curve 3, which can also have a minimum. However, in this case the curve shape is not associated with the unique properties of stationary CD phases; instead, this is a consequence of insolubility or low solubility of sorbates in organic solvents. This behaviour is shown by many amino acids. Analogous dependences for amino acids were obtained also on traditional reversed-phase columns.⁴³

The curve is shifted to the right or left by changing from one organic solvent to another, the character of the dependence remaining unchanged.

b. Salt effect and influence of pH of a mobile phase

In some cases, the nature of the organic solvent is of less importance than pH and the ionic strength of the mobile phase. The effect of the concentration of the salt additive on the retention and enantioselectivity was studied for 5-dimethylaminonaphthalene-1-sulfonyl derivatives of amino acids (dansyl amino acids). As can be seen from Table 2, the addition of small amounts of a salt to the mobile phase leads to substantial changes in retention (k') and peak resolution (R_s) of enantiomers, whereas it has virtually no effect on the selectivity coefficient (α). The resolution is improved due to a decrease in the chromatographic band broadening. In some cases, the column performance is increased by a factor of 4.¹⁰

A comparison of the experimental data obtained with the use of additives of various salts to a mobile phase shows that the presence of the salt always leads to a decrease in the capacity factor of the column and an increase in resolution (Table 3). The effect of a decrease in retention of sorbates upon the addition of a salt to the mobile phase can be compensated by varying pH and concentration of the salt.

From the published data, it is known that triethylamine acetate is recommended as an additive to a mobile phase, because this reagent allows one to vary pH using buffer solutions. The effect of pH on the retention of dansyl-L-valine is shown in Fig. 4. Curve 2 characterises the dependence of the retention on the concentration of an organic solvent in the mobile phase (a mixture of methanol and water) in the absence of the salt additive. It should be noted that curve 2 has a minimum, which is absent in curves 1 and 3. It should also be emphasised that the behaviour of sorbates in acidic media differs from that in alkaline media (curves

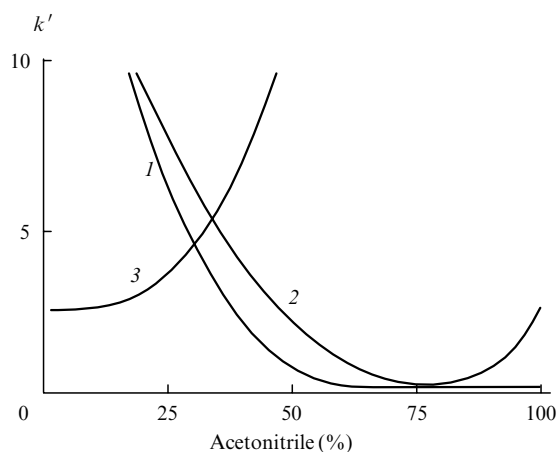


Figure 3. Influence of the composition of a mobile phase on the retention of various compounds.⁴³ The description of curves (1–3) is given in the text.

Table 2. Effect of the ionic strength of a mobile phase on the separation of enantiomers of dansyl amino acids.⁴³

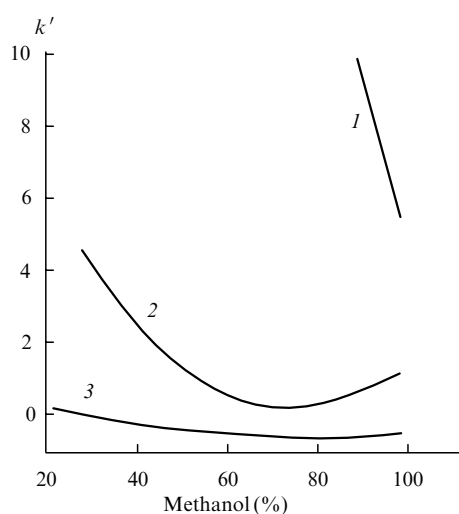
Compound	[Na ₂ HPO ₄] /mol litre ⁻¹	k'_1 (see ^a)	α	R_s
Dansyl-DL-valine	0	3.9	1.16	0.4
	0.005	0.6	1.20	0.5
	0.01	0.7	1.20	0.6
	0.02	1.4	1.17	1.1
	0.03	1.2	1.18	1.1
Dansyl-DL-phenylalanine	0	10.5	1.15	0.5
	0.005	1.7	1.18	0.7
	0.01	2.0	1.19	0.9
	0.02	3.4	1.16	1.1
	0.03	3.2	1.17	1.2

Note. Methanol–water (25:75) as the mobile phase, the flow rate was 1 ml min⁻¹. ^a The capacity factor of the first enantiomer.

Table 3. Influence of various salt additives on the separation of enantiomers of dansyl amino acids.⁴³

Additive ^a	Dansyl-DL-valine			Dansyl-DL-phenylalanine		
	k'_1 (see ^b)	α	R_s	k'_1 (see ^b)	α	R_s
LiClO ₄	1.7	1.16	1.3	3.9	1.17	1.4
NaClO ₄	1.8	1.17	1.4	3.9	1.18	1.5
KClO ₄	2.2	1.16	1.3	4.7	1.16	1.3
CsBr	2.4	1.16	1.5	4.9	1.17	1.6
NH ₄ Cl	2.4	1.16	1.5	5.3	1.19	1.5
Ca(NO ₃) ₂	1.7	1.15	1.2	3.5	1.15	1.3
Cd(NO ₃) ₂	2.3	1.14	1.4	4.6	1.15	1.3

Note. Methanol–water (40 : 60) as the mobile phase, the flow rate was 1 ml min⁻¹. ^a The concentration of the salt was 0.02 mol litre⁻¹; ^b the capacity factor of the first enantiomer.

**Figure 4.** Influence of pH and concentration of an organic solvent on the retention of dansyl-DL-valine.

A 0.1% buffer solution of triethylamine acetate [pH 4.1, curve (1); pH 8.0, curve (3)] and pure water [curve (2)] were used as an aqueous component of the mobile phase.⁴³

1 and 3, respectively). High enantioselectivity of stationary CD phases in separation of compounds of an acidic or neutral nature is most often observed at pH ~ 4.0. This is associated with the ionic state of sorbates and depends on their pK_a . For instance, pH ~ 4 is optimum for most amino acid derivatives separated on β -CD, because compounds exist predominantly in the molecular form under these conditions.

c. Temperature effect

It is known that the constants of interactions between sorbates and the cyclodextrin surface depend on the temperature.¹⁰ As can be seen from Table 4, the selectivity coefficient and resolution increase as the retention temperature decreases. However, an increase in the resolution ability is not always achieved, because at low temperatures the mass transfer rate on the surface decreases and the chromatographic band is broadened. Therefore, an increase in selectivity has no positive effect because of an increase in the peak width at low temperatures. The use of low temperatures becomes favourable if there is a possibility of narrowing the chromatographic band by changing from one organic solvent to another or introducing various additives into the mobile phase.

In the temperature range of 60–90 °C, most inclusion complexes decompose on stationary CD phases. This fact is exploited in elution of sorbates when their retention on the surface is very strong. It should be noted that the influence of the temperature on

Table 4. Effect of the temperature on the separation of enantiomers of dansyl amino acids.⁴³

Compound	T / °C	k'_1 (see ^a)	α	R_s
Dansyl-DL-valine	23	2.4	1.16	1.5
	4	3.7	1.23	1.7
Dansyl-DL-phenylalanine	23	5.3	1.19	1.5
	4	8.8	1.3	1.8

Note. Methanol–0.02 M NH₄Cl (40 : 60) as the mobile phase, the flow rate was 0.5 ml min⁻¹. ^a The capacity factor of the first enantiomer.

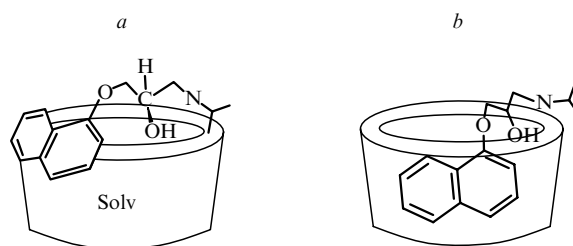
the retention of sorbates on stationary CD phases is more pronounced than that on traditional reversed-phase sorbents.

d. Effect of the rate of a mobile phase

The standard flow rate which is used in commercial 250 × 4.6-mm CD columns packed with a sorbent with a grain size of 5–10 μ m varies from 0.5 to 2 ml min⁻¹. For some compounds, the chromatographic band is substantially broadened at a flow rate of 1–2 ml min⁻¹ in the absence of a buffer or salt additives to a mobile phase. This broadening occurs due to the characteristic features of the kinetics of formation of an inclusion complex, for which the mass transfer rate on the surface of a stationary phase is low. A decrease in the rate of the mobile phase from 1–2 ml min⁻¹ to 0.4–0.5 ml min⁻¹ can improve the column performance by a factor of 1.5–3.¹⁰

3. Enantiomer separation at high concentrations of an organic solvent in a mobile phase ('polar organic' method)

The characteristic features of separation by chromatography with mobile phases containing from 90% to 100% of acetonitrile or methanol differ substantially from those of separation by reversed-phase chromatography. If an organic solvent is dominant in a mobile phase, no inclusion complexes are formed because the CD cavities are occupied by solvent molecules (Fig. 5). Armstrong and co-workers^{22,44} hypothesised that this is a new modification of chromatography, which was called a 'polar organic mode of liquid chromatography'.

**Figure 5.** Scheme of the enantioselective mechanism of retention on β -cyclodextrins in the 'polar organic' mode (a) and normal-phase (b) chromatography.¹⁰

a. Structural characteristics of chiral recognition

In elution with mobile phases in which an organic solvent prevails, the retention and enantioselectivity of separation on CD are determined by hydrogen bonding and dipole–dipole interactions between the sorbate molecules and hydroxy groups of CD rather than by hydrophobic interactions (formation of inclusion complexes).^{10,22} In addition, steric factors can be of considerable importance in chiral recognition, which is typical of stationary phases based on CD derivatives.

Compounds separated in the 'polar organic' mode should be able to form hydrogen bonds. For instance, the replacement of

hydrogen at the secondary nitrogen atom adjacent to the chiral centre by the methyl group leads to a decrease or loss of enantioselectivity. This example suggests that the presence of the acidic hydrogen atom, *i.e.*, the proton donor, is of importance for recognition of enantiomers.⁴⁴

To separate enantiomers on nonmodified CD, it is necessary that the sorbate molecules contain at least two groups capable of hydrogen bonding.¹⁰ The retention and separation on cyclodextrin derivatives occur due to the formation of $\pi-\pi$ complexes or hydrogen bonding. Groups grafted to the CD surface also contribute to chiral recognition as a result of the appearance of steric interactions.

Mobile phases with a high content of an organic solvent offer advantages over the reversed-phase and normal-phase modes of liquid chromatography and allow one to extend substantially the range of racemates which can be separated. For example, separation of compounds such as β -blockers (propranolol, atenolol, timolol, *etc.*) can be carried out on β -CD only in the 'polar organic' mode.¹⁰

b. Influence of the mobile-phase composition

The retention and enantioselectivity of sorbates in the 'polar organic' mode of chromatography depend on the nature and concentration of an organic solvent. Acetonitrile is most commonly used in enantiomer separations.

Since molecules of acetonitrile serving as the major component of a mobile phase, unlike sorbate molecules, do not form hydrogen bonds with cyclodextrin, the retention of the compounds analysed may be very high. The presence of small additives of methanol, which can form hydrogen bonds with cyclodextrin and sorbate molecules, in a mobile phase leads to a decrease in retention to a reasonable time. However, a high excess of methanol can cause a loss of enantioselectivity. To improve recognition and efficiency of separation, small amounts of triethylamine and acetic acid ($\leq 1\%$) are recommended to be added to a mobile phase.^{10,44} The ratio between these additives in a mobile phase is determined primarily by selectivity of separation and depends on the nature of the sorbates.

One of the advantages of the 'polar organic' mode of chromatography is that it allows one to separate a series of water-insoluble organic salts. This problem cannot be solved by normal-phase chromatography in which sorbates should be electro-neutral.²³

4. Enantiomer separation by normal-phase high-performance liquid chromatography

Cyclodextrin-based stationary phases are used for separation of some compounds by normal-phase chromatography.^{10,23} Hexane-isopropanol mixtures in different ratios are used as mobile phases. In this case, components of a nonpolar mobile phase tend to occupy cyclodextrin cavities and, hence, the retention and separation occur through hydrogen bonding between the sorbate and hydroxy groups of cyclodextrin and also due to $\pi-\pi$ interactions. Satisfactory results were obtained in separations of various structural isomers (substituted benzoic acids, phenols, anilines, *etc.*) by normal-phase chromatography.²³

Studies of enantiomer separations on CD-based stationary phases by normal-phase liquid chromatography are few in number. All these studies were devoted to β -CD derivatives. In most cases, their enantioselectivity is higher than that of traditional chiral polysaccharide phases for normal-phase chromatography.

5. Practical application of enantiomer separation

Molecules of most compounds which are of interest from the viewpoint of pharmacology and biochemistry contain one or several asymmetric centres. Since optical isomers differ generally in pharmacological and biological activities, the enantiomer separation has attracted growing interest. High-performance liquid chromatography has gained wide acceptance, because it

provides high efficiency and selectivity of enantiomer separation, analyses being relatively inexpensive and time-saving.

The differences in the physiological activity of enantiomers of β -adrenoblockers (so-called β -blockers) gave impetus to investigations of chromatographic separation of enantiomers of such compounds. It is known that (*S*) enantiomers of such compounds are often 50–100 times more efficient than (*R*) enantiomers. The latter can even be toxic. These compounds are too polar to be separated by gas chromatography without preliminary derivatisation. Therefore, HPLC is the method of choice. Data on the use of β -CD and its derivatives for the determination and separation of enantiomers of β -blockers have been published in the literature. The recognition ability of the following cyclodextrins was examined: β -CD,^{9,45} perphenylcarbamate (PPC) β -CD,⁴⁶ carboxymethyl- β -CD (CM- β -CD),⁴⁷ heptakis(2,3-di-*O*-methyl)- β -CD,⁹ phenylcarbamate (PC) β -CD⁴⁸ and mono-6-azido-6-deoxy-PPC- β -CD.⁴⁹ In addition, the determination of β -blockers is of great interest in studies of the composition of human blood and urine. For example, propranolol enantiomers were quantified in human urine and plasma; the sensitivity of analysis was 1.5 ng ml^{-1} for each enantiomer. It was experimentally found that the concentration of the (*S*) enantiomer is always higher than that of the (*R*) enantiomer.⁵⁰

Enantiomer separations of hydantoin and its derivatives exhibiting anticonvulsive activity were carried out with the use of chiral additives of β -CD;^{51,52} β -CD, charged β -CD and CM- β -CD;⁵³ α -CD, β -CD and their permethylated (PM) derivatives;⁵⁴ and chiral stationary phases based on β -CD and trimethyl- β -CD (TM- β -CD).⁵⁵ Charged β -CD was also used as a stationary phase for separation of antiinflammatory drugs.⁵⁶

The chromatographic behaviour of the following compounds was investigated: antidepressants and their metabolites on acylated β -CD;⁵⁷ drugs used in cancer treatment⁵⁸ and anticonvulsive drugs and their metabolites on β -CD;⁵⁹ antiepileptics and their metabolites,⁶⁰ drugs used for treatment of allergic rhinitis⁶¹ and imidazole derivatives^{62,63} with the use of an additive of β -CD to a mobile phase and imidazole derivatives on β -CD;⁶⁴ the local anaesthetic procaine⁶⁵ and the antiinflammatory drug naproxen^{66,67} using various β -CD derivatives both as chiral additives to a mobile phase and as a stationary phase; profens on β -CD.⁶⁸ A procedure was developed for the detection of the anti-anxiety agent lorazepam in human plasma on a β -CD derivative.⁶⁹

Pentostatin was detected and separated with the use of a mobile phase in the presence of an additive of sulfated β -CD;⁷⁰ methylsalsolinol and its derivatives were detected and separated with the use of an additive of β -CD to a mobile phase. The biological and toxic properties of these compounds were studied.⁷¹ The behaviour of substituted decalins on various chiral stationary CD phases was investigated.⁷² The detection of the following pharmaceuticals and biologically active compounds was examined in a series of studies: methadone and its metabolites in main human biological liquids on β -CD and its derivatives,⁷³ 7-desmethylormeloxifene (metabolite of levormeloxifene)⁷⁴ with an additive of sulfated β -CD to a mobile phase, pirlindole on β -CD,⁷⁵ tropicamide on 2-hydroxypropyl- β -CD (HP- β -CD),⁷⁶ doxazosin on CM- β -CD,⁷⁷ trimipramine with the use of an additive of β -CD to a mobile phase;⁷⁸ carbisocaine on β -CD,⁷⁹ simendan and levosimendan on β -CD,⁸⁰ salsolinol and methylsalsolinol,^{81,82} terfenadine,⁸³ thalomid⁸⁴ using an additive of β -CD to a mobile phase; zopiclone and its metabolites on β -CD,⁸⁵ *etc.*^{9,47}

Cyclodextrins as chiral additives to a mobile phase (α -CD,⁸⁶ β -CD⁸⁷ and α -CD together with β -CD⁸⁸) are used also for separation of terpenes [($\pm$)- α -pinene, ($\pm$)- β -pinene, ($\pm$)-camphene and ($\pm$)-limonene]. The enantiomeric purities of these hydrocarbons were, generally, determined by polarimetry, because separation of these nonpolar compounds devoid of functional groups which can undergo derivatisation or interact with a selector presents difficulties. Consequently, a chromatographic method for the enantioselective separation of racemates of satu-

rated hydrocarbons should be based on the formation of inclusion complexes, because in this case steric effects play a decisive role. That is the reason why enantiomer separations are carried out with the use of cyclodextrins.

The separation of amino acid derivatives on chiral cyclodextrin stationary phases was extensively studied in the early 1990s. Amino acid derivatives containing the following modifying substituents were investigated in most detail: 4-dimethylaminoazobenzene-4'-sulfonyl (dabsyl), dansyl, 9-fluorenylmethoxycarbonyl (Fmoc), 2,4-dinitrophenyl (DNP), 3,5-dinitropyridyl (DNPY), phthalyl, benzyloxycarbonyl (Z), benzoyl, *tert*-butoxycarbonyl (BOC) and derivatives of *o*-phthalic anhydride (OPA).^{10,23} The mechanism of retention and separation of enantiomers was studied for the following compounds: dansyl amino acids on PM- β -CD,⁸⁹ dansyl- and 3,5-dinitrobenzoylamino acids on methyl- β -CD (M- β -CD),⁹⁰ DNP-amino acids on 3-*O*-methyl- β -CD,⁹¹ dansyl and dabsyl amino acids on β -CD,⁹² Fmoc amino acids and selected peptides on β -CD and γ -CD,⁹³ Fmoc and dansyl derivatives of DL-serine on γ -CD,⁹⁴ dansyl amino acids on β -CD, heptakis(2,3-di-*O*-methyl)- β -CD⁹ and γ -CD, which was modified with azobenzene derivatives,⁹⁵ 3,5-dinitrobenzoyl and dansyl amino acids on naphthylethylcarbamate (NEC) β -CD,⁹⁶ 1-fluoro-2,4-dinitrophenyl-5-L-alanineamido derivatives of amino acids on β -CD,⁹⁷ Z, benzoyl, dansyl, DNP, DNPY, OPA, BOC, Fmoc and phthalyl derivatives of amino acids on heptakis(6-amino-6-deoxy)- β -CD.¹³ The chiral ability of this aminated β -CD was compared with that of nonmodified β -CD¹⁴ for various derivatives of amino acids.

Interesting experimental chromatographic data were obtained in the separation of dansyl derivatives of amino acids on a chiral stationary phase based on β -CD modified with L-tyrosine.⁹⁸ Separations of nonmodified amino acids, *viz.*, enantiomers of DL-selenomethionine⁹⁹ and various amino acids from tobacco,¹⁰⁰ were carried out on β -CD.

As can be seen from the above-considered data, most separations were carried out on CD as chiral stationary phases. However, in some cases chiral additives of CD to a mobile phase were used. As an example we refer to the separation of naphthalene-sulfo derivatives of amino acids.¹⁰¹

Enantiomer separations of the following compounds were carried out: bicyclic 1,3-amino alcohols on NEC- β -CD,¹⁰² analogues of crown ethers on β -CD and heptakis(2,3-di-*O*-methyl)- β -CD,⁹ polychlorobiphenyls and certain pesticides on heptakis(tri-*O*-methyl)- β -CD (HTM- β -CD),¹⁰³ enantiomers of warfarin on β -CD,¹⁰⁴ phenoxypropionates on permethylated β -CD,¹⁰⁵ a number of carboranes on β -CD and acylated β -CD,¹⁰⁶ compounds analogous to isoflavone on β -CD,¹⁰⁷ fluoxetine and norfluoxetine with the use of CD both as chiral additives to a mobile phase and as a stationary phase.^{108, 109}

A number of studies were devoted to the quantification and separation of biologically active compounds, in particular, of amino alcohols belonging to one of the most important classes of chiral compounds. These compounds play an important role in metabolic processes in organisms and find extensive application in medicine and pharmacology. The optical purity of adrenaline was determined using 2,6-DM- β -CD as the stationary phase.¹¹⁰ Adrenaline and its analogues were quantified in biological liquids using additives of TM- β -CD to a mobile phase.¹¹¹ Quantification of adrenaline and noradrenaline was carried out on β -CD.¹¹² Ephedrine and methylamphetamine were quantified on β -CD.¹¹³ Methylenedioxymphetamines were detected on β -CD and HP- β -CD,¹¹⁴ and methamphetamine was quantified on phenyl- β -CD.¹¹⁵

IV. Enantiomer separation by capillary electrophoresis

Capillary electrophoresis is a modern method which allows one to perform rapid and highly efficient separations of compounds. Since enantiomers possess identical physicochemical properties, it

is necessary to change selectively their effective, *i.e.*, intrinsic, electrophoretic mobilities with the aim of carrying out their successful separation by CE. This is achieved upon the formation of stereoselective complexes through hydrophobic, π - π , dipole-dipole and van der Waals interactions and hydrogen bonds. To separate enantiomers by capillary electrophoresis, a chiral selector is either added to a supporting electrolyte (SE) or chemically grafted to a capillary wall or a stationary phase. In separations with the use of cyclodextrins as chiral selectors, the compounds are either completely or partially included into the CD cavity to form inclusion complexes stabilised by secondary bonds between polar groups of the chiral selector and the compounds that are separated.

1. Selected aspects of the mechanism of chiral separations by capillary electrophoresis

The model of separation of an enantiomer pair by CE was first proposed in 1992.¹¹⁶ It is assumed that chiral separation takes place if enantiomers have different affinities for a chiral selector, *i.e.*, different binding constants K_1 and K_2 , and if the electrophoretic mobility of the free enantiomer differs from that of the enantiomer involved in a complex. The difference in the electrophoretic mobilities is expressed by the following equation:¹¹⁶

$$\Delta\mu = \frac{[C](\mu_1 - \mu_2)(K_2 - K_1)}{1 + [C](K_1 + K_2) + K_1K_2[C]^2}, \quad (1)$$

where μ_1 and μ_2 are the electrophoretic mobilities of the free enantiomer and the enantiomer involved in a complex, respectively (it is assumed that these parameters are identical for both enantiomers) and $[C]$ is the concentration of the chiral selector. The optimum concentration of the chiral selector can be determined by solving the equation $d\Delta\mu/d[C] = 0$. In this model, the concentration depends only on the binding constants K_1 and K_2 :

$$[C]_{\text{opt}} = \frac{1}{\sqrt{K_1K_2}}. \quad (2)$$

From Eqn (1), it follows that the difference in electrophoretic mobilities is larger if the enantiomer-chiral selector complex migrates in a direction opposite to the direction of migration of the free enantiomer. This is confirmed by experimental results obtained with the use of charged CD, when the compounds that are separated and the chiral selector migrate in different directions.

The influence of the following two factors providing enantioselective separation of dansyl amino acids by CE was examined:¹¹⁷ the difference in the binding constants of enantiomers with the chiral selector (HP- β -CD) and the enantioselective change in pK_a upon complex formation in the pH range $pK_a \pm 2$ resulting in different charges of enantiomer-chiral selector complexes and, consequently, in different effective mobilities of the complexes. Intra- and intermolecular interactions often have a strong effect on acid-base equilibria and lead to changes in pK_a of acidic and basic groups in the molecule. Enantiomers are included into the CD cavity in different fashions to form hydrogen bonds which differ in strength and direction. Enantiomers also differ in the involvement in dipole-dipole interactions, which leads to different changes in pK_a of the amino and carboxy groups for two enantiomers. An enantioselective change in pK_a upon complex formation can lead to a difference in pK_a for two enantiomers up to 0.4 (for the carboxy group of dansyl tryptophan). In the pH range $pK_a \pm 2$, a change in the concentration of a chiral selector leads to the reversal of the enantiomer migration order. This phenomenon is observed if a more stable enantiomer-chiral selector complex possesses a higher effective mobility and the mobility of the complexes is lower than that of the free enantiomers.

The pH-dependent reversal of the migration order of di- and tripeptide enantiomers with the use of β -CD and its derivatives

was investigated.¹¹⁸ The possibility of this reversal depends on the structure of cyclodextrin, the amino acid composition and amino acid sequence in peptides. Phenylalanine containing the carboxy group at one end of the amino-acid chain is favourable for the reversal of the migration order. It was noted that the pH-dependent reversal of the migration order in the case of di- and tripeptides is observed at $\text{pH} \approx \text{p}K_a$ for carboxy groups.

2. Factors influencing enantiomer separation in capillary electrophoresis

The efficiency of enantiomer separation by CE is influenced by the following factors: the type and concentration of a chiral selector, pH and the composition of SE, organic and inorganic agents modifying SE and the capillary temperature. The effects of all the above-mentioned factors are briefly discussed below.

a. Type and concentration of a chiral selector

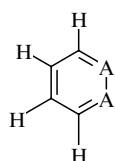
α -, β - and γ -Cyclodextrins contain different numbers of glucose residues and, consequently, their cavities differ in the inner diameter. Since the mechanism of enantiomer separation is based on the possibility of inclusion of a substrate into the CD cavity, both the sizes and shapes of the guest and host molecules are of great importance in chiral separation. These effects were examined in the studies.^{119–129} The importance of the choice of the type of CD as a chiral agent was demonstrated in different CE methods (capillary gel electrophoresis, isotachopheresis, capillary zone electrophoresis).^{119–121}

Various methylated β -CD as applied to the enantiomer separation of dansyl derivatives of amino acids were examined.¹³⁰ Methylation of CD at position 6 has no effect on the stereoselectivity of separation compared to the starting (native) CD, whereas the modification of position 2 renders chiral separation impossible. These data are indicative of the key role of the hydroxy groups of CD in the chiral recognition of dansyl amino acids. The importance of the type of CD in the chiral separation of several herbicides using selectively modified α -, β - and γ -CD was demonstrated in the study.¹³¹

The influence of the concentration of new positively charged CD, *viz.*, heptakis(6-deoxy-6-methoxyethylamino)- β -CD, on separation of enantiomers of profens and herbicides (chlorophenoxypropionic acids) was studied.¹³² The order of the decrease in the degree of complex formation of profen enantiomers with a chiral selector was revealed (from the difference in the migration times in the presence and absence of the selector). It was noted that the peak resolution decreases in the reverse order independently of the concentration of the CD derivative. The best resolution of enantiomer peaks was achieved for indoprofen and fenoprofen (R_s are 11 and 14, respectively). For chlorophenoxypropionic acids, the formation of more stable complexes with the chiral selector improves the peak resolution. A mixture of enantiomers of six different herbicides was successfully separated.

Various cyclodextrins were extensively investigated.^{133–136} For example, racemates of 42 of 86 drugs under study were separated with the use of HP- β -CD.

The review¹³⁷ surveyed data on the study of enantiomer separation using TM- β -CD. Of 86 pharmaceuticals, 47 compounds were successfully separated. The influence of the structures of the compounds analysed and chiral selectors (TM- α -CD, TM- β -CD, TM- γ -CD) on enantiomer separation was examined. Based on abundant data, it was found that the so-called 'substructure 4H',



where $A = C, N, \text{etc.}$, influences substantially the electrophoretic separation. Compounds containing this substructure not only

have high affinity for cyclodextrins but also can be separated with a high probability into enantiomers using the above-mentioned chiral selectors.

Interesting results were obtained with the use of various CD¹²³ (α -, β -, γ -, DM- α -, DM- β -, TM- α -, TM- β -CD) for separation of enantiomers of dansyl amino acids.

The advantage of charged CD in the chiral separation was demonstrated in the study¹²² devoted to separation of enantiomers of dansyl amino acids on charged mono-(6-amino-6-deoxy)- β -CD.

Sulfobutyl ether of β -CD (SBE- β -CD) is an important chiral selector, which finds wide application in CE. The advantages of this CD derivative for separation of a large number of racemates of chiral compounds were demonstrated in many investigations.^{138–146} It should be noted that peaks observed in capillary electrophoresis with the use of charged CD are often smeared, particularly at low pH in analysis of basic compounds.¹⁴⁷ A mixture of sulfated cyclodextrins, which differ in the degree of substitution, was used¹⁴⁸ for separation of enantiomers of 56 drugs.

The separation of dansyl amino acids with the use of new CD derivatives, *viz.*, 6-deoxy-6-*N*-histamino- β -CD and 6-deoxy-6-[4-(2-aminoethyl)imidazolyl]- β -CD, was investigated.¹⁴⁹ The former chiral selector is a monosubstituted positively charged β -CD in which the histamine moiety is bound to the C(6) atom of the monosaccharide fragment of the CD ring through the amino group. In the latter chiral selector, the histamine moiety is bound to the C(6) atom through the imidazolyl group. The number of positive charges in the molecules of these chiral selectors can be varied depending on pH, because the amino and imidazolyl groups have different $\text{p}K_a$. The best separation of dansyl amino acids was achieved with the use of the latter chiral selector. The same CD derivatives were used in the separation of enantiomers of α -hydroxy and carboxylic acids.¹⁵⁰ Separation with the use of the former chiral selector was attained at a concentration of 1 mmol litre⁻¹, whereas separation with the use of the latter chiral selector did not occur, which indicates that a short distance between the positive charge and the CD cavity is of importance for chiral separation.

New CD derivatives were proposed^{151–153} for separation of enantiomers of neutral and charged compounds. Heptakis(2,3-dimethyl-6-sulfo)- β -CD forms less stable complexes with the compounds analysed compared to two other derivatives, *viz.*, heptakis(2,3-di-*O*-acetyl-6-sulfo)- β -CD (HDAS- β -CD) and heptakis(6-sulfo)- β -CD, and exhibits the highest stereoselectivity of these three derivatives. An increase in the concentration of the chiral selector leads to a change in the elution order of enantiomers of neutral compounds. Enantiomers of weak bases and acids were separated at pH lower and higher than 7, respectively.¹⁵¹

Cyanoethylated β -CD was proposed for separation of basic and acidic racemic compounds.¹⁵⁴ The advantage of this chiral selector is that its solubility in water and organic solvents is relatively high.

Mono(6-glutamylamino-6-deoxy)- β -CD is a zwitterionic CD suited to the separation of uncharged compounds.¹⁵⁵ The charge of the chiral selector can be varied by changing the pH of SE: the chiral selector is positively charged at pH 2.3 and negatively charged at pH 10.3–11.2.

Enantiomers of herbicides, dansyl amino acids and profens were separated on heptakis(6-hydroxyethylamino-6-deoxy)- β -CD.¹⁵⁶ The stereoselectivity of enantiomer separation depends on the pH of SE. Chiral separations were obtained in the pH range 4–7.

Soluble polymers, which were prepared by the reactions of β -CD or carboxymethyl- β -CD with epichlorohydrin, were successfully used in chiral CE.^{157–161}

The concentration of CD in the supporting electrolyte is of primary importance in CE. Chiral separations very often do not take place, although the addition of CD causes a decrease in effective mobilities of enantiomers. One of the reasons is an

improper choice of the CD concentration. The existence of the optimum CD concentration (Eqn 2), at which the maximum enantiomer separation would be expected, was theoretically described in the study.¹¹⁶ In some cases, the maximum peak resolution is not attained (R_s increases as the concentration of CD is increased), because the optimum concentration of cyclodextrin cannot be achieved due to its low solubility in water.

Based on the data published in the literature, it can be concluded that the β -CD cavity (unlike the α - and γ -CD cavities) is most suitable for the chiral separation of a large number of compounds, particularly those involved in modern drugs. Most commercially available cyclodextrin derivatives were synthesised based on β -CD. As mentioned above, modified cyclodextrins differ substantially in their properties from native β -CD (they are readily soluble, can form secondary bonds and their cavities have different hydrophobicities), which can be used for improving the selectivity of enantiomer separation. The experimental difficulties in using charged cyclodextrins are associated with the fact that most commercially available selectors are complex mixtures containing a large number of isomers. A change in the concentration of charged cyclodextrins in SE leads to substantial changes in the ionic strength. In the presence of cyclodextrins, it is difficult to determine the precise rate of electroosmotic flow (EOF).

Charged β -CD derivatives find application in separations of enantiomers of neutral and charged compounds. In the case of the latter, the use of charged chiral selectors leads to larger R_s compared to neutral selectors. As mentioned above, the migration of a chiral selector in a direction opposite to the direction of migration of the compounds analysed facilitates enantiomer separation, because it increases the difference in the electrophoretic mobilities of the free enantiomer and the enantiomer involved in a complex.¹¹⁶

b. Concentration and pH of a supporting electrolyte

The choice of an appropriate supporting electrolyte (the type and concentration of a buffer solution, ionic strength, pH) is of great importance for achieving the optimum experimental conditions for enantiomer separation. The electroosmotic flow can be controlled and the ionic state of both the compounds separated and a chiral selector can be changed by varying the pH. The influence of the pH of a supporting electrolyte on the enantioselectivity was examined in virtually all the above-mentioned studies. The ionic strength influences both EOF and migration times of the compounds separated. Electromigration dispersion can be decreased by increasing the ionic strength of the buffer, which is, however, accompanied by an increase in the current in the system. The effect of the ionic strength on separation of enantiomers of warfarin was studied;¹⁶² *N*-tris(hydroxymethyl)methyl-3-aminopropanesulfonate containing CD as a chiral additive was used as the buffer; the ionic strength was increased by adding sodium chloride. An increase in the ionic strength of the buffer led to a decrease in the rate of EOF, an increase in the migration time and an improvement of peak resolution of warfarin enantiomers. In the study,¹⁶³ the optimum separation of isoproterenol enantiomers was achieved at relatively high SE concentrations (250 mM sodium acetate) with maximum efficiency, selectivity and peak resolution.

c. Capillary temperature

The capillary temperature is a very important parameter, which is necessary to control in chiral analyses by electromigration methods. The temperature influences the mobility of the compounds analysed, the kinetics and thermodynamics of complex formation with cyclodextrins, etc. The influence of the capillary temperature on the chiral separation was examined in the studies.^{164–171} It was found that the migration time and the peak resolution decrease as the temperature increases. In some cases, a reverse dependence was observed.^{172, 173}

d. Organic and inorganic modifying agents of supporting electrolytes

The addition of achiral compounds to SE changes the electroosmotic flow, viscosity, solubility of the compounds analysed and/or the chiral selector with a resulting change in electrophoretic mobilities giving rise to enantiomer separation. Enantiomers of *threo*-chloramphenicol and ketotifen were separated using heptakis(2,6-di-*O*-methyl)- β -CD with the addition of hydrophilic cellulose derivatives to SE.¹⁷⁴ In the cited study, an improvement of separation was attributed to a decrease in both EOF and adsorption of the compounds analysed on capillary walls. An analogous effect was observed in the study of the influence of polyvinyl alcohol on the chiral separation of several tocainides.¹⁷⁵ The introduction of short-chain alkyl ammonium cations into SE has a strong effect on the chiral separation of some pharmaceuticals. Separations of enantiomers of 22 drugs using β -CD, DM- β -CD, TM- β -CD, HP- β -CD with additives of tetramethyl- or tetrabutylammonium bromide were investigated.¹⁷⁶ The use of ammonium salts causes the reversal of EOF, an increase in the migration time and improvement of resolution of enantiomer peaks. The separation of enantiomers of several anaesthetics was also improved with the use of the tetrapropyl- and tetrabutylammonium cations in DM- β -CD-containing SE.¹⁷⁷ The influence of small organic cations on the chiral separation of compounds possessing basic properties was examined in the study.¹⁷⁸ Optical isomers of alprenolol, amphetamine, anisodamine, isoprenaline, pinacidil, synephrine and verapamil were separated with the use of HP- β -CD in the presence of tris(hydroxymethyl)methylamine (Tris), diethanolamine, triethanolamine, diethylamine or triethylamine. Of the additives used, triethanolamine proved to be most efficient for improving the selectivity.

Enantiomers of nonpolar primary amines are difficult to separate by CE with the use of only CD. To perform or improve the chiral separation of amines, DM- β -CD, hydroxyethyl- β -CD (HE- β -CD) and γ -CD in combination with 18-crown-6 were used.¹⁷⁹ The compounds analysed form inclusion complexes both with the chiral selector, which recognises amine enantiomers, and 18-crown-6. The mechanism of enantiomer separation with the use of CD and 18-crown-6 was elucidated in the study.¹⁸⁰ Compounds containing the amino group were separated on β -CD or its derivatives in the presence of an achiral crown ether (30 mmol litre⁻¹). A combination of a chiral selector (β -CD or succinyl- β -CD) and an achiral complex-forming agent (a borate buffer) made it possible to separate enantiomers of phenylethane-1,2-diol, 3-benzoyloxypropane-1,2-diol, hydroxybenzoin and 3-(*N*-benzyl-*N*-methylamino)propane-1,2-diol.¹⁸¹ The borate anion serves as a complex-forming agent for vicinal diols. The cationic ion-pair reagent quinine has a strong effect on separation of enantiomers of acidic and basic compounds on cyclodextrins.¹⁸²

The introduction of organic modifying agents into SE can change parameters, such as the binding constants of the chiral selector and enantiomers, the rate of EOF, conductivity of SE, solubility of the chiral selector and/or compounds analysed with a resulting change in the time required for analysis. The introduction of organic modifying agents into SE can either improve or impair the enantiomer separation. Chiral separations of several amino acids were performed in a capillary filled with polyacrylamide gel with the addition of 10% of methanol to CD-containing SE.¹¹⁹ Propranolol was separated into enantiomers only in the presence of methanol (10%–30%) in SE (phosphate buffer–urea– β -CD).¹⁸³ An improvement of chiral separation upon the addition of methanol was observed for mandelic acid,¹⁷⁰ warfarin¹⁶² and imidazole derivatives.¹⁸⁴ The influence of the organic modifying agents on the chiral separation was theoretically examined in the study.¹⁸⁵ In some cases, the addition of this agent impairs the chiral separation because the binding constants and the difference between the effective mobilities of enantiomers decrease when the optimum CD concentration is attained. Examples are separations of clenbuterol,¹⁸⁶ denopamine and trimetoprim,¹⁸⁷ deprenyl,¹⁸⁸ dioxypromethazine,¹⁸⁹ verapamil and

propafenone,¹⁹⁰ dansyl derivatives of phenylalanine, leucine and propranolol with the use of β -CD and in the presence of additives of alcohols containing from one to six carbon atoms in SE.¹⁹¹

3. Methods for optimisation of separation using cyclodextrins

The use of a large number of commercially available cyclodextrins in CE makes it difficult to formulate general rules for choosing conditions of enantiomer separation. The present knowledge of the processes of enantiomer separation does not allow one to choose *a priori* the best chiral selector for a particular racemate. The charged resolving agent migration (CHARM) model proposed by Williams and Vigh¹⁹² can be used for a rational choice of conditions for separation. This model enables one to estimate rapidly the ability of various charged cyclodextrins to perform chiral separation of any racemate.

Successful enantiomer separation depends on many parameters. Instrumental factors (separation potential, temperature) are rather well and predictably controlled in most modern instruments. The selectivity of separation in CE is determined by the ratio between the effective mobilities of the compounds separated and can be optimised based on the dependence of the effective mobility on the composition of the supporting electrolyte. However, the effect is predictable only for some of the compositional variables of SE (pH, the concentration and charge of the chiral selector used, the effective charge of the enantiomer, the rate of EOF). Such factors as the structure of a chiral selector and the addition of organic or inorganic modifying agents can cause essential but unpredictable changes. The CHARM model is based on the consideration of equilibria between protonation and complex formation of enantiomers with a charged chiral selector (the assumed enantiomer:selector ratio is 1:1) and the influence of these equilibria on the effective charges of enantiomers, their effective mobilities and selectivity of separation. Analytical expressions for calculations of the above-mentioned parameters of compounds of differing nature (non-electrolytes, strong and weak electrolytes) were reported in the study.¹⁹² It was demonstrated that the calculated values depend on the ionic mobilities of enantiomers involved in a complex and the free protonated and non-protonated forms of enantiomers, the protonation constants, the formation constants of enantiomer-selector complexes for protonated and non-protonated forms, pH and the concentration of the selector in SE. The theoretical resolution can be calculated if the binding constants, ionic charges and ion mobilities of different forms of enantiomers are known.

The CHARM model helps one in making a rational choice of the composition of the supporting electrolyte. For selectors which are strong multicharged electrolytes, the separation of neutral and charged analytes is independent of pH in the absence of EOF. For weak electrolytes, R_s is high at low pH for separation of weak acids in a non-dissociated form and for separation of weak bases as ions. At high pH, R_s is high for separation of weak acids as ions and for separation of weak bases in a non-dissociated form. Consequently, in the absence of EOF (*i.e.*, in a capillary with a neutral coating), it is necessary to perform only two series of measurements to find the best conditions for separation: at low pH of the supporting electrolyte (for example, at pH 2.2) and at high pH (for example, pH 9.5). At each pH, the type and concentration of CD are varied to find the maximum R_s . If the optimum chiral selector is known, the rate of EOF can be varied by changing the properties of capillary walls (anionic or cationic coating, uncoated walls) to improve the peak resolution, accelerate separation or change the enantiomer migration order. Finally, to carry out or improve separation, one can try to use organic modifying agents, surfactants or systems consisting of two chiral selectors. However, this does not necessarily improve the results.

Electromigration dispersion caused by the difference in mobilities of the ions of the sample and buffer often leads to broadening of the peaks (frontal peaks or peaks with 'tails'). This phenom-

enon can be reduced by increasing the ionic strength of SE or with the use of a buffer whose conductivity is equal to that of the band of the sample.

4. Micellar electrokinetic chromatography

Micellar electrokinetic chromatography (MEKC) allows one to separate uncharged components of a sample due to the difference in the probability of their presence in an aqueous mobile and pseudostationary phases. Sodium dodecylsulfate (SDS) is the surfactant most generally used in capillary electrophoresis for separation of enantiomers in the presence of cyclodextrins (CD-MEKC method). Micelles of SDS bear a negative charge and, consequently, possess electrophoretic mobility toward the anode. A scheme of electrophoretic separation of uncharged compounds by CD-MEKC with the use of SDS is shown in Fig. 6; the electroosmotic flow is directed toward the cathode. If the contribution of electrophoretic mobility of micelles is smaller than the contribution of electroosmotic mobility, micelles move toward the cathode, *i.e.*, the detector. Uncharged enantiomers form inclusion complexes with CD in an aqueous phase or are included into micelles and move at the rate of the latter. The separation of neutral enantiomers is based on the difference in their distribution between a CD-containing buffer solution and the interior of micelles. Since molecules of a sample interact with a pseudostationary phase, the metrological characteristics of CD-MEKC correspond to the characteristics of chromatography. It should be emphasised that MEKC on CD allows one to separate both uncharged and charged enantiomers if they are included into micelles.

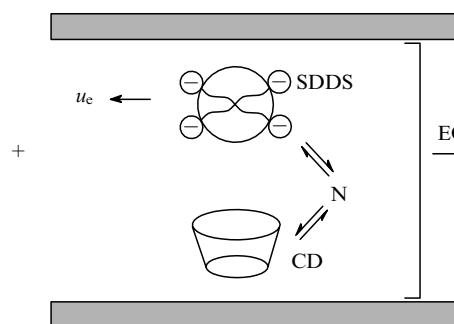


Figure 6. Scheme of electrophoretic separation of an uncharged compound by CD-MEKC;³⁹ u_e is the rate of electrophoretic migration, N is an enantiomer.

In the first study devoted to separation of enantiomers by CD-MEKC,¹⁹³ the influence of the nature of a chiral selector on the chiral separation of thiopental, pentobarbital, phenobarbital and barbital was examined using α -, β -, γ -, DM- β - and TM- β -CD in a buffer containing 50 mM SDS and 4 M urea (pH 9.0) as examples. γ -Cyclodextrin containing a cavity with the largest diameter proved to be the most efficient chiral agent. The addition of other chiral compounds together with CD (for example, with D-camphor-10-sulfonate) improved the chiral separation of the compounds under study.

The MEKC method was employed in chiral separations of various compounds: amino acid derivatives,^{194–197} aromatase and barbiturate inhibitors,¹⁶⁵ β -blockers,¹⁹⁸ triazole derivatives,^{199,200} dihydropyridine derivatives,²⁰¹ cicletanine,²⁰² mephénytoin, phenýtoin and their 4-hydroxy derivatives,²⁰³ peptide derivatives,^{204,205} pesticides,²⁰⁶ *etc.* In CD-MEKC, bile acids belonging to chiral surfactants and their salts are also used for separating enantiomers of dansyl amino acids,^{207–209} baclofen and its analogues, mephénytoin and fenoldopam and their derivatives,²⁰⁷ amino acid derivatives, such as *N*-substituted 1-cyano-benzo[*f*]isoindoles (CBI amino acids),²⁰⁸ OPA amino acids,²¹⁰

phenylethylamines (diclofenac, ephedrine, methamphetamine, β -blockers)²¹¹ and binaphthyl derivatives.²¹² Mixed micellar mixtures of SDDS and taurodeoxycholic acid with β -CD are used to separate CBI-selenomethionine and selenoethionine enantiomers.²¹³ Enantiomers of dansyl amino acids were separated²¹⁴ with the use of an achiral polymeric surfactant (sodium salt of butyl acrylate–butyl methacrylate–methacrylic acid copolymer) in combination with β -CD; the peak resolution obtained in the cited study was better than that attained with the use of the β -CD–SDDS system.

5. Non-aqueous chiral capillary electrophoresis

The review³¹ surveyed data on enantiomer separations by non-aqueous CE. The effects of the concentration and the nature of the chiral selector used, apparent pH, the ionic strength, temperature and the nature of organic solvents on the mobility of enantiomers, selectivity and efficiency of enantiomer separation were discussed.

One of the most important advantages of non-aqueous CE is that it enables one to study compounds insoluble or poorly soluble in water. Solubility of cyclodextrins in many solvents is much higher than that in water. For example, the solubility of β -CD in *N*-methylformamide is higher than 700 mmol litre⁻¹, whereas its solubility in water is 18 mmol litre⁻¹.²¹⁵ Therefore, the chiral separation can be improved at higher cyclodextrin concentrations in organic media.^{215–223} The chiral separation of basic tricyclic drugs was investigated²¹⁶ with the use of β -CD, M- β -CD, HP- β -CD and γ -CD in formamide, *N*-methylformamide and *N,N*-dimethylformamide. In this case, the character of interactions between enantiomers and the chiral selector changes. It is assumed that hydrophobic interactions between enantiomers and the chiral selector are virtually absent and the formation of inclusion complexes proceeds to a very low extent. Apparently, the planes of the compounds separated lie on the cyclodextrin ‘cone’, and the compounds interact with the hydroxy groups of CD. This assumption is consistent with the binding constants of trimipramine, mianserin and thioridazine, which decrease from $\sim 10^4$ in water to $\sim 10^{-2}$ in *N,N*-dimethylformamide. The formation of inclusion complexes proceeds more readily in a polar solvent, for example, in formamide, than in less polar *N*-methylformamide because the difference in polarity of the solvent and the CD cavity is larger in the former case. The best results of chiral separations of tricyclic compounds were obtained with the use of β -CD and its derivatives, but not with γ -CD, although the diameter of the cavity in the latter is larger and is closer to the size of the molecules separated.

The drawback of the above-mentioned solvents is their intense absorption at 214 nm and at lower field. Ultraviolet-transparent supporting electrolytes can be prepared from methanol or mixtures based on this solvent. Enantiomers of 40 basic compounds in the H₃PO₄–NaOH–CH₃OH supporting electrolyte were separated with the use of heptakis(2,3-dimethyl-6-sulfo)- β -CD.²²⁴ The dependences of the effective mobilities, selectivity coefficients and peak resolution on the concentration of a chiral selector were studied in the range of 0–40 mmol litre⁻¹ and it was found that these dependences obey the theoretical predictions of the CHARM model with the use of a charged chiral selector.¹⁹²

6. Electrochromatography

Capillary electrochromatography (CEC) is a modern method which combines the advantages of HPLC and CE. Chiral CEC employs the principles of molecular recognition of enantiomers by a chiral stationary phase (CSP) and the electric field as the driving force for the transfer of enantiomers. The main advantage of CEC over HPLC is a higher column performance, which is a result of a planar plug-like profile of the mobile phase flow.

The main principles of chiral CEC were discussed in the review.²²⁵ The transfer of enantiomers through a capillary column occurs primarily due to EOF caused by the electric double layer in the vicinity of the charged surface of a stationary phase. The linear

rate of osmotic flow u_{eo} is proportional to the ζ potential, which characterises the electric double layer and depends also on the properties of a mobile phase (dielectric permeability ϵ , viscosity η , ionic strength) and the electric field strength E . In addition to the transfer caused by EOF, charged compounds have inherent electrophoretic migration in a direction determined by the ion charge. The linear migration rate of compounds can be increased by applying pressure to a column. The apparent linear migration rate of a compound u_{app} is the sum of the linear rate of EOF u_{eo} , the rate of electrophoretic migration u_{ep} and an increase in the rate due to the applied pressure u_{press} :

$$u_{app} = u_{eo} + u_{ep} + u_{press} \quad (3)$$

The chiral separation is always based on enantioselective molecular interactions between the compound and CSP or pseudo-SP (chiral additives), whereas the electrophoretic migration makes a contribution only to the total transfer of compounds, because enantiomers possess identical electrophoretic mobilities. The elution time t_e depends on the column length L , the chromatographic retention factor k and the linear migration rate of the compound u_{app} .²²⁶

$$t_e = \frac{L(1+k)}{u_{app}} \quad (4)$$

Two varying approaches are used for the direct separation of enantiomers in CEC: a chiral selector can be added to a mobile phase or immobilised on a solid support or a capillary wall (CSP).

Commercial reversed-phase achiral columns are generally used for the enantiomer separation in the presence of chiral additives in a mobile phase. In this version of CEC, the mechanism of separation is rather complex because it includes electrophoretic (for charged enantiomers) and chromatographic components. The enantioselectivity of separation is achieved due to the difference in the formation constants of enantiomer–chiral selector complexes, the difference in effective mobilities of the free enantiomer and the enantiomer involved in a complex and separation of diastereomeric complexes on SP.²²⁶ If EOF and electrophoretic migration of charged compounds occur in different directions, the elution order of enantiomers can be reversed by changing the mobile phase (this effect is well known in CE).¹¹⁷ It should be noted that α -, β -, γ -CD and their derivatives are most commonly used as additives to a mobile phase. Chlorthalidone enantiomers were separated on a column packed with octadecyl silica gel (ODS) (3 μ m) with HP- β -CD as a chiral selector.²²⁷ Enantiomers of phenylephrine and synephrine were separated on a silica gel column using HP- β -CD as a chiral selector.²²⁸ In the study,²²⁶ salsolinol enantiomers were separated by CEC on a column based on ODS in the presence of β -CD as a chiral additive and sodium heptanesulfonate as an achiral ion-pair reagent. The mechanism of separation in CEC in the presence of an additive of a chiral selector in MP was discussed in detail, and a theoretical model of enantioselectivity in such systems applicable to both neutral and charged compounds was proposed. Capillary electrochromatography with the use of a chiral selector in a mobile phase has no advantages over enantioselective CE.

A chiral stationary phase holds the most promise for separating enantiomers by CEC. There are three different approaches to CSP-based capillary columns.²²⁹

1. Open tubular columns, whose walls are chemically or physically modified with a chiral selector. Tubular columns with an inner diameter of ~ 50 μ m, which is optimum simultaneously for high column performance and UV detection (standard detection in most apparatus for CE) are required for enantiomer separation. The electroosmotic flow is created by residual silanol groups on a silica gel surface (for neutral chiral selectors). The only drawback of this approach is a small surface area accessible for the modification with a chiral selector. As a consequence, columns can be easily overloaded, which is manifested in peak

asymmetry and deterioration of the efficiency. The efficiency of separation is influenced by the thickness of the SP layer. Larger theoretical plate (t.p.) numbers are obtained on thinner films.

Enantiomer separation on an open tubular column using a 0.2- μm thick film of polydimethylsiloxane with permethylated β -CD (16%) (Chirasil-Dex) covalently grafted through the octamethylene spacer was first carried out for 1-phenylethanol and other compounds.²³⁰ In another study,²³¹ a capillary modified with permethylated γ -CD (Chirasil- γ -Dex) was used for the chiral separation of ibuprofen, flurbiprofen, cicloprofen and 1-phenylethanol. The effects of the pH of the buffer, the applied stress and the thickness of the SP layer were studied. An increase in the film thickness from 0.2 to 0.4 and 0.8 μm led to a substantial loss of efficiency: from 30 500 (300 000 t.p. m^{-1}) to 24 000 and 9500 t.p. per column, the selectivity of separation remaining virtually unchanged (1.17, 1.19 and 1.12, respectively). Enantiomer separations with the use of Chirasil-Dex films in open tubular columns were discussed in the review.²³²

2. Packed columns with CSP using standard chromatographic supports (silica gel or polymers) chemically modified with a chiral selector. For such chiral stationary phases, quartz capillaries with an inner diameter of 75 or 100 μm are used. Columns of this type are analogous to standard chromatographic columns but allow one to obtain a larger theoretical plate number. For CSP, smaller particles and/or longer columns can be used, because there are no such strong limitations on the pressure in CEC compared to HPLC. It should be noted that external pressure applied to a capillary can decrease the time of analysis but simultaneously leads to distortion of the planar profile of the flow typical of electromigration systems to give a parabolic profile of the flow resulting in a decrease in the column performance. As mentioned above, enantiomer separation can be performed using normal-phase, reversed-phase and 'polar organic' modes of HPLC. The latter two modes are predominantly used for CEC; the conditions of separations by HPLC can often be directly extended to CEC without loss of enantioselectivity. The mechanism of separation of enantiomers by CEC is identical to that by HPLC and was discussed above. The strength of interactions between an enantiomer and a chiral selector can be controlled by varying the composition of a mobile phase. This is more difficult to perform in CEC than in HPLC, because control over the retention and/or selectivity of separation in CEC always influences the rate of EOF and, in the case of charged compounds, the electrophoretic migration. In most cases, mobile phases include acetonitrile-based mixtures, which produce large EOF, and buffers with a low ionic strength. Acetonitrile as an organic modifying agent is best suited to attain a high rate of EOF and is, generally, preferred over methanol. A high rate and stability of EOF are important conditions in CEC. The ζ potential of the operating conditions as well as the rate and direction of electroosmotic flow are determined by the properties of mobile and chiral stationary phases. The choice of the corresponding support for the preparation of CSP is of more importance in CEC than in HPLC. Silica gels can differ substantially in the number of silanol groups resulting in differences in the rate of EOF for CSP prepared based on these silica gels. Examples of the use of this type of column are given below. Enantiomers of benzoin, hexobarbital, dansyl and 3,5-DNP amino acids were separated on capillary columns packed with CSP containing β -CD (5 μm , Cyclobond I).²³³ The use of a solution of triethylammonium acetate instead of a phosphate buffer led to the reversal of EOF and improved the separation of acidic compounds. This reversal of EOF observed for mobile phases containing small amounts of methanol (no more than 15%) cannot be attributed to adsorption of the triethylammonium ions on the SP surface and the formation of a dynamic anion exchanger. Chlorthalidone and mianserin enantiomers on CSP based on HP- β -CD (5- μm commercial column Cyclobond I 2000 RSP) were separated in the study.²²⁷ In the investigation,²³⁴ CSP

based on permethylated β -CD (pore size was 300 Å, 5 μm) was used for the enantiomer separation of several barbiturates, benzoin, glutethimide, methylthiohydantoin proline and methyl mandelate (the efficiency varied from 20 000 to 40 000 t.p. m^{-1}). A comparison of the separation of mephobarbital enantiomers by micro-HPLC and CEC on this capillary column demonstrated that the use of CEC led to a threefold increase in the efficiency of separation and improved the peak resolution from 2.08 to 3.39 without loss of enantioselectivity. Separations of enantiomers of the same compounds and esters of aryloxy-carboxylic acids performed on permethylated β -CD covalently bound through a spacer (octamethylene) to polydimethylsiloxane on silica gel (pore size was 300 Å, Chirasil-Dex) led to a further improvement of the column performance to 70 000 t.p. m^{-1} .²³⁵ The hydrophobic microenvironment and protection of polar silanol groups with a polysiloxane film improve the enantioselectivity. For example, 1-(2-naphthyl)ethanol was separated only on Chirasil-Dex rather than on covalently grafted permethylated β -CD as a chiral stationary phase.

3. Specially designed monolithic CSP prepared by *in situ* polymerisation in a capillary; such CSP have chiral selectors or chiral cavities introduced into a continuous polymeric matrix. Positively and negatively charged polyacrylamide gels (which give cathodic and anodic EOF, respectively) physically or chemically modified with β -cyclodextrin were prepared in capillaries, which already contained methacrylate groups.^{236–238} The advantage of these monolithic CSP is that there is no need to introduce an organic modifying agent, which can decrease enantioselectivity, into a mobile phase with the aim of performing enantiomer separation. Separations of terbutaline, propranolol and benzoin enantiomers were carried out using negatively charged gel.^{236, 237} Dansyl amino acids and some other acidic compounds were separated on positively charged polyacrylamide gel with covalently grafted allylcarbamoyle- β -CD.²³⁸ The column performance was as high as 150 000 t.p. m^{-1} .

7. Practical application of enantiomer separation

Data on enantiomer separations by CE with the use of cyclodextrins as chiral selectors were generalised in the reviews.^{29, 39, 239–244} Examples of chiral separations carried out in 2000–2002 (which were grouped according to the type of CD) are given in Table 5.

In spite of abundant data on the application of cyclodextrins in chiral separations by CE, studies devoted to quantification of enantiomers in real samples are few in number. Enantiomers in real samples are quantified in pharmaceuticals, medicine, biology and investigations of environmental objects. It should be emphasised that when performing stereoselective analyses of drugs, it is necessary to quantify an undesirable enantiomer at a concentration lower than 1%. The precise determination of the enantiomer ratio of 99.9:0.1 is often a more complicated problem than the 'simple' separation of racemates. Examples of quantification of enantiomers in real samples were given in the reviews.^{29, 39} The results obtained in 2000–2002 are presented in Table 6.

The principles and most important aspects of chiral analysis of pharmaceuticals were discussed and the data on quantification of enantiomers of drugs and their metabolites in biological liquids were surveyed in the reviews.^{245, 246} These reviews also gave examples of the practical application of the determination of enantiomers for an explanation of the possible mechanisms of pharmacokinetics and stereoselectivity of drug metabolism.

The review²⁴⁷ was devoted to chiral separations of amino acids and peptides. A large number of examples which illustrate the state-of-the-art separation of enantiomers and diastereoisomers of amino acids and peptides were offered. Ways of improving the selectivity and methods for optimisation of the parameters of chiral separation using the mathematical design of experiments were discussed.

Table 5. Examples of enantioselective separations by CE using various types of cyclodextrins.

Compound	CD	Supporting electrolyte, method of detection ^a	Ref.
Aromatic derivatives of aminophosphorous and aminohypophosphorous acids	α -CD	100 mM phosphate buffer, pH 7.5, and 40 mM CS ^b	248
5,11-Dihydro-11-[2-[2-[(<i>N,N</i> -dipropylaminomethyl)-piperidin-1-yl]ethylamino]carbonyl]-6 <i>H</i> -pyrido[2,3- <i>b</i>][1,4]benzodiazepin-6-one	sulfo- α -CD	25 mM triethylammonium phosphate, pH 2.5 and 5% CS	249
Lobeline, benzhexol	β -CD	50 mM Tris – phosphoric acid, pH 2.5 and 14% of a mixture: β -CD, P ₂ O ₅ , L-glutamic acid	250
Brompheniramine	β -CD	100 mM phosphoric acid – triethanolamine, pH 3.0 and 18 mg ml ⁻¹ CS	251
OPA amino acids	β -CD	40 mM borate buffer, pH 9.0, 60 mM sodium taurocholate, 15% propan-2-ol and 30 mM β -CD	210
Promethazine	β -CD	30 mM Na ₂ HPO ₄ , 15 mM citric acid, pH 2.5 and 1 mM CS; amperometric detection	252
Ibuprofen	β -CD	200 mM MES, ^c pH 4.4, 0.3% hydroxyethylcellulose and 15 mM CS	253
Thioureas (products of the reaction of fluorescein-5-isothiocyanate with amino acids)	β -CD	80 mM borate buffer, pH 9.3, 30 mM sodium taurocholate and 20 mM β -CD; FD ^d	254
Dextromoramide	HP- β -CD	100 mM phosphoric acid – triethanolamine, pH 3.0 and 15 mM CS	255
2-(4,5-Dihydro-1 <i>H</i> -imidazol-2-yl)-5-fluoro-2-methoxybenzo[1,4]dioxane	HP- β -CD	50 mM ammonium formate, pH 4 and 10 mM CS; CE-MS ^e	256
Cizolirtine and its dehydration products	HP- β -CD	50 mM borate buffer, pH 9.2, 150 mM SDDS, 5% n-butanol and 60 mM CS	257
3,4-Methylenedioxyamphetamine and two of its metabolites	HP- β -CD	50 mM phosphoric acid, pH 2.5 and 50 mM CS	258
Bis(phenethyl)amines, their cyclic analogues	HDAS- β -CD	50, 100 mM phosphate buffer, pH 3.0, 6.0, 7.5 and 0.5–9 mM CS	259
Synthetic analogue of wasp poison	HDM- β -CD ^f	50 mM 6-aminocaproic acid, pH 4.0 and 30 mM CS	260
1-(1-Naphthyl)ethylamine, 1-aminoindan, 1,2,3,4-tetrahydro-1-naphthylamine	HDM- β -CD ^f	200 mM Tris – 300 mM borate buffer, pH 7.0, 10 mM 18-crown-6 and 10 mM CS	261
Mianserin, cyclopentolate, fluoxetine, nisoxetine, verapamil, aminoglutethimide, dimethindene, doxapram, hydroxyzine, meclozine, ketoprofen	HDMC- β -CD ^g	50 mM phosphate buffer, pH 7.0 and 18–72 mM CS	262
[5-(4-Hydroxybutyl)-5'-methyl-2,2'-bipyridyl]-bis(2,2'-bipyridyl)Ru(II) bis(hexafluoroantimonate)	CM- β -CD	40 mM borate buffer, pH 9.5 and 7.5 mg ml ⁻¹ CS	263
4-(3-Isobutylamino-2-hydroxypropoxy)-3-alkoxymethylacetophenone derivatives	CM- β -CD	80 mM Tris-acetate buffer, pH 4.7 and 10 mM CS	264
Chlorpheniramine, methadone	CM- β -CD	100 mM phosphoric acid – triethanolamine, pH 4.0; 3.5 and 5 mM CS	265
Adrenaline, noradrenaline (1), ephedrine, pseudoephedrine (2)	CM- β -CD	(1) 20 mM phosphate buffer, pH 2.5, 12 mM 18-crown-6 and 5.2 mg ml ⁻¹ CS; (2) 100 mM NaOH, pH 12.9 and 16; 3.9 mg ml ⁻¹ CS; amperometric detection	266
Selenomethionine, selenocysteine, selenoethionine	sulfo- β -CD	35 mM citrate buffer, pH 7 and 1% CS	267
Fungicides	sulfo- β -CD	phosphate buffer, pH 3.0 or phosphate buffer, 2 M urea, pH 3.0 and 2% CS	268
Ormeloxifene and its derivatives	sulfo- β -CD	10 mM NaH ₂ PO ₄ , pH 3.0 and 2% CS	269
Spiro(2 <i>H</i> -benzofuro[2,3- <i>a</i>]quinolizine-2,4'-(1' <i>H</i>)-pyrimidine)-2'-(3' <i>H</i>)-one derivative, <i>cis</i> -aminoindanol	sulfo- β -CD	25 mM Na ₃ PO ₄ , pH 2.5 and 1.5% CS, PVA-coated capillary; 25 mM Na ₃ PO ₄ , pH 6.5 and 0.3% CS	270
Clenbuterol, salbutamol, tulobuterol	sulfo- β -CD	50 mM phosphate buffer, pH 2.24 and 25% CS	271
Nicardipine	sulfo- β -CD	20 mM triethanolammonium phosphate, pH 3 and 5% CS	272

Table 5 (continued).

Compound	CD	Supporting electrolyte, method of detection ^a	Ref.
Voriconazole	SBE- β -CD	50 mM NaH ₂ PO ₄ , pH 7.0 and 1 mM CS	273
Flobufen	HTM- β -CD	87.5 mM acetate buffer, pH 5.5, 10% methanol and 30 mM CS	274
Dimethindene	HTM- β -CD	100 mM phosphoric acid – triethanolamine, pH = 3.0 and 150 mg ml ⁻¹ CS	275
Naproxen	HTM- β -CD	25 mM H ₃ PO ₄ – 25 mM CH ₃ COOH – 25 mM H ₃ BO ₃ – NaOH, pH 5.0 and 3 mM CS, polyacrylamide-coated capillary	276
Propranolol, mexiletine, lobeline, propafenone, isoprenaline, bupivacaine, verapamil, ketamine	MPC- β -CD ^h	40 mM borate buffer, pH 9.18 and 2.5 mM CS	190
Methyl 4-(3,4-difluorophenyl)-6-methoxymethyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate, hydrolysis products	QA- β -CD ⁱ	25 mM Tris-acetate buffer, pH 8.3 and 2.5% CS	277
2-(2,4-Dichlorophenoxy)-, 2-(4-chloro-2-methylphenoxy)propionic acids	EC- β -CD ^j	45 mM NaH ₂ PO ₄ , pH 5 and 12 mM CS	278
Di- and tripeptides	β -CD, PM- β -CD, HDM- β -CD, HTM- β -CD, HP- β -CD	50 mM phosphate buffer, pH 2.5 – 3.5 and 20 mg ml ⁻¹ CS	118
3-(3,4-Dihydroxyphenyl)alanine, 3-(3,4-dihydroxyphenyl)-2-hydrazino-2-methylpropionic acid	HDAS- β -CD, CM- β -CD	20 mM phosphate buffer, pH 2.5 and 20 mM CS	279
1,3,4-Thio-, 1,3,4-selenodiazine derivatives	HE- β -CD, HP- β -CD, M- β -CD	25 mM CH ₃ COONH ₄ – 1 M CH ₃ COOH or 25 mM citric acid – 12 mM Tris in methanol, formamide or a formamide : acetonitrile mixture (1 : 2) and 200 mM CS	280
Alkyl esters of amino acids, BOC and Z amino acids	HP- β -CD, CM- β -CD, SBE- β -CD	100 mM phosphoric acid – triethanolamine, pH 2.5; 4.0; 5.5; 0% – 30% methanol and 5 – 30 mM CS	281
Propranolol, hydrobenzoin, atenolol, nefopam, chlorcyclizine, 1,1'-binaphthyl-2,2'-diyl phosphate, trimipramine, primaxin, canadine, piperoxan	sulfo- β -CD, phosphated β -CD	50 mM phosphate buffer, pH 5.0 and 2% CS	282
Synthetic arginine-containing peptide and its derivatives	SBE- β -CD + β -CD	50 mM citrate buffer, pH 2.5 and 20 mM CS ₁ + 5 mM CS ₂ , PVA-coated capillary	283
Sertraline	sulfo- β -CD + HP- β -CD	20 mM borate buffer, pH 9.0, 50 mM sodium cholate, 15 mM CS ₁ + 5 mM CS ₂	284
Fenoprofen, flurbiprofen, ibuprofen, ketoprofen	sulfo- β -CD + HTM- β -CD	100 mM phosphoric acid – triethanolamine, pH 2.5 and 2 – 3 mM CS ₁ + 10 – 20 mM CS ₂	285
Aminogluthethimide	α -CD + HDM- β -CD; α -CD + HTM- β -CD	100 mM phosphate buffer, pH 2.5 and 10% – 95% CS ₁ + 90% – 5% CS ₂ , total concentration of CD was 15 mM	286
DNP derivatives of aspartic acid, alanine, glutamine, homoserine, proline, norvaline and glutamic acid	copolymer of allylamine and '2-hydroxy-3-methacryloyl- β -CD'	50 mM acetate buffer, pH 4.0 and 4 – 20 mM CS	287
2-Phenoxy-, 2-(4-chlorophenoxy)-, 2-(3-chlorophenoxy)propionic acids	trehalose cysteine-HSD ^k	22 mM Na ₃ PO ₄ , pH 6.0 and 2.5 mM CS	288
	trehalose cysteine-HSD, trehalose ammonium-HSD, trehalose β -alanine-amide-HSD	22 mM phosphate buffer, pH 6.0 and 1.50 – 5.00 mM CS; 22 mM borate buffer, pH 9.5 and 5.00 mM CS	289
Reaction product of homocysteine with 4-aminosulfonyl-7-fluoro-2,1,3-benzoxadiazole	γ -CD	50 mM Na ₃ PO ₄ , pH 2.25 and 50 mM CS	290
1-Methyl-3-phenylpropylamine, 1,2,3,4-tetrahydro-1-naphthylamine	γ -CD	50 mM phosphate buffer, pH 2.0, 10 mM 18-crown-6 and 40 mM CS	291

Table 5 (continued).

Compound	CD	Supporting electrolyte, method of detection ^a	Ref.
Thioureas (reaction products of isothiocyanates with amino acids)	γ -CD	100 mM borate buffer, pH 9.4, 30 mM SDDS and 10 mM CS; FD	292
1-Aminoindan, β -blockers, bupivacaine, bupropion, chlophedianol, 4-chloroamphetamine, chlorpheniramine, epinephrine, isoproterenol, ketamine, metaproterenol, methoxyphenamine, 1-(1-naphthyl)ethylamine, oxyphenyclimine, phenylpropanolamine, piperoxan, propafenone, terbutaline, tetrahydropapaveroline, tetrahydrozoline, tolperisone, trihexyphenidyl	ODAS- γ -CD ¹	25 mM H ₃ PO ₄ , 12.5 mM NaOH, CH ₃ OH and 2.5–30 mM CS	293
Alkyl aryl phosphates	ODAS- γ -CD ¹	25 mM MES, 12.5 mM NaOH, 0%–10% methanol and 5–20 mM CS	294
Uniconazole, diniconazole	CM- γ -CD	50 mM phosphate buffer, pH 6.5 and 5 mM CS	295
Ephedrine and amphetamine derivatised by 4-fluoro-7-nitrobenzofurazan	sulfo- γ -CD	50 mM phosphate buffer, pH 7.35, 1.5 mM SDDS and 10 mM CS; FD	296
Promethazine, ethopropazine, trimeprazine, thioridazine	β -CD, HP- β -CD, γ -CD	40 mM phosphate buffer, pH 3.0 and 0.02–3.0 mM CS ₁ or 0.4–6.0 mM CS ₂ or 2.5–6.0 mM CS ₃	297
Acebutolol, bepridil, cloperastine, diperodon, disopyramide, doxylamine, homochlorcyclizine, hydroxyzine, ketamine, oxyphenonium bromide, pheniramine, propiomazine	CM- β -CD, CM- γ -CD	100 mM phosphate or borate buffer, pH 6, 7, 8 and 2.5% CS	298
Polychlorobiphenyls	CM- γ -CD, β -CD, PM- β -CD	50 mM MES, pH 6.5, 2 M urea and 20 mM CS ₁ + 10 mM CS ₂ or 20 mM CS ₁ + 20 mM CS ₃	299
26 Drugs and their synthetic intermediates	SBE- β -CD + γ -CD + HDM- β -CD	50 mM NaH ₂ PO ₄ , pH 2.5 and 5% CS ₁ + 25 mM CS ₂ + 25 mM CS ₃	300

^a The method is not given if a UV detector was used; ^b CS is a chiral selector; ^c MES is 2-morpholinoethanesulfonic acid; ^d FD is fluorescence detection; ^e MS is mass spectrometry; ^f HDM is heptakis(2,6-di-*O*-methyl); ^g HDMC is heptakis(2-*N,N*-dimethylcarbamoyl); ^h MPC is mono-3-*O*-phenylcarbamoyl; ⁱ QA is quaternary ammonium salt; ^j EC is ethyl carbonate; ^k HSD is hemispherodextrin; ^l ODAS is octakis(2,3-diacetyl-6-sulfo).

Table 6. Enantioselective separations using cyclodextrins in analysis of real samples by CE.

Compound	Sample	CD	Supporting electrolyte, method of detection ^a	Ref.
Epimers of amygdalin	Chinese herbal remedies	α -CD	20 mM Tris–HCl, pH 9.0, 80 mM sodium deoxycholate and 25 mM α -CD	301
CBI baclofen	plasma	α -CD	50 mM borate buffer, pH 9.5 and 7 mM CS; FD	302
Rogletimide	serum	α -CD	10 mM NaH ₂ PO ₄ –5 mM Na ₂ B ₄ O ₇ , pH 2.5, 0.03 mM HTAB ^b and 60 mM CS	303
CBI aspartic acid	rat brain	β -CD	50 mM borate buffer, pH 9.0, 50 mM SDDS, 15% methanol and 20 mM CS; FD	304
CBI derivatives of seleno-methionine and selenoethionine	commercial L-SeMet	β -CD	30 mM NaH ₂ PO ₄ –10 mM H ₃ BO ₃ , pH 7, 50 mM SDDS, 50 mM taurodeoxycholic acid and 20 mM β -CD	213
Methadone, cocaine, amphetamine and its 3,4-methylene-dioxy derivatives	heroin	β -CD	100 mM K ₃ PO ₄ , pH 3.23 and 20 mM CS	305
Lactic acid	food products	HP- β -CD	90 mM phosphate buffer, pH 6.0 and 240 mM CS	306
	biological liquids	HP- β -CD	200 mM phosphate buffer, pH 6.0 and 413 mM CS, polyacrylamide-coated capillary	307
Terbutaline	the same	HP- β -CD	50 mM phosphate buffer, pH 2.5 and 10 mM CS	308
Methylphenidate	commercial samples	HDM- β -CD	100 mM H ₃ PO ₄ –triethanolamine, pH 3.0 and 15 mM CS	255

Table 6 (continued).

Compound	Sample	CD	Supporting electrolyte, method of detection ^a	Ref.
Ephedrine, propranolol, adrenaline, phenylalanine	spinal puncture, pharmaceuticals Gripex and Nurofen	CM- β -CD	20 mM Na ₂ B ₄ O ₇ , pH 7.5 and 20 mM CS	309
Amphetamine, methamphetamine	biological liquids	CM- β -CD	100 mM phosphate buffer, pH 2.5 and 10 mM CS	310
Metoprolol, its metabolite, <i>O</i> -desmethyl metoprolol	the same	CM- β -CD	100 mM acetate buffer, pH 4.0, 5% propan-2-ol and 10 mM CS	311
Albendazole sulfoxide	spinal puncture	sulfo- β -CD	20 mM Tris, pH 7.0 and 3% CS	312
Atropine	ophthalmological solution	sulfo- β -CD	55 mM phosphate buffer, pH 7 and 2.9 mM CS	313
Ofloxacin	biological liquids	sulfo- β -CD	50 mM phosphate buffer, pH 2.5 and 0.35 mM CS	314
Praziquantel, <i>trans</i> -4-hydroxy-praziquantel	plasma	sulfo- β -CD	20 mM borate buffer, pH 10, 20 mM sodium deoxycholate and 2% CS	315
Disopyramide, mono- <i>N</i> -des-alkyl disopyramide	"	sulfo- β -CD	20 mM acetate buffer, pH 5.0 and 0.2% CS	316
Eticlopride, sulpiride	serum	sulfo- β -CD	20 mM citrate buffer, pH 2.90 and 2% CS	317
Ofloxacin, desmethyl ofloxacin, ofloxacin <i>N</i> -oxide	biological liquids	SBE- β -CD	100 mM phosphate buffer – triethylamine, pH 2.0 and 0.65 mg ml ⁻¹ CS; FD	318
Tramadol, its metabolites	plasma	SBE- β -CD	40 mM ammonium acetate, pH 4.0 and 2.5 mg ml ⁻¹ CS; PVA-coated capillary; CE-MS	319
Venlafaxine, its metabolite	clinical samples	phosphated γ -CD	50 mM phosphate buffer, pH 2.5 and 20 mg ml ⁻¹ CS	320
Tramadol	biological liquids	CM- β -CD + M- β -CD	50 mM borate buffer, pH 10.0 and 40 mg ml ⁻¹ CS ₁ + 22.5 mg ml ⁻¹ CS ₂ ; FD	321
Carvedilol	plasma	succinyl- β -CD + M- α -CD	150 mM phosphate buffer, pH 3.0 and 7.5 mg ml ⁻¹ CS ₁ + 15 mg ml ⁻¹ CS ₂ ; FD	322
Amphetamine, methamphetamine, ephedrine, nor-ephedrine, their derivatives (simultaneous detection)	biological liquids	β -CD + HDM- β -CD	75 mM Tris – H ₃ PO ₄ , pH 2.5 and 3 mM CS ₁ + 10 mM CS ₂	323
Diastereomers of flavanone-7- <i>O</i> -glucosides	citron juice	γ -CD	200 mM borate buffer, pH 10.0 and 5 mM CS	324
Vestitone, medicarpin (simultaneous detection)	extracts from transgenic plants	HP- β -CD + HP- γ -CD	25 mM borate buffer, pH 10.0, 10% methanol and 2 mM CS ₁ + 20 mM CS ₂	325

^a The method is not given if a UV detector was used; ^b HTAB is hexadecyltrimethylammonium bromide.

V. Conclusion

A huge amount of the published data on the application of cyclodextrins in enantiomer separations demonstrates the important role of these chiral selectors in various methods of chromatography and capillary electrophoresis. Each method has advantages and limitations. Hence, it is useful to compare the possibilities of chiral separations by capillary gas chromatography, high-performance liquid chromatography, capillary electrochromatography and capillary electrophoresis and to discuss the prospects of the use of CD-based chiral phases.

High-performance liquid chromatography finds the most extensive application. Enantiomers are separated with the use of various CD and their derivatives (both polar and hydrophobic). The advantages of HPLC are associated with the availability of commercial columns, their high selectivity and rather high performance, diversity and high sensitivity of detectors, good reproducibility of the results and a large amount of published data on separations of enantiomers of differing nature.

Capillary gas chromatography with cyclodextrin phases is employed more rarely because of technological difficulties in the column manufacture. However, the number of CD used in capillary gas chromatography is rather large (like in liquid chromatography). This method enables one to separate enantiomers with a boiling point of no higher than 260 °C. Unlike HPLC, gas chromatography allows one to separate compounds devoid of an aromatic ring. The development of capillary gas chromatography with CD phases provided a deeper insight into processes responsible for separation of optical isomers. Depending on the type of CD, either the formation of inclusion complexes (β -CD and its polar derivatives) or surface interactions, *viz.*, hydrogen bonding and π – π interactions with substituents in the ring of CD (γ -CD and hydrophobic derivatives of β -CD), can play a decisive role. A predominance of hydrogen bonding and π – π interactions with substituents in the ring of CD provides an increase in the efficiency of chiral separations, because the rates of these processes are substantially higher than the rate of formation of inclusion complexes. Such selectors make it possible

to separate enantiomers possessing similar thermodynamic characteristics.

The advantages of capillary electrophoresis are a higher efficiency of separation and the ease of variation in the nature of a selector by adding various CD to a supporting electrolyte. The choice of chiral selectors in CE is limited by their solubility in aqueous solutions serving as SE. In some cases, aqueous–organic mixtures (with acetonitrile, methanol or dimethyl sulfoxide) can be used. This is the main limitation on the application of CE to separation of optical isomers. This difficulty is partially compensated by the ease of variation in the composition of a supporting electrolyte. Thus, a selector, its concentration and the pH of an electrolyte can be varied, mixed chiral selectors can be used and specific achiral additives can be introduced.

An essential problem in capillary electrophoresis is associated with the reproducibility of the results. To solve this problem, each subsequent separation must be performed using a fresh solution of the supporting electrolyte and the capillary must be washed with this solution between separations. This leads to a high consumption of a chiral selector and an increase in the time of analysis.

Yet another problem is the detection of enantiomers. A UV detector is most commonly used. Sorbates are detected as diastereomeric complexes with a chiral selector. Due to adsorption of the selector involved in SE, the sensitivity of determination of sorbates decreases. The sensitivity can be substantially different for various enantiomers that form diastereomeric complexes with different stability.

The experimental technique used in capillary electrochromatography approaches that employed in HPLC. Therefore, the nature of a selector can be varied over a wider range, which increases the sensitivity of determination and improves the reproducibility of the results. The retention of sorbates increases substantially (the capacity of a stationary phase increases), which improves the selectivity of separation, the efficiency of separation remaining comparable with that in CE.

All the aforesaid provides evidence that CEC holds considerable promise. In the future, CEC may displace both CE and HPLC as applied to chiral separations. However, the necessary condition is the development of technology for the production of columns for CEC, an increase in the stability of their characteristics and availability of various types of commercial columns.

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Artificial ion channels

I I Stoikov, I S Antipin, A I Konovalov

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Abstract. The approaches to the design of artificial ion channels are systematised and the data on their structure, stability and electrical conduction are summarised. The bibliography includes 104 references.

I. Introduction

The transport of ions through phospholipid membranes is among the most important requisites of functioning of living organisms.^{1–4} The key function of the phospholipid bilayer is to create a barrier preventing the hydrophilic molecules and ions present in the aqueous phases near the cell from penetrating inside the cell. This function is performed by the hydrophobic internal layer of the phospholipid membrane. Nevertheless, some polar compounds and ions are able to penetrate the membrane at a high rate. This selective permeability of natural membranes for certain particles is needed for many biological processes to occur.

The transport of ions through a membrane can be accomplished by carrier molecules (transporters) or through transmembrane channels. In biological systems, the ion transfer (biological transport) takes place mainly through ion channels formed most often by appropriate proteins (channel proteins), which produce channel structures in phospholipid membranes; the sites of binding of the transported substances in such proteins are accessible simultaneously from both sides of the membrane. In this case, the ion transport occurs very rapidly (10^6 – 10^8 ion s^{−1} per channel protein).^{4–7}

The rate of ion transport through a membrane by carrier molecules is lower by several orders of magnitude. This difference

between the rates is due to several reasons. An important reason is the fact that channel proteins do not undergo serious conformational changes upon the transport of ions from one side of the membrane to the other, whereas carrier molecules do undergo conformational changes when they bind the ions to be transported on one side of the membrane and liberate them on the other side. In addition, the binding sites for molecules being transported in the carrier molecules are accessible only on one side of the membrane.

The carrier molecules are used more often for artificial transport of ions than transmembrane channels. This is due to the fact that artificial transmembrane channels are compounds with complex organisation. The synthesis and elucidation of the three-dimensional structure of such compounds are faced with substantial difficulties. Nevertheless, artificial transport systems are very important because study of these systems is favourable for deeper understanding of the properties of channel proteins at the molecular level and forms the basis for the development of new pharmaceuticals and drug delivery systems.^{1,8} Transmembrane channels perform the ion transport through membranes by a flow or jumping mechanism.^{1–4}

The last decade has seen intensive research into biomimetic tubular structures mimicking natural ion channels^{9–17} which can be inserted into 3–5-nm thick bilayer membranes. Depending on the type of molecule that forms the channel and general features of its structure and also on the nature and mutual arrangement of the ion binding sites, synthetic ion channels are classified into different types. Some of them are sketched in Fig. 1.

The natural channel proteins consist of two key functional units, namely, the 'gate' and the 'pore'.⁸ The 'pore' implies the way of ion penetration through the membrane, while the 'gate' means the mechanism of switching on and off the ion flow. The ions that pass through the channel are considered as an ion flux. The ion flux through the membrane depends on the difference between the electrochemical potentials on the two sides of the membrane. The conductance, *i.e.*, the reciprocal of the resistance, serves as the measure of the efficiency of the ion flux.

Let us consider three main characteristics of ion channels:^{2,8} (i) the time it takes for the channel to attain a constant conductance (*i.e.*, the time of maintenance of an invariable geometric structure of the channel, for example, the critical length and pore diameter); (ii) ion selectivity caused by the energetic and geometric complementarity of the ions and the channel pores; and

I I Stoikov, I S Antipin, A I Konovalov Department of Chemistry, Kazan State University, ul. Kremlevskaya 18, 420008 Kazan, Russian Federation. Fax (7-843) 231 54 16.

A E Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Centre of the Russian Academy of Sciences, ul. Arbuzova 8, 420088 Kazan, Russian Federation. Fax (7-843) 238 75 77. Tel. (7-843) 231 54 62. E-mail: IvanStoikov@ksu.ru (I I Stoikov). Tel. (7-843) 231 54 63. E-mail: iantipin@ksu.ru (I S Antipin). Tel. (7-843) 238 75 97. E-mail: konovalov@mail.knc.ru (A I Konovalov)

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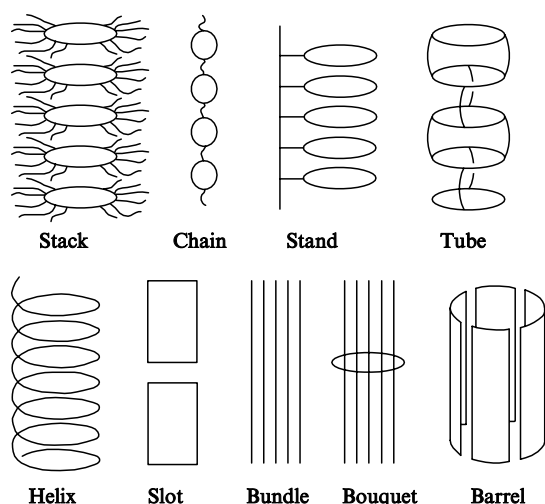


Figure 1. Types of structures of ion channels.

(iii) the type of gate mechanism (gate opening–closing) acting in the channel.

The conductance of an ion channel depends on the pore size and length and on the dielectric constant. The ion selectivity also depends on many factors such as the size of the pores, the energy of ion dehydration, the electrostatic interaction between the ions and the amino acid residues that form the pore. (The channel activity of synthetic peptides is often measured using the method of planar bilayers.⁸)

Depending on the type of gate mechanism, ion channels are classified into sensing, ligand and mechanical ones. In the sensing

(voltage-controlled or electrically excitable) channels, the channel opening is induced by an electric signal. Examples of such channels are fast Na^+ -channels² or voltage-gated K^+ -channels, which respond to the change in the potential of nerve cells (Fig. 2 *a*).⁸ In the ligand (ligand-gated or chemically excitable) channels, opening or closing of the channel is induced by the chemical changes that take place under the action of an appropriate ligand. These channels can be exemplified by nicotinic cholinergic receptor (Fig. 2 *b*). In mechanical (mechanosensitive) channels, opening of the channel is due to expansion of the cell membrane. Channels of this type participate in muscle contraction and in the control of the osmotic pressure and cell volume.

A number of approaches to the design of ion channels and ion-sensitive membrane systems distinguished by high sensitivity and selectivity have now been proposed.¹⁸ The increase in interest in detecting biologically active substances *in vitro* and *in vivo* (for example, in individual cells and in tissue sections and organs) and in the development of nano-sized drugs and ion–molecular devices is stimulating studies aimed at the design of synthetic ion channels.

II. Compounds used as models of natural channels

A lot of data on the structure and properties of channel proteins which perform biological transport has been collected.^{1–4} The amino acid sequences in many channel proteins have been decoded. However, in investigations of the structure and the mechanism of channel operation, it was necessary to resort to model systems, due to the complexity of X-ray diffraction studies of transport proteins. Considerable capabilities for this modelling are provided by the use of oligo- and polypeptides [for example, some toxins^{19,20} and polyene (nystatin, amphotericin B) and peptide (gramicidin A, alamethicin and mellitin)^{21–23} antibiotics] capable of forming channel-like associates in bilayer phospholipid membranes.

1. Nystatin and amphotericin B

The polyene antibiotics — amphotericin B,^{24–26} filipin²⁵ and nystatin²⁷ — are membrane-active antimycotic agents.

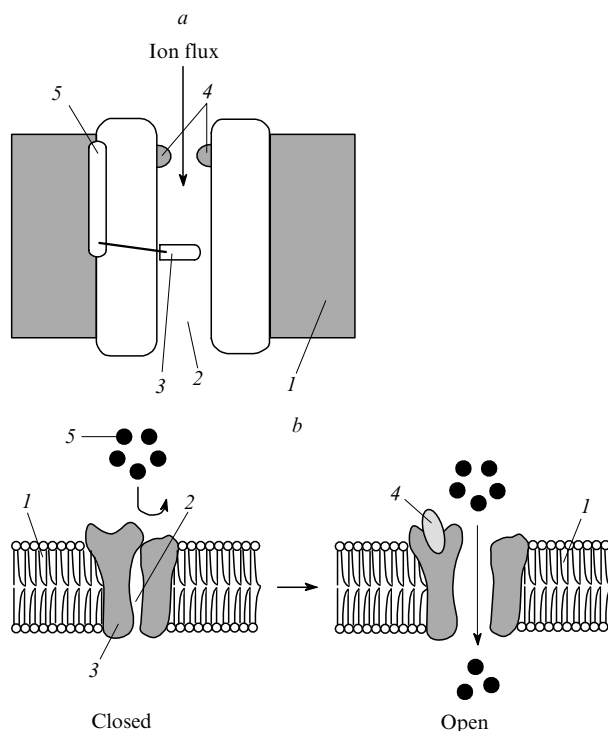
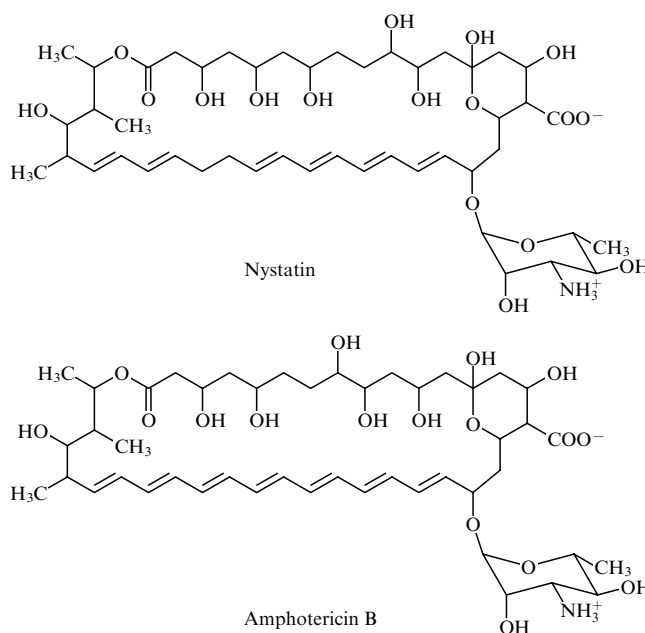


Figure 2. Schematic view of ion voltage-gated (*a*) and ligand-gated (*b*) channels.

Designations in (*a*): (1) membrane, (2) pore, (3) gate, (4) ionic filter, (5) potential-sensitive fragment.

Designations in (*b*): (1) membrane, (2) pore, (3) ligand-gated fragment; (4) ligand; (5) ions.

Apparently, the lytic activity[†] and the ability of this type of antibiotic to induce the removal of low-molecular-weight compounds from cells with low selectivity are due to the association of

[†] Lytic activity is the ability of a compound to cause rupture of the cell wall.

these agents with steroid membranes to form pores. The formation of these complexes has been detected by NMR.^{21,26}

The molecules of polyene antibiotics 8 to 10 in number form a tubular structure (pore) with the hydroxy groups directed inwards in the membrane bilayer.^{22,28} The diameter of this pore is about 8 Å and water molecules are loosely accommodated inside. For the formation of a channel in the phospholipid bilayer, two cylindrical structures arranged according to the tail-to-tail pattern are required. This channel would be nonpolar from the outside but hydrophilic from the inside and would end with polar fragments of amino sugars. The association and dissociation of the tubular ensemble of polyene molecules result in opening and closing of the channel, respectively.^{22–28}

2. Gramicidin A and alamethicin

The best known ion channel is that formed by gramicidin A,^{2,29,30} which is a hydrophobic peptide composed of alternating L- and D-amino acids³¹ (HCO–L-Val–Gly–L-Ala–D-Leu–L-Ala–D-Val–L-Val–D-Val–L-Trp–D-Leu–L-Trp–D-Leu–L-Trp–D-Leu–L-Trp–NHCH₂CH₂OH). This ion channel is formed by two gramicidin A molecules arranged in the head-to-head mode by their N-end fragments to form a β (LD)-helical configuration³² (Fig. 3 a). In this helical structure, all the side chains are located outside, while the carbonyl groups are inside the channel. The total length of the gramicidin channel is equal to ~ 30 Å; the external and internal diameters are 15 and 5 Å, respectively. Owing to the small internal diameter of the channel, the transport through the channel can be performed only by a single molecule. The gramicidin channel is cation selective,³³ although gramicidin A itself is extremely hydrophobic and contains no polar amino acid. The conductance of a single channel formed by gramicidin is rather high. When the concentration of RbCl in the solution surrounding the membrane is 100 mmol litre⁻¹, the cationic conductance of the channel (for Rb) amounts to $30 \times 10^{-12} \Omega^{-1}$ per channel,² whereas the permeability for chloride anions is zero.³⁰ This selectivity is related to the electrostatic repulsion of the anions by the carbonyl group dipoles at the gate of the channel. The permeability of the gramicidin channel for single-charged cations changes in the following sequence: Cs⁺ > Rb⁺ > K⁺ > Na⁺ > Li⁺. The selectivity exhibited by the gramicidin channel with respect to these cations is not very high: it corresponds to a fivefold change in the permeability coefficients. The gramicidin channel is opened due to association of monomers to form a dimer and closed upon dissociation of the dimer (Fig. 3 a). The lifetime of the dimer is $\sim 10^{-3}$ to 10 s, depending on the lipid composition of the membrane and other factors.^{2,29,30} It is noteworthy that the gramicidin channel is not voltage-dependent.

Alamethicin (Alm) is a peptide antibiotic consisting of 20 amino acid residues, which forms transmembrane channels with a variable number of associated subunits in artificial^{34–37} and biological³⁸ membranes. The mechanism of ion transport by alamethicin has been studied rather comprehensively. The peptide

forms α -helices in the bilayer, which are associated with each other forming a channel which consists of several interconnected α -helices^{39–43} (Fig. 3 b). The conductance of this channel, unlike that of the gramicidin channel, depends on the potential applied to the surface of the bilayer membrane. Alamethicin channels start conducting ions (Na⁺, K⁺) only at a positive transmembrane potential (> 60 mV). Thus, they represent nano-sized ionic diodes which can conduct current only in one direction, like macroscopic diodes. The voltammetric characteristics of the alamethicin channel formed in a planar bilayer on the basis of a mixed lipid (egg phosphatidylcholine–egg phosphatidic acid–cholesterol in a molar ratio of 8 : 2 : 1) are shown in Fig. 4.

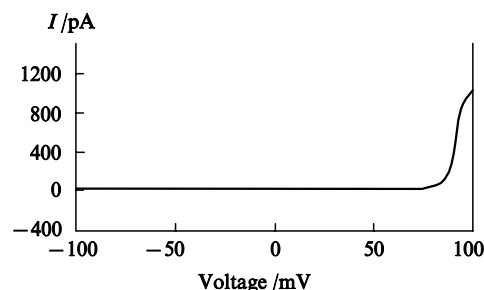


Figure 4. Average macroscopic current–voltage relationships for alamethicin channel (130 pmol of alamethicin, 1 M KCl, egg phosphatidylcholine–egg phosphatidic acid–cholesterol, 10 cycles from –100 to 100 mV at 5.7 mV s⁻¹).

3. Ion channels based on modified peptides and antibiotics

Futaki *et al.*³⁴ have prepared the channel peptide Alm–LeuZ by covalent linking of a leucine-enriched oligopeptide (LeuZ) to an ionophore, namely, alamethicin (Alm). As a result of this linking, it is possible to perform the extramembrane control of the association of the channel peptides Alm–LeuZ (Fig. 5) and thus to change the channel conductance. Here Alm–LeuZ = Ac–Alm–Gly–Gly–Gly–Gly–LeuZ–CONH₂, Alm = UP.
.UAUAQUVUGLUPVUUEQF, LeuZ = RXKQLEDKVEEL.

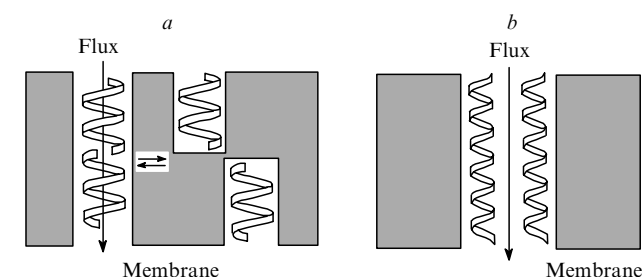


Figure 3. Schematic view of the ion channels formed in phospholipid membranes by peptide antibiotics, gramicidin A (a) and alamethicin (b) under the action of osmotic pressure.

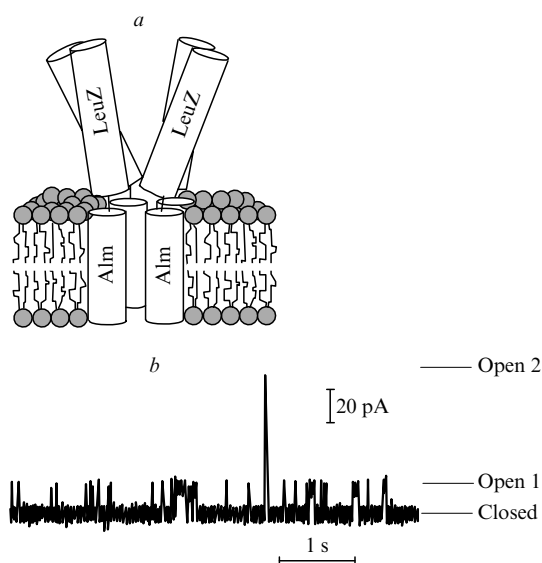
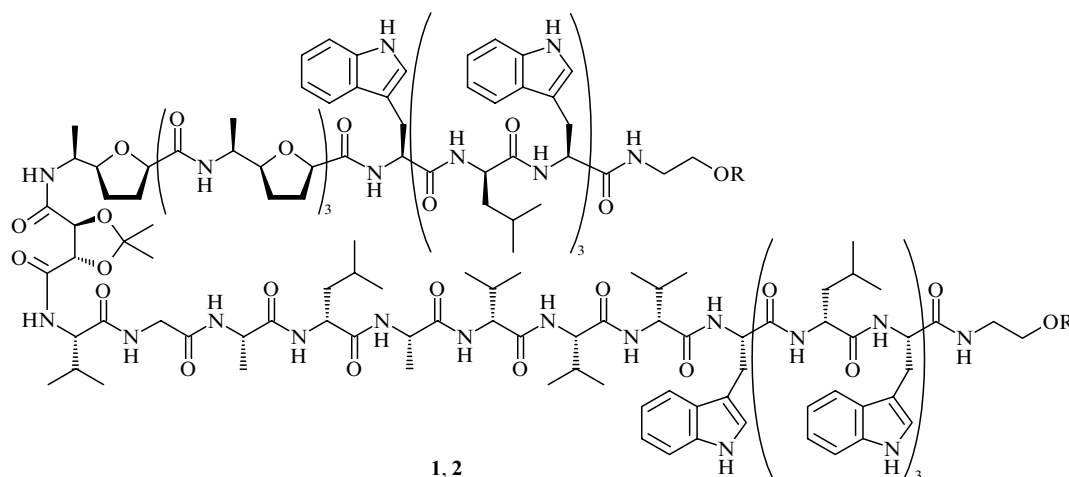


Figure 5. Schematic view of a single channel formed in a lipid bilayer by an association of modified alamethicin subunits Alm–LeuZ (50 nmol Alm–LeuZ) (a) and current through this single channel at 100 mV (b).³⁴ Open 1 and Open 2 are the current levels observed for two different conformations of the channel.



R = Bu^tPh₂Si (**1**), H (**2**).

.LSKNYHLENEVARLKKLVGE, where U is (*R*)-aminoisobutyric acid (Aib), X is norleucine (Nle), A is Ala, D is Asp, E is Glu, F is Phe, G is Gly, H is His, K is Lys, L is Leu, N is Asn, P is Pro, Q is Gln, R is Arg, S is Ser, V is Val, and Y is Tyr.

The conductance of this single ion channel in 1 M KCl is $120 \times 10^{-12} \Omega^{-1}$. The channel behaviour is voltage dependent. The conformational transitions from the helical to the disordered structure which take place in extramembrane segments regulate the ionic conduction of the channel. Thus, it is possible to control the functioning of the channel by varying the conformation of the attached synthetic extramembrane fragment.

In 1977, Bamberg and Janko⁴⁴ connected two gramicidin A molecules by a malonic acid bridge and thus obtained malonylbis(deformyl)gramicidin. It was shown that this covalent dimer forms a channel in the bilayer lipid membrane, the conductance and the ion selectivity of this channel being the same as those of the gramicidin channel, while the time the channel remains open significantly increases. Whereas the open lifetime is 1–2 s for the single gramicidin channel, in the case of a single malonylbis(deformyl)gramicidin channel, it is several minutes.

Arndt *et al.*⁴⁵ also used gramicidin A molecules as building blocks for the design of artificial ion channels with a long-lived active conformation (unlike the natural short-lived gramicidin dimers). For this purpose, two gramicidin molecules were cross-linked by C₄-linkers based on succinic acid. To study the phenomenon of the active conformation of the channel protein, a series of gramicidin-based synthetic channels with a long open duration in solution has been developed. The compounds synthesised for this purpose contained gramicidin molecules connected by various C₄-linkers. The influence of the linkers on the channel behaviour was studied.⁴⁵

In the last decade, ion channels based on gramicidin and other antibiotics and on modified peptides have been used as sensing elements. These channels incorporated in a bilayer lipid membrane are highly sensitive and selective.¹⁸ Sensors making use of chemically modified gramicidin and alamethicin have been reported.^{46,47} Gramicidin ion channels bound to antibodies by covalent bonds were used to design biosensors for determination of proteins, viruses, antibodies, DNA, electrolytes, drugs, and pesticides. The ionic conductance of these channels is regulated by the interaction of substrates with the antibodies connected to gramicidin molecules through biotin bridges.

It is well known that tetrahydrofuran can efficiently solvate metal cations. Therefore, in the development of cation-conductive synthetic peptide channels, it has been proposed to use oligotetrahydrofurans and THF-substituted amino acids. On the basis of THF-containing amino acids, cation channels with biomimetic entrance and exit have been synthesised.⁴⁸

The biomimetic fragment present in the obtained structures **1** and **2** is gramicidin A. The entrance and the exit of the channels **1**

and **2** contain four tryptophan residues. Apparently, the indole side groups of tryptophan contribute to stabilisation of the structures of channels **1** and **2** through hydrogen bonding to the polar groups of the lipid membrane and electrostatic dipole–dipole interaction with the surface charge of the membrane. The compounds **1** and **2** contain a heptapeptide (L-Trp–D-Leu)₃–L-Trp, a tetra-THF-peptide fragment, a linker based on tartaric acid[‡] and a pentadecapeptide, namely, gramicidin A.

In the compound **1**, the terminal fragments of ethanolamine are protected by lipophilic *tert*-butyldiphenylsilyl groups, while in the compound **2**, they are free. Upon incorporation in the lipid bilayer, the compound **1** forms a channel with different levels of conductance, indicating the existence of several active conformations of the channel. The first conformation with a conductance of $15.4 \times 10^{-12} \Omega^{-1}$ and an average open-state duration of 500 ms is responsible for passage of ~30% of the cations through the channel. The second conformation ($19.7 \times 10^{-12} \Omega^{-1}$) is more rarely encountered; however, its contribution to the total cation flux is greater, as its lifetime in the open state is ~15 s. Channel **1** demonstrated selectivity with respect to single-charged cations (NH₄⁺ > Cs⁺ > K⁺ > Na⁺). Since the cations lose their hydration shells, at least partially, when passing through the channel, this selectivity is due to the difference in the dehydration energies of the cations.

The electrochemical experiments with gramicidin D carried out by Wang's group⁵⁰ have dealt with the effect of the gramicidin concentration in the bilayer lipid membrane on the properties of the channels formed by gramicidin. When the concentration of gramicidin D is high, its structure in the bilayer lipid membrane is represented only by dimers.

Futaki⁸ reported a new approach to the design of sodium ion channels on the basis of the peptide template H–Cys(Acm)–Lys–Cys(SH)–Pro–Gly–Cys(MBzl)–Glu–Cys(Ad)–Gly–OH (Fig. 6). He synthesised a compound containing four different α-peptides ([NaI]–[NaIV]) attached to the given peptide template.

The assembly of such a peptide ion channel is shown in Fig. 7. Chloroacetyl-γ-aminobutyric acid was attached as a spacer to the N-end fragments of the amino acid sequences of the [NaI]–[NaIV] peptides. All the [NaI]–[NaIV] α-peptides were linked to the template through the interaction of chloroacetyl fragments with the free SH groups of the template after selective removal of the S-protective groups. The protein thus produced showed an ion-channel activity in lipid bilayers, dependent on the conformational changes in the channel induced by the change in the voltage applied to the membrane.

[‡] (*S,S*)-Tartaric acid has already been successfully used as the bridge for the head-to-head covalent attachment for the gramicidin dimer.⁴⁹

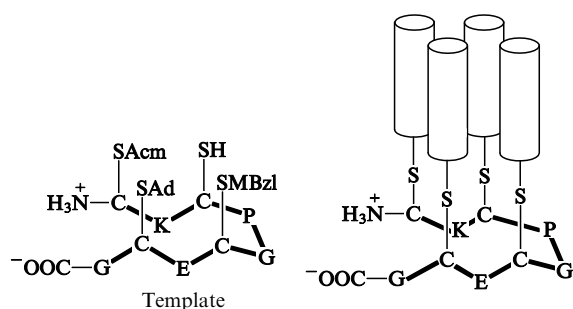


Figure 6. Nonapeptide template and artificial ion channel assembled from it.

Designations: C is Cys, K is Lys, P is Pro, G is Gly, E is Glu, AcM is acetamidomethyl, MBzl is *p*-methoxybenzyl, Ad is 1-adamantyl.

4. Toxins

Toxins capable of forming channels in a bilayer membrane are often used to model ion channels. The problem of spontaneous

incorporation of these water-soluble hydrophilic proteins in the membrane bilayer appears to be most interesting. This problem has been studied using thionins and ϵ -toxin.^{4,19} Thionins are small cysteine-containing amphipathic plant proteins. Many of them are toxic for microorganisms and mammal cells. Hughes *et al.*¹⁹ have shown that β -purothionin isolated from wheat flour can form cation-selective ion channels in artificial and biological bilayer lipid membranes (plasma membrane of neurons of the rat hippocamp); this apparently is responsible for the toxicity of β -purothionin and other thionins with respect to cells.

Petit *et al.*²⁰ demonstrated that the ϵ -toxin produced by the *Clostridium perfringens* microbe forms in lipid membranes wide channels capable of carrying substances with a molecular mass of up to 1 kDa, for example, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide. The ionic conductance of this toxin in a synthetic bilayer membrane amounts to $50 \times 10^{-12} \Omega^{-1}$ at a KCl concentration of $100 \mu\text{mol litre}^{-1}$.

The method of template assembling of synthetic peptides has also been used to prepare a branched peptide containing a δ -toxin fragment.⁵¹ This peptide was used as a model to study the structure and the transport properties of the δ -toxin.

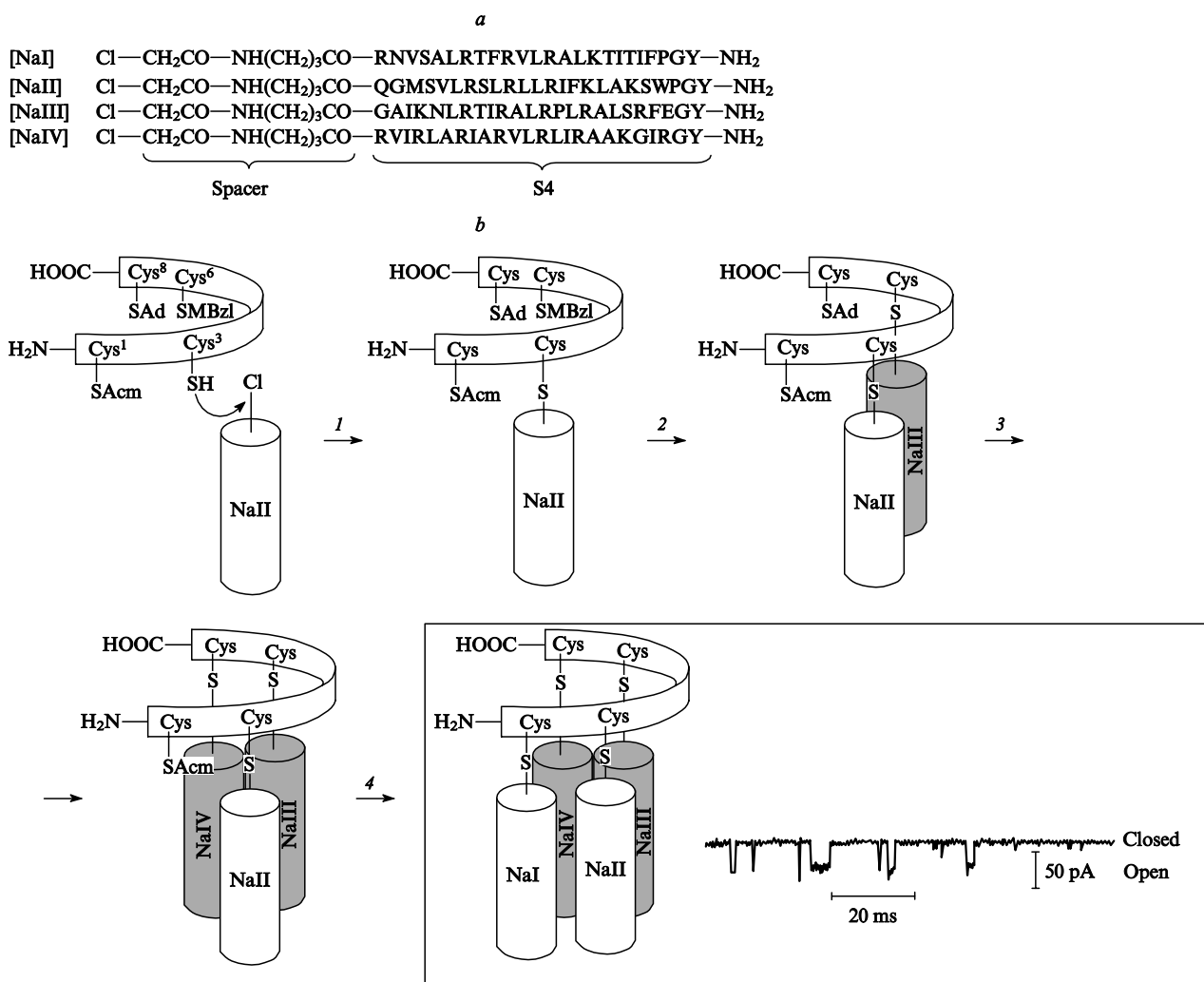


Figure 7. Synthesis of four-helical bundle-type peptide sodium channel [NaI]–[NaIV] containing peptide potential-sensitive segments (S4). For designations of amino acid residues, see the text, I is isoleucine, T is threonine.

(a) Design of peptide segments, (b) assembling and profile of a single peptide channel.

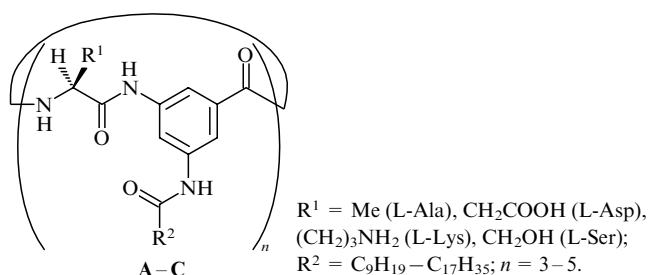
(1) Introduction of [NaII] in a 6 M solution of guanidine hydrochloride–0.1 M Tris-buffer (pH 8) system, (2) removal of the MBzl-protective group by treatment with 1 M Me_3SiBr –thioanisole in THF and introduction of [NaIII] (under conditions 1), (3) removal of the Ad-protection on treatment with 1 M $\text{CF}_3\text{SO}_3\text{H}$ –thioanisole in THF and introduction of [NaIV] (see 1), (4) removal of the AcM protection on treatment with AgOSOCF_3 in THF and introduction of [NaI] (see 1).

III. Artificial transmembrane ion channels based on cyclic peptides

1. Cyclic peptides consisting of alternating natural and abiotic amino acids

Usually, cyclic peptides form hydrophilic ion channels shaped like stacks in bilayer membranes. These channels are formed as a result of specific intermolecular interactions either between the peptide fragments of the macrocycle or between the amino acid residues of the side chains. The possibility of formation of this type of associate by cyclic peptides (see Fig. 1) was predicted back in 1972 by Hassal *et al.*⁵² Later, it was shown by X-ray diffraction¹¹ that cyclic tetrapeptides composed of alternating α - and β -amino acid residues are packed into stacks through hydrogen bonding of the cyclic fragments thus forming hollow cylindrical structures.

Japanese researchers⁵³ have synthesised cyclic peptides **A–C** containing 3 to 5 dipeptide units on the basis of one abiotic [5-(*n*-alkanoylamino)-3-aminobenzoic acid] and one natural (L-alanine, L-aspartic acid, L-lysine and L-serine) amino acids (Fig. 8). The unnatural amino acid makes the cyclic peptides structurally rigid.



Analysis of the structure of the possible associates formed by such peptides and the data on the voltage-dependent blockade of the channels based on them by Ca^{2+} ions allowed the researchers⁵³ to conclude that ion channels consist of two peptide rings packed according to the tail-to-tail pattern. The peptide parts of the rings form the entrance and the exit of the channel, while the long alkanoyl chains penetrate the membrane. It was also shown that variation of the natural amino acid incorporated in the cyclopeptide, *e.g.*, replacement of the neutral L-alanine by either positively charged L-lysine or negatively charged L-aspartic acid, does not influence the channel selectivity.

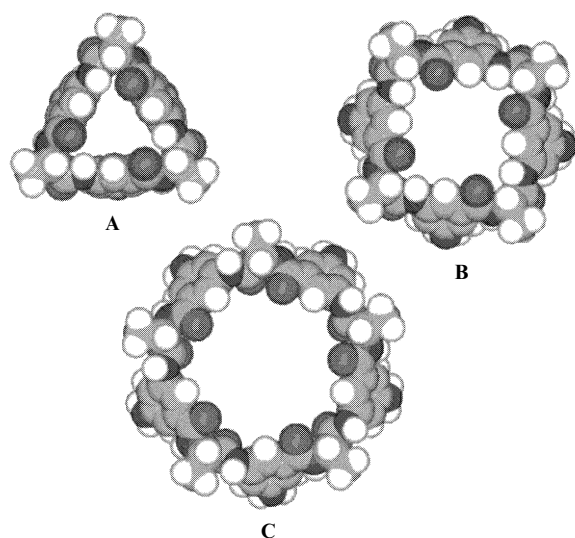


Figure 8. Models of peptides containing 3 (**A**), 4 (**B**) and 5 (**C**) dipeptide units (vertical view).⁵³
 $R^1 = \text{Me}$; for clarity, the alkanoyl chains $\text{R}^2\text{C(O)}$ are not shown.

The ion channels formed by cyclic peptides **A–C** with systematically varied pore size, shape and lipophilicity had a conductance of $\sim 9 \times 10^{-12} \Omega^{-1}$ in a 500 μM aqueous solution of KCl. The selectivity of transport of the potassium cation with respect to the chloride anion ($P_{\text{K}^+}/P_{\text{Cl}^-}$) was 5.9, while that with respect to the sodium cation ($P_{\text{K}^+}/P_{\text{Na}^+}$) was ~ 12.5 .

Under conditions that mimic the biological conditions (addition of equal amounts of solutions of sodium and potassium gluconates), the sodium/potassium selectivity ($P_{\text{Na}^+}/P_{\text{K}^+}$) for the tetrapeptide $n = 4$ (Fig. 8, structure **B**) is equal to 0.40. The Li^+ cation cannot pass through this channel, despite the substantially smaller size (1.56 Å) compared to the K^+ cation (2.66 Å), because of the great energy expenditure required for dehydration (it has been noted above that dehydration is a necessary stage involved in the transport of cations through the channel²).

2. β^3 -Peptides

β^3 -Peptides represent a class of biopolymers of abiotic origin, which tend to form unusual types of secondary structures.^{11, 54–57} Gellman and co-workers^{54, 56} have shown that homooligomers of *trans*-2-aminocyclohexane- and -cyclopentanecarboxylic acids form helical structures. The cyclic oligomers formed by α -unsubstituted β -amino acids with the β -chiral carbon atom can adopt planar ring conformations; in the solid state, these can be combined through hydrogen bonding to form hollow tubular ensembles (cyclic β^3 -peptide nanotubes).⁵⁷ These ensembles are structurally similar to self-assembling associates of cyclic peptides consisting of alternating D- and L- α -amino acids (cyclic DL- α -peptide nanotubes).^{58–62} These two classes of nanotubes supplement each other in the structure and functions.¹¹

Ghadiri and co-workers¹¹ have shown that β^3 -peptides **3–5** with appropriately selected hydrophobic side chains can be self-assembled in the lipid bilayer membranes to form highly efficient transmembrane ion channels (Fig. 9).

Owing to their unusual structure, cyclic β^3 -peptide nanotubes of abiotic origin exhibit unique properties (selectivity, solubility). In particular, due to the unidirectional arrangement of the polar amide groups in space, the nanotubes based on cyclic β^3 -tetrapeptide subunits possess a macrodipole moment (Fig. 10 *a*), whereas the nanotubes based on cyclic DL- α -octapeptides (Fig. 10 *b*) are not dipoles. The dipole moment of the amide groups (macro-dipole) enhanced by the parallel arrangement of the macrocycles

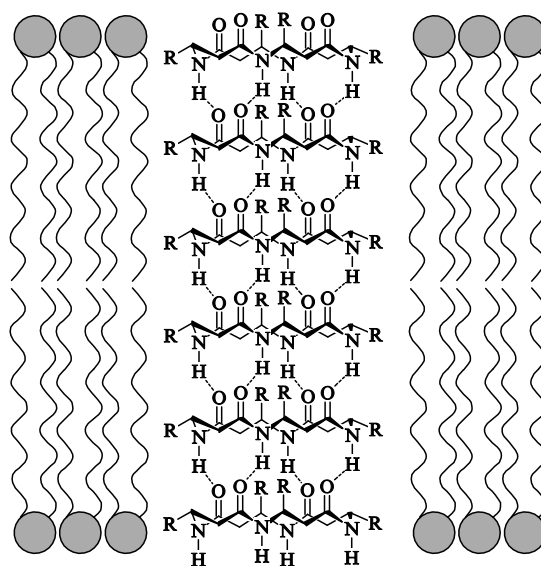


Figure 9. Presumptive structure of self-assembling transmembrane channels formed by β^3 -peptides **3–5**.¹¹

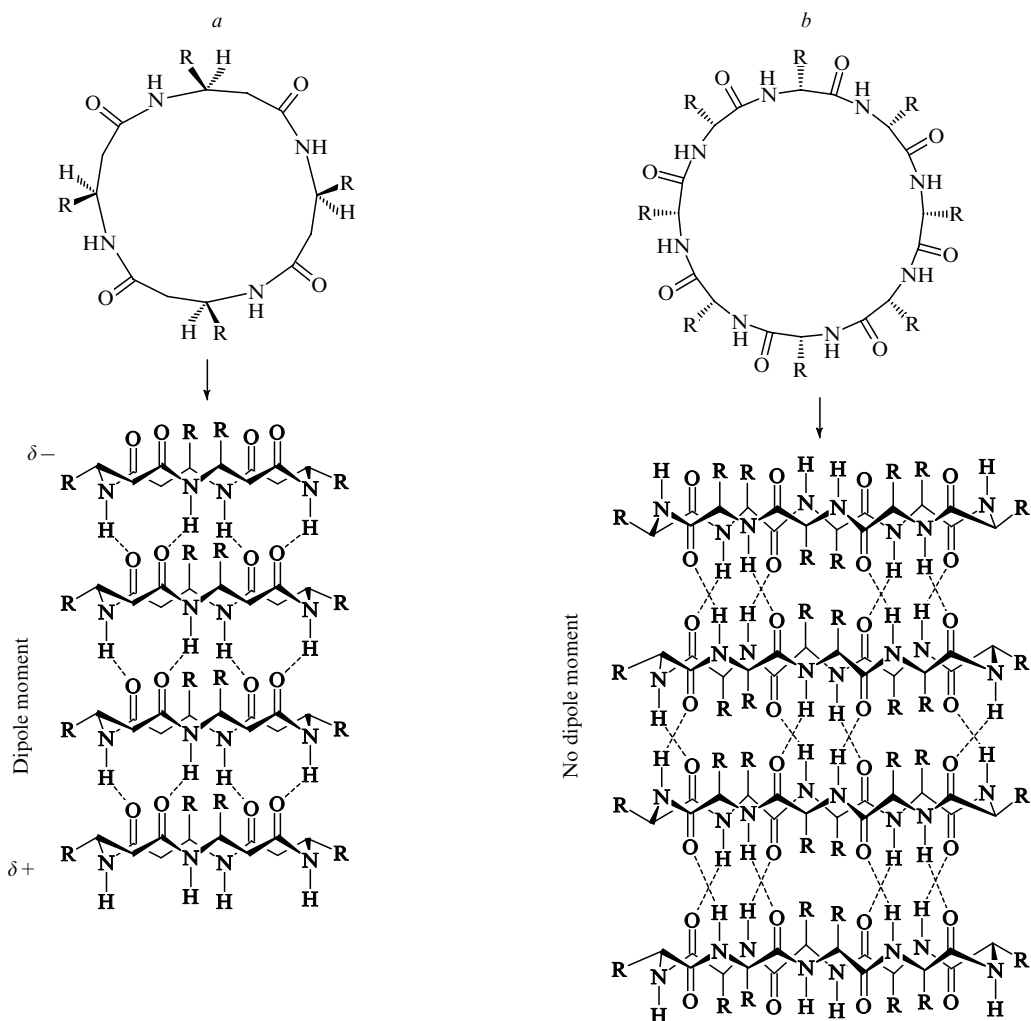
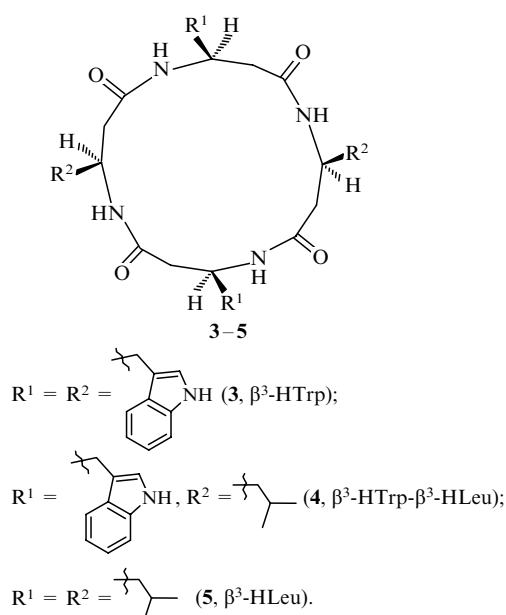


Figure 10. Cyclic peptide nanotubes consisting of cyclic abiotic β^3 -tetrapeptides (a) and cyclic DL- α -octapeptides (b).¹¹

increases the selectivity of the ion channel formed by β^3 -tetrapeptides. The β^3 -tetrapeptide **3**, containing indole groups in side fragments, is readily soluble in polar solvents such as DMSO and DMF.



Cyclic β^3 -tetrapeptides possess a higher conformational rigidity and a higher degree of pre-organisation for self-assembly than larger β^3 -penta- and β^3 -hexapeptides. Powder X-ray diffraction and molecular modelling have shown that the β^3 -tetrapeptide molecule can exist as both C_2 - and C_4 -symmetrical conformations (Fig. 11).

The results of calculations of the diameters of macrocycles suggest that in the lipid membrane, β^3 -tetrapeptides occur in the C_4 -symmetrical conformation, because in this case, the ring diameter equals 2.6–2.7 Å, which allows water molecules and

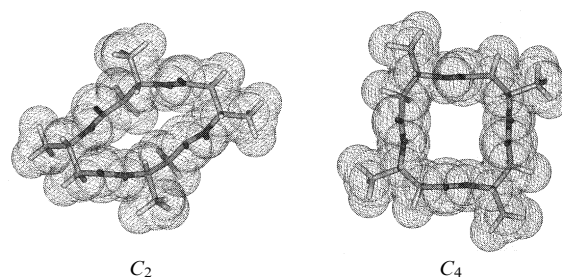


Figure 11. Cyclic β^3 -tetrapeptides in C_2 - and C_4 -symmetrical conformations.¹¹ For clarity, the side groups are shown as methyl groups.

relatively small ions to pass through the central pore of the transmembrane channel.

A synthetic transmembrane channel based on the cyclic β^3 -tetrapeptide **3** has demonstrated a K^+ -conductance of $56 \times 10^{-12} \Omega^{-1}$ (Fig. 12), which is higher than the K^+ -conductance of the channel based on gramicidin A under the same conditions. The peptides **3** and **5** ensure a proton conductance through a liposome membrane.



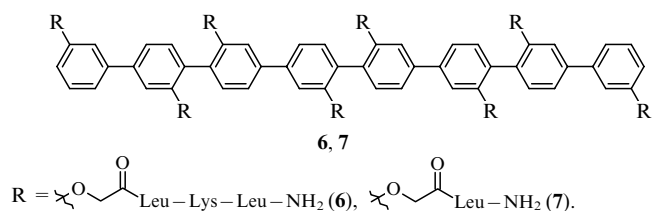
Figure 12. Conductance of the K^+ ions at 60 mV (peptide **3**, the probability of channel opening is 0.14).¹¹

Experiments confirmed the possibility of using cyclic peptides as channels for water molecules and small ions. The jumps of the measured current (see Fig. 12) point to opening or closure of the channel caused by fast conformational transitions (see Fig. 11) or changes in the channel structure.

IV. Supramolecular ion channels based on extended linear molecules

1. β -Barrels based on functionalised oligo(*p*-phenylene)

Matile and co-workers^{14–17} have reported the development of giant transmembrane channels (β -barrels) (see Fig. 1), which consist of rigid bars of octa-*p*-phenylenes **6** and **7** connected by short antiparallel β -sheet structures (Fig. 13). The rigidity of the channel structure is based on the electronic repulsion of the phenylene groups which form the internal surface of the β -barrel. Recording of the current in a single channel at -50 mV revealed a fluctuation-induced appearance of fluxes amounting to 178 pA.

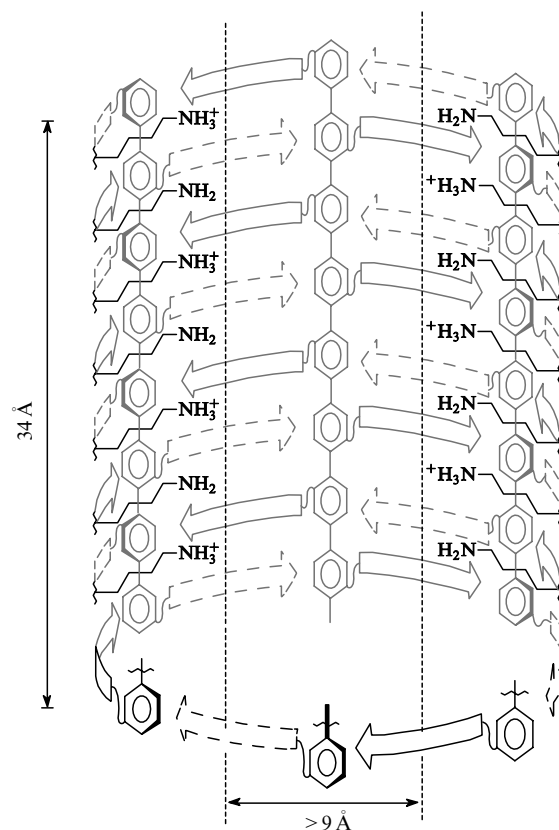
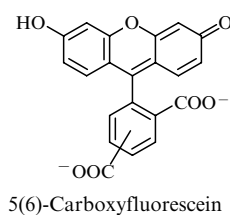


The channel **6** incorporated into monolamellar vesicles can convey an anionic fluorophore, 5(6)-carboxyfluorescein, by means of the cationic NH_3^+ groups of lysine, which line the internal surface of the hexamer of the compound **6** (see Fig. 13). For estimating the internal diameter of the β -barrel self-assembled in the membrane, the transport of carboxyfluorescein was studied (Fig. 14). Since a carboxyfluorescein molecule has a diameter of more than 9 Å, it can be carried through channels with a diameter of at least 20 Å. This nanopore is comparable in size with the natural β -barrel formed by the polypeptide α -hemolysin containing 293 amino acids.

2. Biomimetic oligo(oxyethylene) esters of carboxylic acids

Not only peptides but also various non-peptide structures can be used to construct artificial ion channels. In 1990, Menger *et al.*⁶³ synthesised a number of compounds with the general formula $R^1O(CH_2CH_2O)_nR^2$ (**8**), which facilitated the transport of ions through bilayer membranes.

The highest activity was found for compound **8a** [$R^1 = n-C_{11}H_{23}C(O)$; $R^2 = PhCH_2$, $n = 5$], whose molecules are



6: $\text{NH}_2\text{--Leu--Lys--Leu--COCH}_2\text{O--OCH}_2\text{CO--Leu--Lys--Leu--NH}_2$.

Figure 13. Structures of self-assembling hexamer **6**.¹⁵

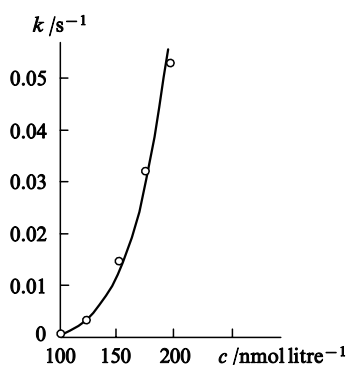
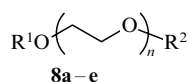


Figure 14. Observed fluxes of carboxyfluorescein as a function of the concentration of octa-*p*-phenylene **6**.



- 8a–e**
8a: $R^1 = n-C_{11}H_{23}C(O)$; $R^2 = PhCH_2$, $n = 5$;
8b: $R^1 = n-C_{13}H_{27}C(O)$; $R^2 = PhCH_2$, $n = 4$;
8c: $R^1 = n-C_{11}H_{23}C(O)$; $R^2 = PhCH_2$, $n = 4$;
8d: $R^1 = n-C_9H_{19}C(O)$; $R^2 = PhCH_2$, $n = 5$;
8e: $R^1 = n-C_7H_{15}C(O)$; $R^2 = PhCH_2$, $n = 5$.

stretched throughout the whole thickness of the lipid membrane thus forming channels. The spontaneous inclusion of compound **8a** in the lipid membrane is due to both the hydrophobic section of the fatty acid and the interaction of the π -electron system of the benzyl substituent with the quaternary ammonium group of the membrane lipids. The ion flux through the vesicle membrane was determined by time-resolved fluorescence spectroscopy using a fluorescent dye (pyranine) as the pH indicator. It was found that for a concentration of **8a** equal to 75 molecules per vesicle 30 ± 5 nm in diameter, the equilibrium between the exterior and interior ions is established almost instantaneously. Comparison of the efficiency of the transport of protons by compound **8a**, gramicidin D and 18-crown-6 ether has shown that compound **8a** surpasses gramicidin, while 18-crown-6 does not influence at all the ion flux through the bilayer lipid membrane. The last-mentioned fact deserves particular attention, because experiments with bulky liquid chloroform membranes (in this case, the ion transport is accomplished by ion carriers) give the opposite result, namely, 18-crown-6 transports the K^+ cations through a chloroform liquid membrane, whereas compound **8a** is completely inert. This is due to the fact that crown ethers are potent ligands, able to carry cations through a chloroform membrane,⁶⁴ while compound **8a** is a weak ligand for K^+ . This finding supports the assumption that compound **8a** carries the cations due to the formation of channels in the bilayer membrane. Some other facts also attest to the formation of an ion channel in the membrane. Indeed, ether **8a** is active even when present in nanomolar concentrations; in addition, the efficiency of cation transport is structurally specific, in particular, analogues of compound **8a** having either higher ($n > 5$) or lower ($n < 5$) hydrophilicity do not change the membrane permeability.

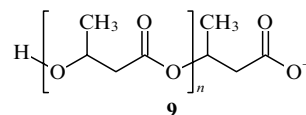
In order to elucidate the influence of the length of the fatty acid residue and the length of the oligo(oxyethylene) fragment on the efficiency of cation transport by compounds **8**, Schafer and co-workers⁶⁵ have synthesised and studied derivatives **8b–e**. Study of the transport of the Li^+ , K^+ and Cs^+ cations through the phospholipid membrane showed that only compounds **8b–d** form single channels (determined on the basis of the current). The highest efficiency was found for compound **8d**, which is probably due to the most favourable ratio of the total chain length and the number of ethylene glycol fragments. The increase in the conductance of this channel in the series $Li^+ < K^+ < Cs^+$ is correlated with the increase in the ion radius of the cation (Li^+ , 78; K^+ , 133; and Cs^+ , 169 pm) and also with the decrease in the radius of the hydrated cation (Li^+ , 382; K^+ , 331; Cs^+ , 329 pm). Apparently, in this case, the pore diameter varies from 340 to 660 pm.

When comparing the compound **8d** and gramicidin D regarding their ability to carry cations, it should be noted that in the case of gramicidin D, the highest ionic conductance of vesicles is observed when its concentration is as low as $1 \mu\text{mol litre}^{-1}$ (further increase in the gramicidin D concentration to $5 \mu\text{mol litre}^{-1}$ does not increase the ionic conductance). Conversely, an increase in the concentration of compound **8d** up to $20 \mu\text{mol litre}^{-1}$ still induces an increase in the conductance of the vesicle. This implies that the formation of the ion channel involves more than two molecules of **8d**, unlike gramicidin D. It was assumed⁶⁵ that the molecules of **8** are associated according to the 'head-to-tail' pattern, because only in this case can the hydrophilic part of the channel-forming compound extend throughout the whole membrane.

3. Biomimetic oligo-(*R*)-3-hydroxybutyrate

The low-molecular-mass polyhydroxybutyrates composed of 50–150 residues of (*R*)-3-hydroxybutyrate and oligohydroxybutyrates composed of less than 50 residues are common in prokaryotic and eukaryotic cells, where they form numerous coordination bonds with cations. They are able to transport ions through a phospholipid membrane in model planar bilayer systems and in liposomes. However, these channels have low selectivity and low sensitivity to the change in the transmembrane potential.⁶⁶ In

addition, for ion transport, it is necessary to build-in large amounts of these substances ($> 0.1\%$) in the membrane.⁴ Das *et al.*⁶⁶ have gained a higher efficiency from this transport system. They prepared complexes of oligo-(*R*)-3-hydroxybutyrates **9** ($n = 18–22$) with inorganic polyphosphates, which demonstrate a higher cationic conductance ($275 \times 10^{-12} \Omega^{-1}$) compared to that of the complexes formed by poly-(*R*)-3-hydroxybutyrates ($n = 120–140$) with polyphosphates ($100 \times 10^{-12} \Omega^{-1}$).



$n = 18–22$.

However, the selectivity of the transport of Ca^{2+} cations with respect to Na^+ cations by means of these oligomers is much lower than the selectivity of transport by polymers: 4:1 and $> 90:1$, respectively. These results confirm the hypothesis that polyphosphate fragments play the crucial role in the cation selectivity, while oligo- and poly-(*R*)-3-hydroxybutyrates are solvating agents (Fig. 15). Thus, the monodisperse biomimetic oligo-(*R*)-3-hydroxybutyrate/polyphosphate system can be efficiently used for the development of voltage-activated synthetic ion channels with a limited cationic selectivity (Fig. 16).

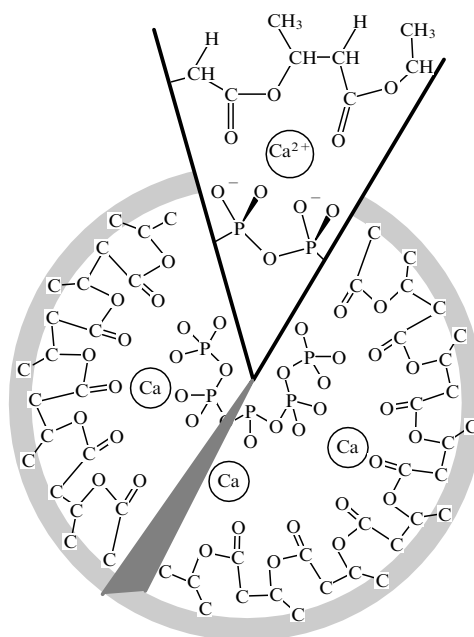


Figure 15. Structure of the channel formed by oligo-(*R*)-3-hydroxybutyrates with inorganic polyphosphates (vertical view).⁶⁸

The formation of ion-selective voltage-activated channels by poly-(*R*)-3-hydroxybutyrate/polyphosphate complexes has been considered in detail.⁶⁷ Complexes of these two polymers isolated from the plasmatic membranes of bacteria or obtained from synthetic polymers form voltage-dependent Ca^{2+} -selective channels in a planar bilayer membrane. The key factor in the solvation of calcium polyphosphates by polyhydroxybutyrates is the flexible core of the polymer and the optimal distance between the carbonyl groups of the ester fragments. In the models of channel complexes proposed by Reusch⁶⁸ and Seebach,⁶⁹ the highly polar poly-anionic polyphosphates are shielded from the hydrophobic region of the bilayer by amphiphilic polyhydroxybutyrates. As a result, numerous sites of cation binding are formed between the two polymers, *i.e.*, irregular binding cavities formed by the phosphoryl oxygen atoms belonging to the polyphosphate and the oxygen

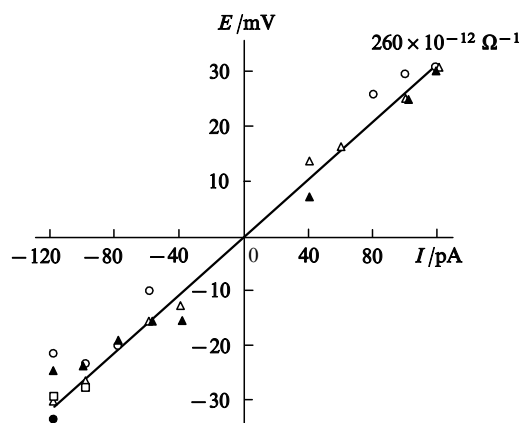


Figure 16. Current–applied voltage dependence for the channel complexes of oligo-(*R*)-3-hydroxybutyrate with polyphosphates. Different designations of experimental points correspond to values obtained in parallel experiments.

atoms of the ester groups of poly-(*R*)-3-hydroxybutyrate, which bind more readily the Ca^{2+} cation than the Mg^{2+} cation.

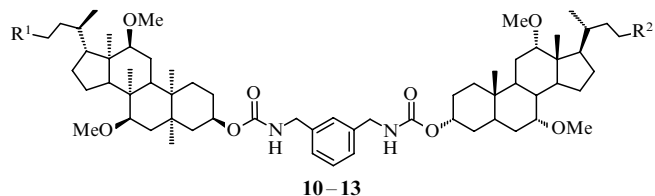
4. Voltage-dependent channels based on cholic acid derivatives

The natural transport proteins are characterised by a high degree of controllability. Transition from the closed to the open (or conductive) state is usually induced by a particular process: phosphorylation, binding of small molecules (acetylcholine, Ca^{2+} and so on) or a change in the transmembrane potential. Conversely, most synthetic ion channels cannot be controlled: they switch from the closed to the open state as a result of random aggregation processes in the lipid bilayer.

The regulation of the permeability of bilayer membranes by applying a voltage is one of the fundamental approaches to the control of the overall conductance of ion channels and to the design of new supramolecular ionic devices (selective filters, conductors and so on) and pharmaceuticals. Voltage-dependent channels are opened or closed upon application of a voltage higher or lower than a certain critical value. Only a few studies dealing

with the preparation of synthetic voltage-dependent ion channels have been published to date.

The design of voltage-dependent ion channels **10–13** on the basis of cholic acid and its derivatives has been reported.^{70, 71} Compounds **10–13** are formed upon cross-linking of two fragments of cholic acid or its derivatives by a *m*-xylylenedicarbamate bridge.



$\text{R}^1 = \text{R}^2 = \text{CO}_2\text{H}$ (**10**), $\text{CH}_2\text{OC(O)CH}_2\text{N}^+(\text{CH}_3)_3\text{Cl}^-$ (**11**);

$\text{R}^1 = \text{OP(O)(OH)}_2$, $\text{R}^2 = \text{CO}_2\text{H}$ (**12**); $\text{R}^1 = \text{CO}_2\text{H}$, $\text{R}^2 = \text{OH}$ (**13**).

The length of channels formed by these compounds approximately corresponds to the thickness of the bilayer membrane (~ 40 Å). The rigid amphiphilic steroidal frameworks of compounds **10–13** have a favourable effect on the stability of the resulting channels. In order to elucidate the effect of the electric asymmetry of the ion channel on the possibility of controlling the channel by means of an applied transmembrane potential, two types of compounds have been prepared, those with identical (compounds **10**, **11**) and different (compounds **12**, **13**) terminal hydrophilic groups. The electric asymmetry of the structures of compounds **12** and **13** was attained by introducing different terminal hydrophilic groups, namely, a carboxy group and a phosphoric acid fragment and a hydroxy and carboxy groups, respectively.

In a bilayer membrane, compounds **10–13** formed stable single ion channels having long open durations (200 ms to 4.7 s); in addition, with a positive potential applied, higher ion currents were observed than on application of a negative potential, *i.e.*, an essential non-linearity of voltammetric characteristics was observed. Taking into account the cation selectivity of the channels formed by compounds **12** and **13** (for example, for channel **12**, the $P_{\text{K}^+}/P_{\text{Cl}^-}$ ratio is equal to 11), the researchers suggested that in a channel formed by compound **12**, the potassium cations move from the phosphoryl end of the molecule to the carboxylate one. The functioning of the channel based on compound **12** is schematically illustrated in Fig. 17.

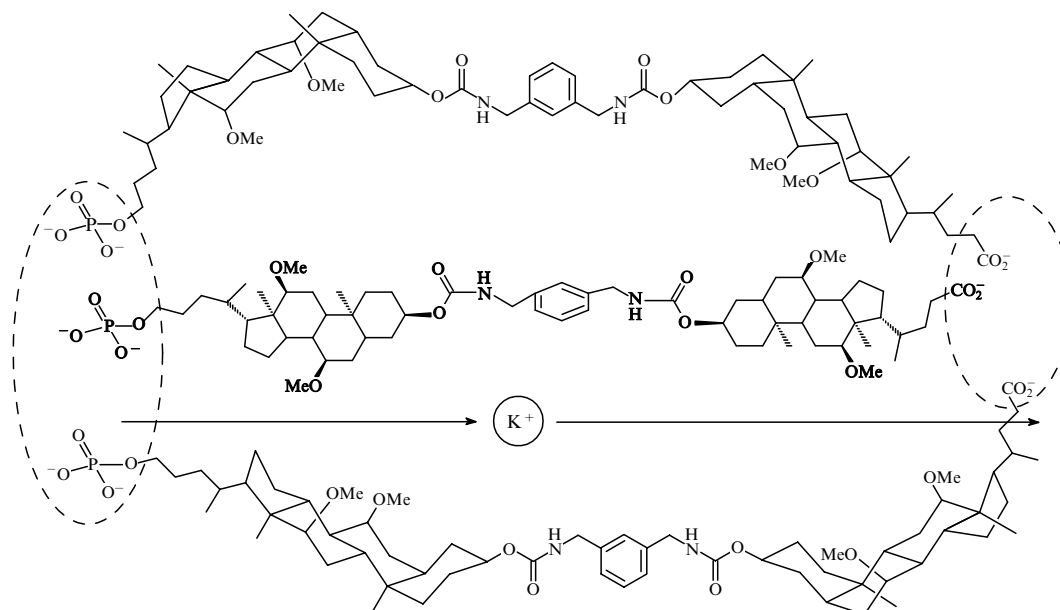
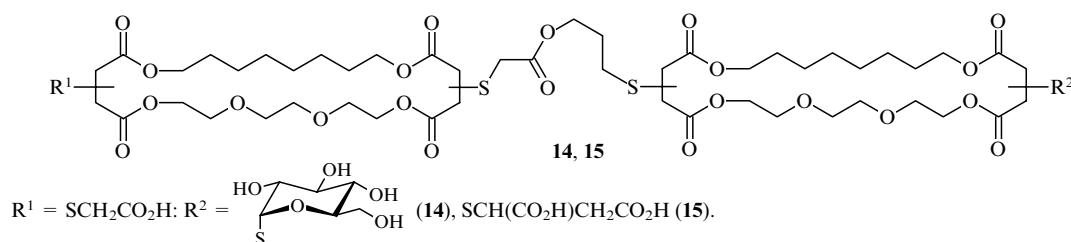


Figure 17. Movement of the potassium cation in channel **12**.⁷¹



5. Voltage-dependent ion channels based on bismacrocylic amphiphiles

Fyles *et al.*¹² described the synthesis of bismacrocylic amphiphilic compounds **14** and **15**, where groups able to carry different charges are located on the opposite ends of the molecule, in particular, a mercaptoacetate (1−) and a thioglucose (neutral) group in compound **14** and a mercaptoacetate (1−) and a mercaptosuccinate (2−) group in compound **15**. The presence of such groups imparts a substantial dipole moment to compounds **14** and **15** and favours fixing of these molecules on the surface of a bilayer membrane.

It was found that the presence of a negatively charged (1−) and neutral end groups in compound **14** gives rise to an ion channel, characterised by regular changes in the ionic conductance. However, the voltammetric characteristics of such a channel proved to be almost linear, *i.e.*, opening of the channel did not depend on the voltage applied. This was attributed to a random orientation of the channel-forming molecules **14** in the membrane. Meanwhile, compound **15** forms a channel due to asymmetric orientation in the diphtanoyl phosphatidylcholine bilayer membrane such that the succinate group is located predominantly on the *cis*-face of the bilayer. As a result, a non-linear voltammetric characteristic of the channel is observed (similar to that typical of the alamethicin channel) with an opening threshold of about −30 mV (Fig. 18, curve 1). The drawbacks of this channel include the unstable behaviour of its opening and functioning. The non-linear voltammetric characteristic is observed only for the first cycles and disappears after 10–15 min of channel operation (Fig. 18, curve 2). The time the channel remains in the open state is exceptionally short, being equal to 0.5–10 ms. The current amplitude is variable and can change by an order of magnitude (1–10 pA). Thus, the qualitative characteristics of these channels, namely, the ‘explosive’ opening, variable flux values per opening, and low cationic selectivity, are indicative of a relatively low degree of structuring of the resulting channels.

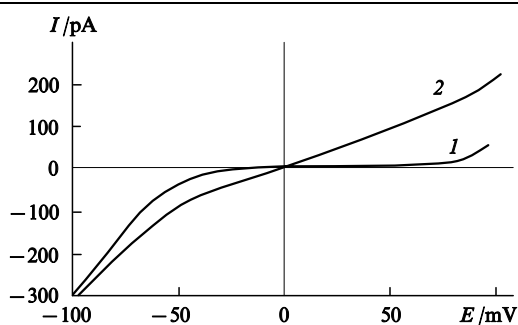


Figure 18. Voltammetric characteristics of the ion channel based on compound **15** (118 nmol of **15**, 1 M LiCl, diphtanoyl phosphatidylcholine) with 1–7 (1) and 8–20 (2) cycles.

The presumptive mechanism of the functioning of voltage-dependent channel **15** is shown in Fig. 19.

Apart from the non-specific pre-association of compound **15** with the bilayer (structure **A**), the researchers also considered

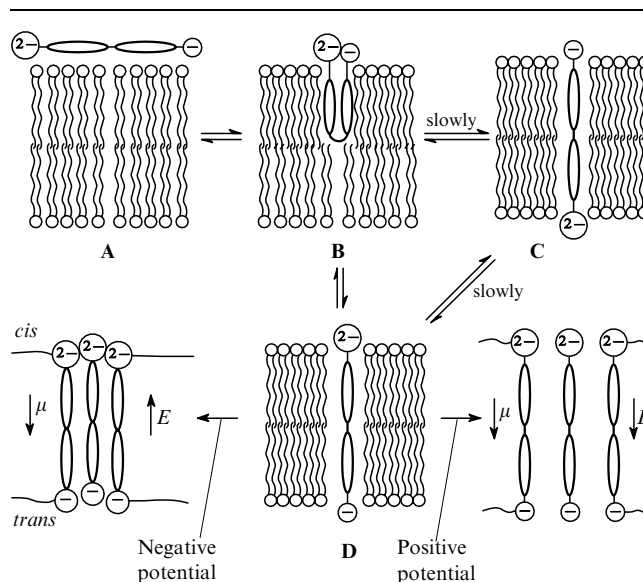


Figure 19. Presumptive mechanism of operation of the voltage-dependent channel formed by **15**.

other types of association of this compound with the bilayer giving intermediate U-shaped (**B**) and transmembrane (**C** and **D**) structures. Since the processes involving penetration of the succinate dianion terminal group through the lipophilic membrane (transition from structure **B** to structure **C** and from structure **D** to structure **C**) occur more slowly than the processes of penetration of the acetate monoanion group (transition from **B** to **D**), it can be suggested that structure **D** with the succinate terminal group located on the *cis*-face of the bilayer is the first to be formed (see Fig. 18). In this case, opening or closure of the channel is due to parallel or antiparallel arrangement of the molecular dipole moment and external field vectors. Since the electrostatic repulsion of the succinate groups should be substantial, the degree of aggregation would depend appreciably on the stabilisation of the resulting supramolecular system due to the external electric field. In the case of antiparallel orientation of the dipole moment and external field vectors, ion-conductive aggregates are formed at negative potentials on the bilayer surface and the system proves to be more stable. The parallel orientation results in destabilisation, predominance of the electrostatic repulsion of likely charged terminal groups and destruction of ion-conductive aggregates.

6. The formation of supramolecular ion channels by amphiphilic ion pairs

Kobuke *et al.*^{72–74} have designed amphiphilic compounds able to be incorporated into bilayer membranes by combining a hydrophilic oligoether and a hydrophobic alkyl chain in an ion pair formed by an ammonium cation and carboxylate or phosphate anions. The researchers synthesised two types of amphiphilic ion pairs with the hydrophilic component represented by either an anion (compounds **16** and **17**) or a cation (compounds **18–21**).

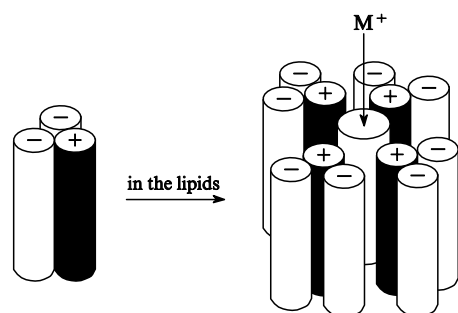


Figure 20. Schematic view of the structure of supramolecular ion half channel formed by an amphiphilic ion pair. The black and white columns designate the hydrophilic and hydrophobic parts of the ion pair, respectively.

The presence of the hydrophilic oligoether moiety in the ion pair results in supramolecular aggregation of ion pairs. The hydrophilic parts of ion pairs in the aggregates are 'expelled' from the hydrophobic lipid membrane to give a half ion channel (Fig. 20). Further tail-to-tail dimerisation of these half channels forms a full single channel. It is evident that the stability of these supramolecular ensembles would depend on the hydrophilic–lipophilic balance within the amphiphilic ion pairs. The most stable channels were found to appear when the hydrophobic parts of the ion pairs contain two alkyl chains (compounds **17**, **19**, and **20**). The ion pairs containing one alkyl chain (compounds **16** and **18**) form channels with low stability. The ion pair **21** does not form channels at all. Probably, in this case, the four hydrophobic chains of cardiolipin mask the oligoether chain of the cation, thus hampering the formation of a supramolecular ensemble in the lipid membrane.

All the ion channels studied showed a cation selectivity (cations are transferred more efficiently than anions). For example, for channels **19** and **20**, the P_{K^+}/P_{Cl^-} values are equal to 4.9 and 16.8, respectively. Moreover, this is observed despite the

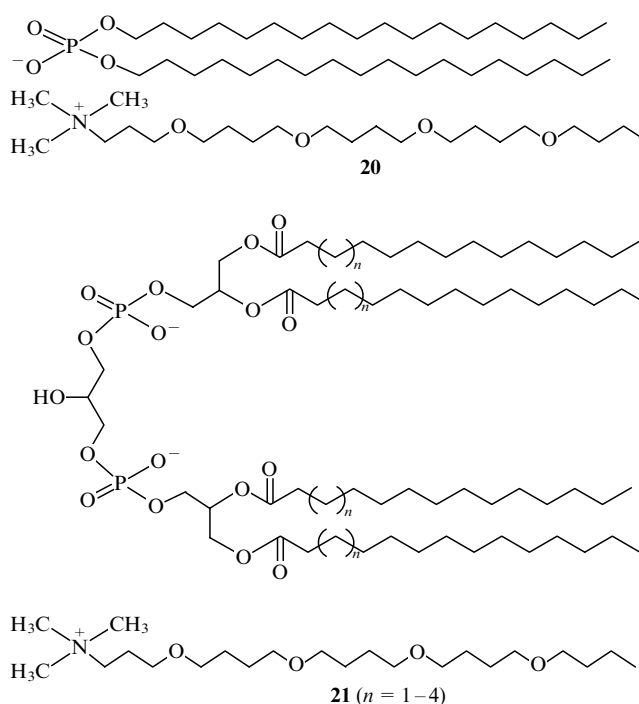
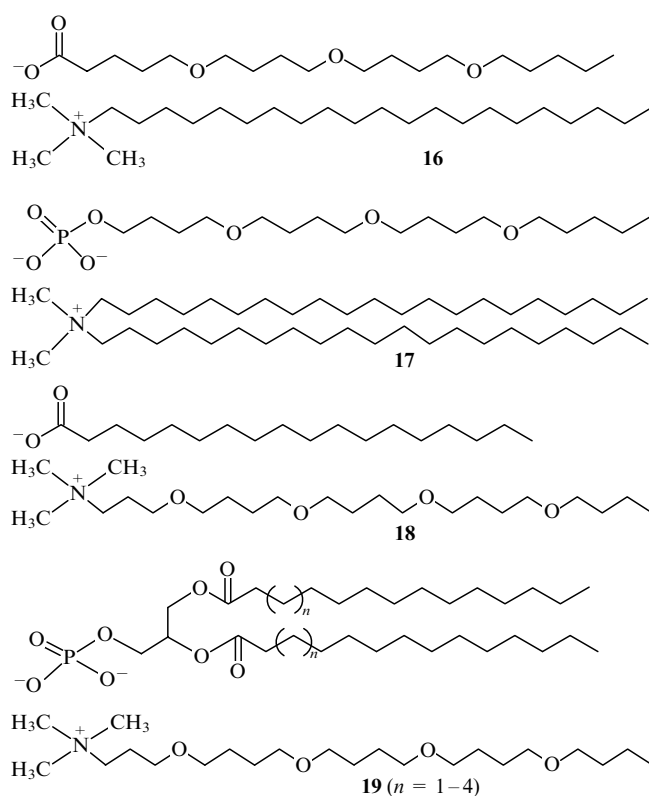
different characters of the anionic terminal groups in the hydrophobic component of the ion pair. Thus, the pattern of selectivity is determined by the nature of the intramembrane walls of the channel rather than by the type of terminal groups which form the entrance of the channel.

The discovery of voltage-dependent ion channels represented one more important result of this study. The probability of opening and closure of the channels formed from ion pairs of the monoammonium cation and the alkyl phosphate dianion (compounds **17** and **19**) depends on the voltage applied. Meanwhile, the ion pairs consisting of the monoammonium cation and the carboxylate (compounds **16**, **18**) or dialkyl phosphate (compound **20**) monoanions do not form voltage-dependent ion channels.

As noted previously, the presence of different charges (dipole moment) on the opposite ends of the channel is a necessary condition for the functioning of voltage-dependent ion channels. It is clear that the degree of aggregation of amphiphilic ion pairs in the half channel depends on many factors, and aggregates of diverse compositions are formed in the membrane. As a result, a single channel assembled from two such half channels has different negative charges on the opposite ends; in other words, it has a dipole moment. However, the dipole moments for different single channels assembled from two half channels in a random way are dissimilar and cannot be controlled. Therefore, the voltammetric characteristics of the resulting channels vary from one experiment to another.

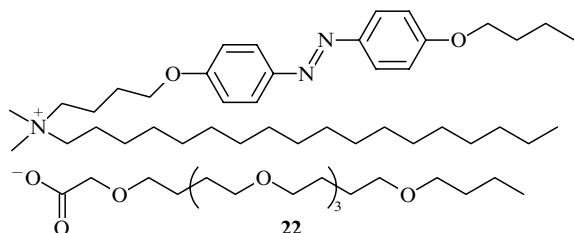
7. Photochemical control of the ion transport using compounds containing an azobenzene fragment

The photochemical method for controlling ion channels based on modified gramicidin peptides has been reported in several publications.^{75–77} Schreiber and coworkers⁷⁵ have found that the gramicidin dimer containing an azobenzene bridging fragment in the *cis*-form acts as an ion channel. Higuchi *et al.*⁷⁶ have shown that in the case of azobenzenes linked to the α -helix of bispolyglutamate, the overall ion flux is controlled by photoisomerisation. Woolley and co-workers⁷⁷ have observed the variation of a single ion flux induced by isomerisation of the azobenzene fragments attached to the channel gate of gramicidin. On exposure to



laser radiation with a wavelength of 337 nm, the channels pass from the *trans*-state characterised by the highest flux levels of 14.9 ± 0.4 pA and lower current levels of 0.6 ± 0.1 pA to the *cis*-state with a flux level of 12.8 ± 0.4 pA and three current levels, 1.1 ± 0.1 pA (first level), 2.6 ± 0.1 pA (second level) and 3.5 ± 0.2 pA (third level). The subsequent illumination of the *cis*-channels by a 100-W table lamp for 10 min resulted in the transition into the *trans*-form.

Kobuke and Ohgoshi⁷⁸ have synthesised and studied a supramolecular synthetic ion channel based on *N,N*-dimethyl-*N*-octadecyl-*N*-[4-(4-butoxy)-*trans*-azophenoxy]butylammonium 3,8,13,18,23-pentaoxaheptacosanoate (**22**). The channel is an amphiphilic ion pair which isomerises on exposure to photo-radiation.



After this ion pair (single channel) had been incorporated into a planar phospholipid membrane, an ion flux was passed through it (Fig. 21). An important characteristic of this channel is that the period when the channel is open is longer than the period when the channel is closed. The channel based on compound **22** has shown different values of electrical conductivity, most of all, in the range of $(2-13) \times 10^{-12} \Omega^{-1}$. The channel was found to be selective for the potassium cation with respect to both the chloride anion and the sodium cation: the permeability ratios are as follows: $P_{K^+}/P_{Cl^-} = P_{K^+}/P_{Na^+} = 6.1$.

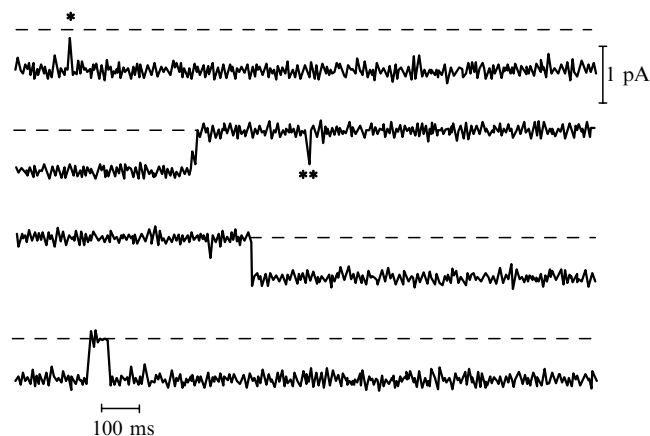


Figure 21. Current created by *trans*-azobenzene ion pair **22** at a voltage of 96.9 mV in a 500 mM solution of KCl and 5 mM Tris – HEPES buffer (pH 7.2) [Tris is tris(hydroxymethyl)aminomethane, HEPES is *N*-2-hydroxyethylpiperazine-*N'*-ethanesulfonic acid]. The dashed line corresponds to a closed channel. The short-lived opening and closure of the channel were observed at the points marked by one and two asterisks, respectively.

Upon photoirradiation at 367 nm, the *trans*-azobenzene fragment passes to the *cis*-form (Fig. 22). This isomerisation results in channel closure and the current does not pass through it. The subsequent transition of the *cis*-azobenzene fragment to the *trans*-form resumes the ion flux through single channels. Thus, the photocontrol of the channel throughput capacity was attained.⁷⁸

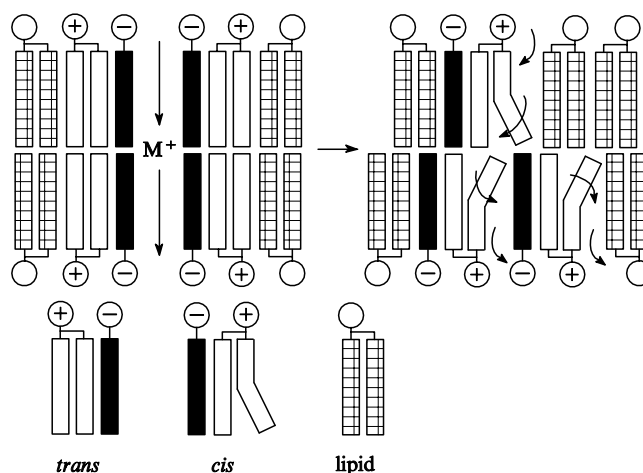


Figure 22. Possible mechanism of the photochemical control of the ion flux with the use of ion pair **22**.

V. Ion channels based on crown ethers

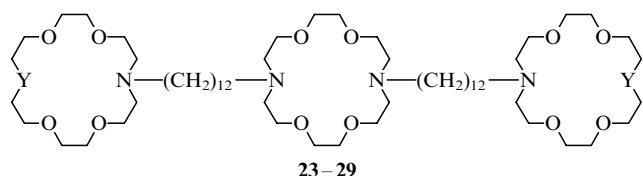
1. Tris- and tetrakis(diazacrown ether) channel-forming structures

Crown ether derivatives are convenient models for investigating the mechanism of functioning of ion channels in bilayer phospholipid membranes. In artificial channel-forming systems, crown ethers are used as either head groups or binding sites for the corresponding ion.

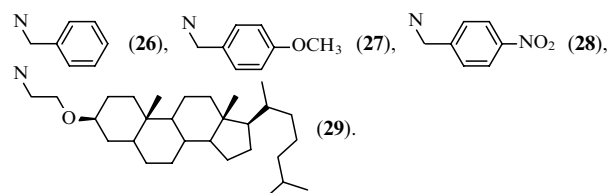
It has been shown^{79,80} that *N,N'*-bisalkylated and *N,N'*-bisbenzylated diaza-18-crown-6 ethers are self-aggregated in the solid phase to form channel-like ensembles. The length of the supramolecular structures thus formed determined by laser light scattering was 2000–3000 Å; the aggregates of alkylated diaza-18-crown-6 derivatives proved to be more stable than the aggregates of benzylated derivatives.

Meadows *et al.*⁸¹ reported that complexes of propargyl-substituted diaza-18-crown-6 with KBF_4 form a channel-like extended structure whose supramolecular organisation indicates that the diaza-18-crown-6 molecule within synthetic channels can play the same role as water that forms the hydration shell in natural proteins. This structure formed by cations and donor groups can mimic the natural cationic channels located in the lipid bilayer.

The amphiphilic nature of crown ethers allows one to use them as the channel gate. A substantial contribution to the understanding of the principles of design and functioning of artificial ion channels based on crown ethers was made by Gokel and co-workers.^{10,13,82,83} In particular, they synthesised a series of tris(diaza-18-crown-6) compounds **23–29**,⁸² which demonstrated the ability to be incorporated into lipid membranes to form ion channels.



Y = O (**23**), NH (**24**), $N(CH_2)_{11}CH_3$ (**25**),



For estimating the efficiency of the ion transport, two methods have been used most often, namely, determination of the exchange rate of the sodium cation in the vesicles by ^{23}Na NMR dynamic spectroscopy using shift reagents and determination of the conductance of planar bilayer membranes.

To establish the mechanism of action of synthetic channels based on tris(macrocyclic) systems, one should answer three main questions. The first one concerns the possibility of explaining the differences in the fluxes of the Na^+ cation through a bilayer membrane by different solubilities of ionophores in the membrane. For this purpose, the distribution coefficients of tris(crown ethers) **23–29** in the octanol–water system were calculated. The calculation showed that all the compounds studied occur preferably in the lipid bilayer: the ratio of the distribution coefficients is $10^{10}:1$ (i.e., the crown ethers occur entirely in the membrane phase).⁶⁰

The second question concerns the ion transport, because the ability of crown ethers to function as cation carriers is well known.⁸⁴ In order to answer this question, it was necessary to determine the mode of functioning of the systems of interest, whether they are ion carriers or ion channels. Therefore, experiments were carried out on Na^+ transport through lipid and bulky chloroform membranes by means of crown ethers **23–29**. It is evident that the transport through a chloroform membrane cannot occur by the channel mechanism, because in this case, the distance between the source and receiving aqueous phases is too great, unlike that in a bilayer lipid membrane. Figure 23 presents the measured rate constants for the transport of the Na^+ cations by crown ethers **23–29** in the lipid bilayer and chloroform membranes. For comparison, similar experiments were carried out with gramicidin (the natural channel-forming peptide) and valinomycin (a natural receptor of Na^+ ions).

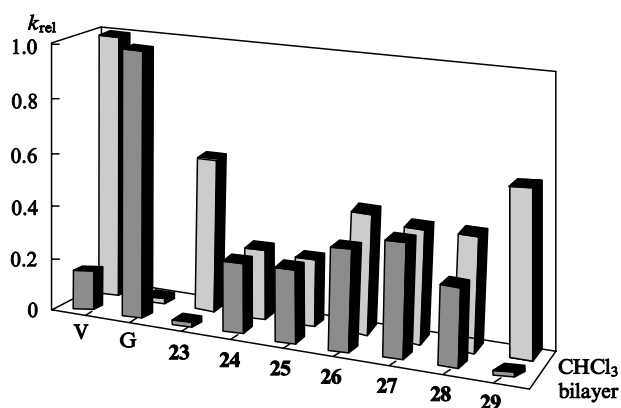


Figure 23. Comparison of the efficiency of Na^+ transport by compounds **23–29**, gramicidin (G) and valinomycin (V) through chloroform and lipid bilayer membranes.

It can be seen from Fig. 23 that most of the compounds **23–29** studied are less active ion carriers than natural compounds. As expected, valinomycin proved to be the most efficient carrier, while gramicidin was the most effective channel-forming compound. The lack of correlation between the rates of transport of Na^+ ions through phospholipid and chloroform membranes by tris(crown ethers) **23–29** confirmed that they function in a bilayer membrane as channel-forming agents rather than mere ion carriers.

Finally, the last question concerns the role of the terminal residues of the crown ethers, whether they are the head groups through which the cations pass when they enter or leave the membrane? If the terminal crown-ether fragments function as the input elements of the channel, the transport efficiency should depend on the electron density on the macrocycle and on the nature of the substituents at nitrogen. Experiments with com-

pounds **26–28**, which differ only in substituents (H, OCH_3 and NO_2) in the benzene ring, showed a positive effect of electron-donating substituents on the ion flux. This influence is quite understandable, as an increase in the electron density at the entrance of the channel is expected to accelerate the transport of cations through the channel. On that ground, Murillo *et al.*⁸² suggested that the terminal residues of crown ethers are the head groups of the ion channel through which the cations pass.

Further investigation of tris(diaza-18-crown-6 ethers) as channel-forming structures in bilayer phospholipid membranes allowed researchers to propose a structure for the ion channel formed (Fig. 24).⁸³ They suggested that water molecules fill the channel and assist in the cation transport. This suggestion was based on the known fact that a chloroform membrane containing some tris(macrocyclic) compounds becomes rapidly saturated with water.

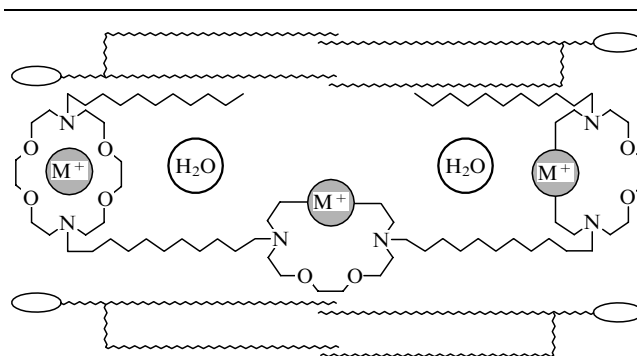
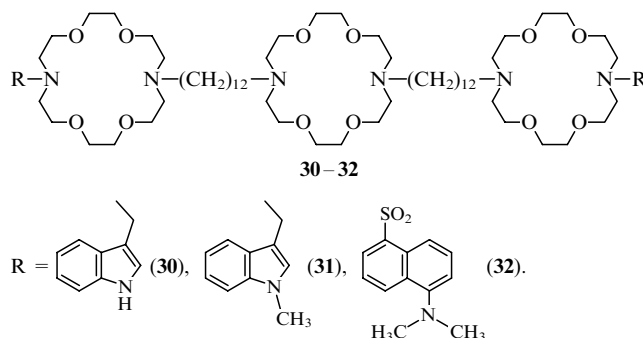


Figure 24. Structure of the ion channel formed by tris(diaza-18-crown-6 ether) **25**.¹³

Subsequently, Gokel and co-workers¹³ proposed using heterocyclic compounds as the terminal fragments of tris(macrocyclic) structures based on diazacrown ethers. It is known that side groups of some amino acid residues in transmembrane proteins serve to fix the protein helices relative to each other and relative to the bilayer membrane.⁴ This role is often performed by the indole fragment of tryptophan. It was shown by NMR spectroscopy that numerous tryptophan residues present in the gramicidin channel are directed toward the water–bilayer membrane interface. Therefore, Gokel chose indole as the terminal heterocyclic fragment. He prepared a series of compounds with the general formulae **30–32**, which were used to create ion channels in phospholipid vesicles. It was demonstrated experimentally that *N*-alkylindoles are able to form stable vesicles with neutral head groups represented by crown-ether fragments which control the cation transport (channel gate). The C_{12} hydrophobic bridge in tris(diazacrown ethers) **30–32** can be oriented in the membrane parallel to the lipid chains. Generally, the length of these tris(macrocyclic) channels proved to be sufficient to bridge the hydrocarbon region of the membrane and to form a channel.

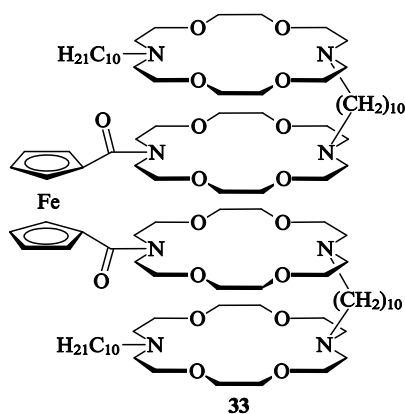


Compounds **31** and **32** are able to transfer the sodium cation in the bilayer membrane, unlike compound **30**. This can be attributed to the fact that compound **30** forms in the membrane a hydrophilic globular conformation due to strong intramolecular hydrogen bonding between the NH groups of the indole substituent and heteroatoms of the macrocycle.

The synthesis of tetrakis(diazacrown ether) **33** has been described.⁸⁵ The researchers linked two macrocyclic fragments connected by long aliphatic chains to the central ferrocene fragment capable of functioning as a cationic 'filter'.

The length of the resulting channel was ~ 30 Å, which corresponded to the thickness of a typical biological membrane. It was assumed that variation of the head groups would create the basis for controlling the cationic selectivity.

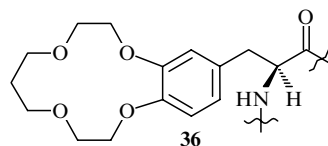
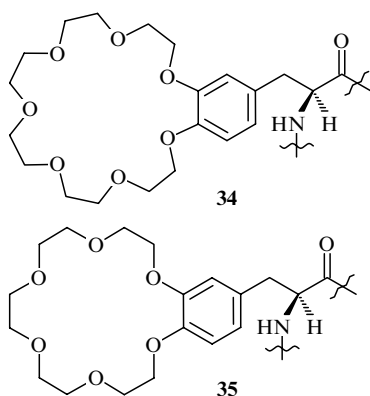
Cyclic voltammetry studies of compound **33** showed that the strength of the coordination interaction of the Na^+ ion with the amide group of the ferrocene fragment decreases as the channel becomes filled with cations, which can be explained by charge repulsion. This does not occur for Ca^{2+} ions, apparently, due to their stronger coordination to the amide groups.



The transport of ions through such channels has been studied using biological membranes (fragments of hamster brain cells). The change in the membrane potential from -60 to $+60$ mV decreased the transmembrane cation flux following the accumulation of positive charge on the inner side of the cell. At -80 mV, the amplitude of the mean K^+ flux through a single channel was -4.0 pA, which corresponded to a conductance of $50 \times 10^{-12} \Omega^{-1}$. For a potential of 80 mV, this value was 2.4 pA ($30 \times 10^{-12} \Omega^{-1}$). These results indicate that the activity of these channels can be controlled to some extent by varying the applied voltage.

2. Artificial ion channels based on peptides containing crown-ether fragments

Voyer and co-workers^{86,87} proposed that crown ether fragments **34–36** be used for the creation of ion channels with a new architecture on the basis of synthetic peptides.



They synthesised a series of peptides **37–41** consisting of 21 amino acid residues carrying six crown ether fragments:

N-BOC-(Leu-**34**-Leu₃-**34**-Leu)₃-OMe (**37**),
N-BOC-(Leu-**35**-Leu₃-**35**-Leu)₃-OMe (**38**);
N-BOC-(Leu-**36**-Leu₃-**36**-Leu)₃-OMe (**39**);
N-BOC-(Leu-**36**-Leu₃-**36**-Leu)₃-OH (**40**);
H₂N-(Leu-**36**-Leu₃-**36**-Leu)₃-OH (**41**).

Since peptide **37** contains 15 L-leucine residues of the total 21 amino acid residues, it is sufficiently hydrophobic to be incorporated in a lipid membrane. Therefore, the channel is formed most likely due to stacking of crown ether rings (Fig. 25).

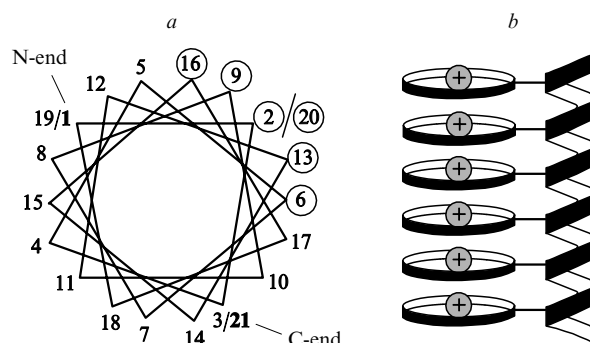


Figure 25. Axial projection of the α -helix of the hexacrown peptides **37–41** (a, the circles mark the sites of attachment of the crown ethers) and scheme of the channel formed by these peptides in the bilayer membrane (b).

Studies of the conformations of hexacrown peptide **37** and its analogues **38–41** by polarimetry and FT IR spectroscopy have shown that they exist as two forms, **A** and **B** (Fig. 26), which occur in equilibrium. Peptides existing in the inactive form **A** are adsorbed on the bilayer surface, while peptides in the active form **B** are arranged parallel to the aliphatic tails of lipids.

Aggregated crown peptide is adsorbed from a solution on the surface of a bilayer membrane. The adsorbed inactive form **A** of the peptide, partially immersed in the membrane, is reorganised to the active form **B** (see Fig. 26). It is noteworthy that in both the membrane and the solution, peptides occur in the stable α -helical conformation.

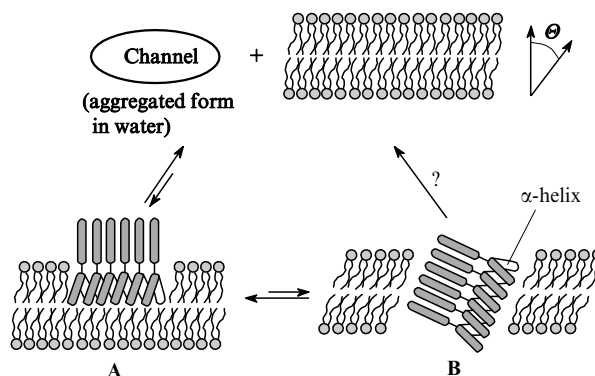


Figure 26. Model of the formation of the channel from peptides **37–41**. **A** is the inactive form, $\theta = 90^\circ$; **B** is the active form, $\theta = 30^\circ$.

VI. The use of 'bouquet' structures for the design of synthetic ion channels

1. 'Bouquets' based on 18-crown-6 and β -cyclodextrin

Lehn and co-workers^{88–91} used polyfunctional macrocycles, β -cyclodextrin and 18-crown-6 as the 'platform' for the design of artificial ion channels. It is common knowledge that crown ethers form labile complexes with alkali metal cations and that cyclodextrins have rigid cavities which are sufficiently large for hydrated alkali metal cations to pass through them. To make these channels amphiphilic, polyoxyethylene or polymethylene chains with polar terminal groups were linked to the macrocyclic 18-crown-6 and β -cyclodextrins.^{88,89} Four compounds differing in the type of central structure and the type of podand chains have been prepared in this way (the structures of two such compounds **42** and **43** are presented below). These compounds have been called 'bouquets'.

The ability of compounds **42** and **43** to be incorporated into phosphatidylcholine bilayers of the vesicles was studied by a number of methods (circular dichroism, UV/Vis spectroscopy, differential scanning calorimetry and so on).^{88,89}

It was found that the 'bouquets' are incorporated in the bilayers in two modes: in the U-mode (both hydrophilic ends are arranged on one side of the membrane) and in the transmembrane mode.

The transport of metal cations (Li^+ and Na^+) induced by the 'bouquet' compounds incorporated in liposomes⁹⁰ has been studied by NMR on alkali metal nuclei with a shift reagent (a 3:1 mixture of tetramethylammonium tripolyphosphate and dysprosium chloride), which allows one to distinguish between the signals from intraliposome metal cations (no shift) and those from extraliposome metal cations (a shift is observed). Upon creation of opposite gradients for the concentrations of Li^+ and Na^+ cations, the 'bouquets' induced the cation transport according to the antiport mechanism. The rate constants for ion transport calculated for the 'bouquets' based on 18-crown-6 with

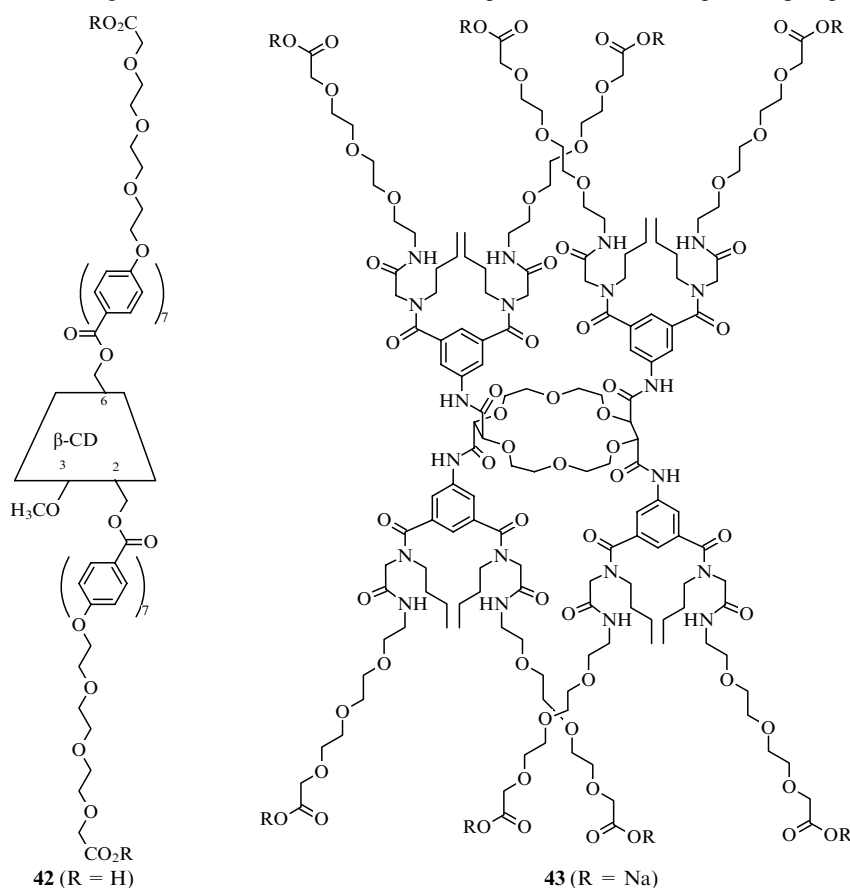
polyoxyethylene and polymethylene chains were, on average, 6×10^{-3} and $10 \times 10^{-3} \text{ min}^{-1}$, respectively. While studying the cation transport along channels based on 18-crown-6, the researchers found out that an increase in the concentration of a compound in a membrane enhanced the transport only for the channel with polymethylene chains.

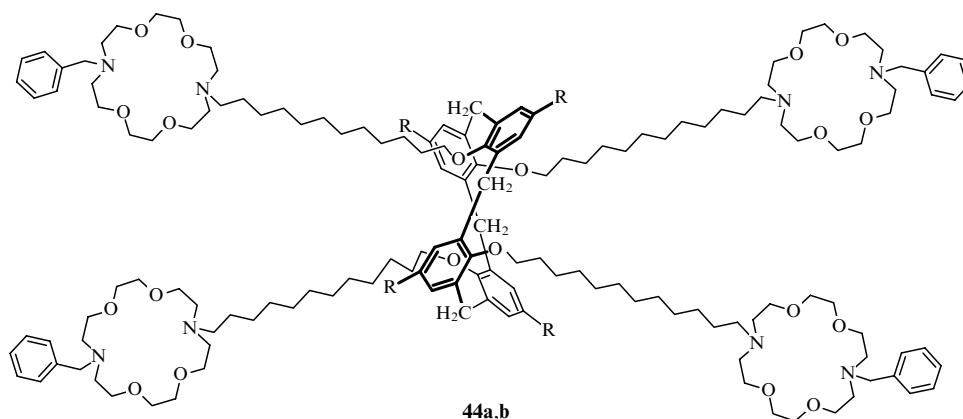
In order to distinguish between two transport mechanisms (an ion channel or an ion carrier), the transport rate through the membrane under usual conditions was compared with the transport rate through a frozen membrane. Switching to the gel state is expected to cause a substantial decrease in the rate of the ion flux for a carrier, which executes shuttle movements in the membrane, but to have almost no influence on the rate of the transport induced by a static channel structure. It was shown that the liquid crystal–gel phase transition did not result in a decrease in the transport rate only for two of the four 'bouquets', those based on cyclodextrin with polyoxyethylene chains and 18-crown-6 with hydrocarbon chains. The behaviour demonstrated by the compounds derived from 18-crown-6 with polyoxyethylene chains and from β -cyclodextrin with hydrocarbon chains does not allow one to classify them as channel structures; however, the results obtained do not indicate that they are ion carriers either.⁹¹

2. 'Bouquet' structures based on calixarenes

A few examples of using calixarenes for constructing artificial ion channels have been reported. A cyclic resorcinol tetramer with long alkyl chains has been synthesised and studied as an ion channel.⁹² It was found that this compound functions as a half channel with K^+ -selectivity. This channel is of interest as a model of natural ion-channel proteins having hydrophobic fragments. The uncharged and highly hydrophobic M2-segment of the nicotine acetylcholine receptor ...MTLSISVLLSLTVFLLVIV... can serve as an example.⁹³

The synthesis of two compounds based on calix[4]arene in the 1,3-alternate conformation (**44a,b**) has been described. In compounds **44a,b**, each phenol group of calixarene is connected





R = H (a), Bu^t (b).

through an oxygen atom to one dodecyl chain which ends with a 10-benzyl-1,10-diaza-18-crown-6 fragment.

The side chains in compounds **44a,b** are arranged on both sides of the central fragment, two chains on each side. The diazacrown fragments acting as head groups stabilise the distribution of side chains within the membrane. The total length of the channel is 34–60 Å, which is sufficient for bridging the lipid part of a typical bilayer membrane, whose average thickness is ~30 Å.⁹

The incorporation of compounds **44a,b** (1 mmol) in a bilayer membrane increases the membrane permeability for alkali metal cations [with smaller amounts of these compounds (1 nmol), the membranes show unstable permeability] (Fig. 27). The repeated introduction of solutions of compounds **44a,b** in the membrane increases the intensity and the frequency of the observed transitions (up to $300 \times 10^{-12} \Omega^{-1}$).

The probability for Na⁺ and K⁺ cations to flow through a calixarene platform has been estimated. In the solid state, the average distance between the centres of the aryl fragments in the 1,3-*alternate* calixarene conformation is 5.9 Å. This distance is sufficient for penetration of Na⁺ and K⁺ cations, because according to theoretical calculations, the benzene–M⁺–benzene distance in an ideal sandwich structure is 4.96 Å (for M = Na) or

5.84 Å (for M = K). Thus, it was shown that Na⁺ and K⁺ cations can flow through calix[4]arenes in the 1,3-*alternate* conformation.^{94,95}

However, in the case of tetra-*tert*-butylcalix[4]arene **44b**, the calixarene platform is completely blocked from both sides by bulky *tert*-butyl groups. To enable the flowing of cations through calixarene **44b**, the conformation must undergo a definite sequence of modifications: two aryl fragments should pass into the open state, to let the cation through, while the other two fragments are closed. Similar changes should take place at the other end of the molecule to let the cations out. However, at room temperature, calix[4]arene is unable to change its conformation. The results obtained by measuring the channel conductance for compounds **44a,b** did not allow the researchers to decide how the ions flow in such a channel, either through the macrocyclic ring of calixarene or outside the ring.

Compounds **44a,b** represent a new class of cation-conductive channels with a high level of conductance for the sodium and potassium cations. In these compounds, calixarenes in the 1,3-*alternate* conformation were used as the basic compounds for the design of ion channels.

VII. The use of the calixarene platform for the design of ion channels

1. The artificial ion channel based on a macrocyclic calix[4]resorcinarene with amphiphilic ester groups of cholic acid

As a result of further development of approaches to the preparation of nonpeptide ion channels — supramolecular and molecular half channels — Kobuke and co-workers⁹⁶ synthesised calix[4]resorcinarene **45** with four alkyl substituents. This compound forms a single ion channel with one conductance level. They also obtained a supramolecular ion channel on the basis of an amphiphilic derivative of rigid methyl cholate **46**. The channel

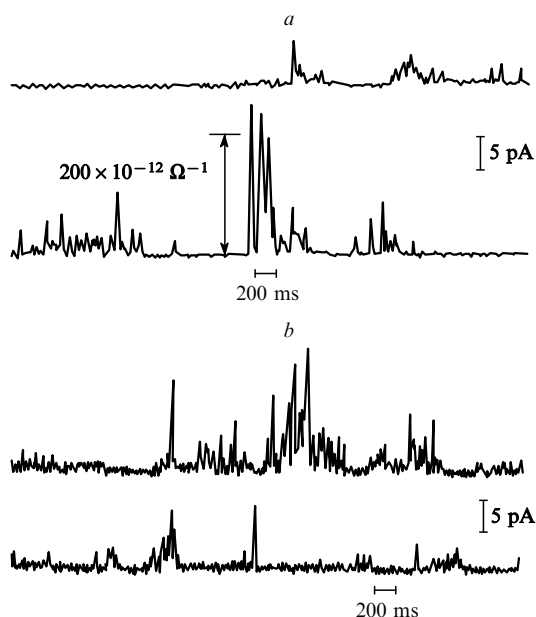
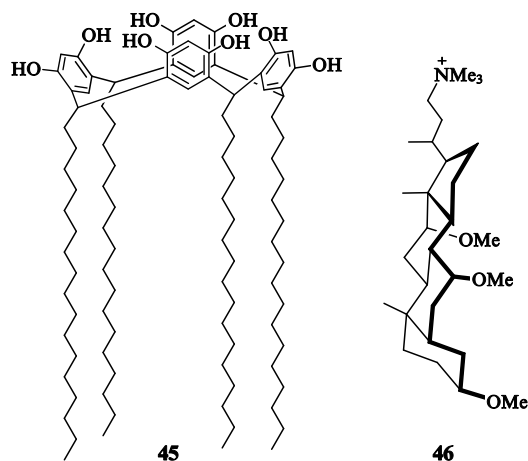


Figure 27. Conductance of compounds **44a** (a) and **44b** (b) (1 pmol each in THF, a 0.5 M solution of NaCl) in a planar bilayer membrane at 100 mV. For each compound, two different time sections are shown. The different patterns of these sections point to an unstable permeability regime.



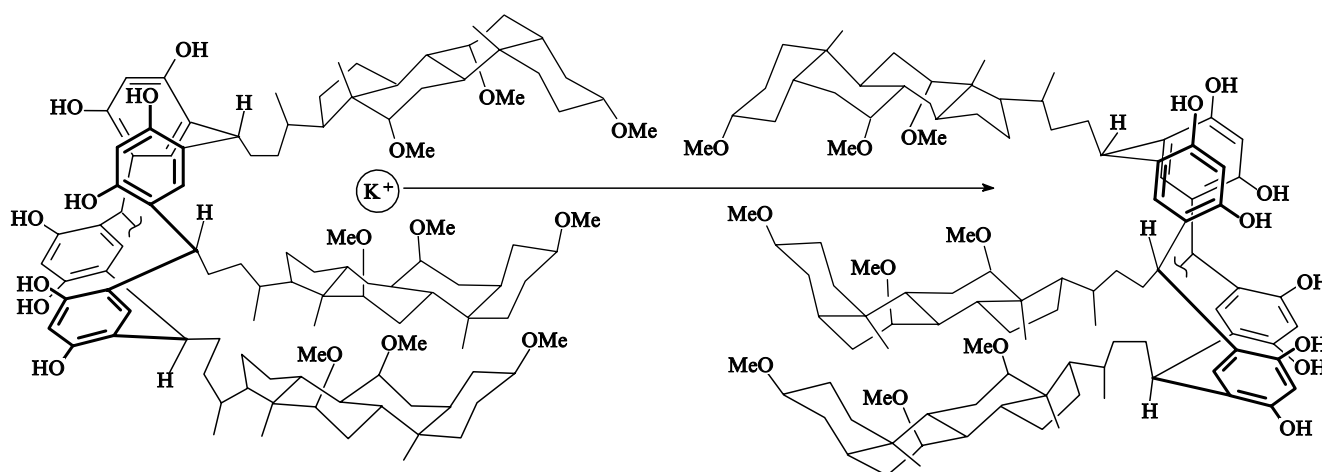


Figure 28. Ion channel formed from two calix[4]resorcinarene **47** molecules connected in the tail-to-tail mode (one methyl cholate residue is omitted for clarity).

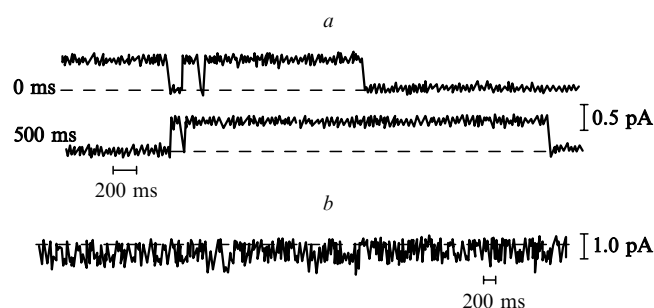
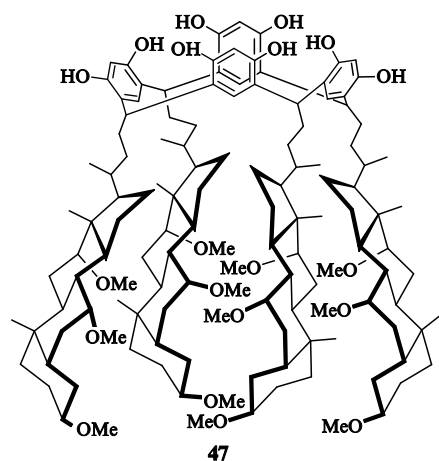


Figure 29. Time profiles of single channels **47** (a) and **45** (b). (a) 0.5 mol of KCl, pH 7.2, 70 mV; (b) 0.5 mol of KCl, pH 7.2, -74.4 mV.

formed by compound **46** in the bilayer membrane has a long open duration.

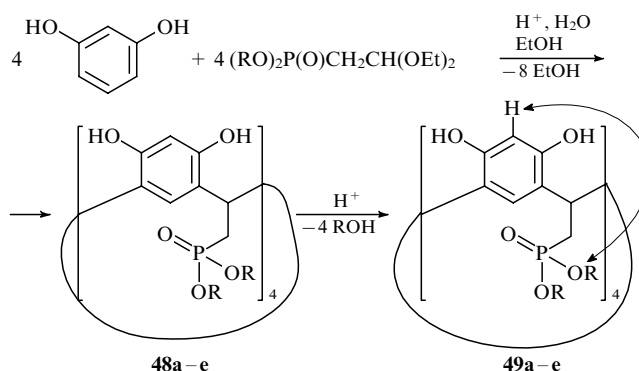
To prepare a molecular ion channel having one conductance level and a long open-state duration, calix[4]resorcinarene **47**, combining calixarene and methylcholine fragments, was synthesised. A study by ^{13}C NMR spectroscopy showed that compound **47** exists in a C_4 -symmetric conformation. The presence of hydrophilic head groups and amphiphilic steroidal fragments in calix[4]resorcinarene **47** allows the molecules in a bilayer membrane to form a tail-to-tail pair, which gives rise to a transmembrane channel (Fig. 28). The hydrophilic parts of the steroid groups form a hydrophilic pore around the central axis, whereas the hydrophobic parts are directed toward the lipid alkyl groups surrounding the channel. The ion channel formed by the molecules of compound **47** exists in the open state for a long time (Fig. 29).

On passing from compound **45** to compound **47**, the electrical conductance increases by 60%, but the cation/anion selectivity decreases simultaneously by 60%: the $P_{\text{K}^+}/P_{\text{Cl}^-}$ ratio decreases from 20 to 8. These changes attest to the formation of a more hydrophilic medium at the centre of the pore when steroidal fragments are used as side groups. The Na^+ and K^+ selectivities found for the channels based on calix[4]resorcinarenes **45** and **47** do not differ much, $P_{\text{K}^+}/P_{\text{Na}^+} = 3$ (for channel **45**) and 2.8 (for channel **47**).

The ion channels constructed from calix[4]resorcinarenes proved to be appropriate models for investigating the structure–function relationship in ion channels, as they exhibit one conductance level and the tail section can be varied. It should be noted that compound **47** has certain advantages over compound **45**, because the steroidal tail stabilises the open state of the channel

and promotes modification of the hydrophilic pore of the channel without a change in the general structure, which is confirmed by the values of conductance and selectivity of this channel with respect to cations.

A new approach to the design of ion channels on the basis of nanotubular structures has been developed by chemists from Kazan.^{97–100} It is based on self-stacking of functionalised calix[4]arenes through specific interactions (mainly, hydrogen bonding) between groups appropriately oriented in space. A series of amphiphilic organophosphorus calix[4]resorcinarenes self-assembled due to the presence of groups, linked to each other by strong hydrogen bonds, on the lower and upper rims of the macrocycle have been synthesised. An original method for the synthesis of calix[4]resorcinarenes **48a–e**, containing dialkoxy-



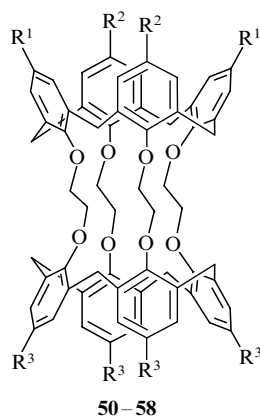
R = Et (a), Pr^n (b), Pr^i (c), Bu^n (d), Bu^i (e).

phosphoryl groups on the lower rim has been proposed.⁹⁹ Partial hydrolysis of these compounds yielded phosphonic monoesters **49a–e**.

Studies of self-aggregation of compounds **49a–e** in deuteriochloroform performed by 2D ¹H NMR techniques (NOESY and ROESY) confirmed the formation of tubular aggregates due to head-to-tail association of molecules in solution. This is also indicated by the presence of cross-peaks between the hydrogen atoms of the alkyl groups of the phosphorus fragments located on the lower rim of the macrocycle and the aromatic hydrogen atom located between two hydroxy groups on the upper rim (marked by arrows).

2. Calix[4]arene tubes as a new class of selective potassium ionophores

Determination of the structure of the potassium channel from *Streptomyces lividans* encouraged researchers to study the structural features of ion channels by using synthetic mimetics. Although the known synthetic receptors for K⁺ cations are rather good, they still do not demonstrate sufficient selectivity. High selectivity was attained by Beer and co-workers.¹⁰¹ They synthesised a new class of cryptand-like ionophores **50–58** derived from the biscalix[4]arene structure. Compounds **50–58** are composed of two calixarene fragments connected by four ethylene groups located on the lower rim. The ion channels based on these compounds show high selectivity for K⁺ cations over other Group I metal cations and Ba²⁺ cations.



50: R¹ = R² = R³ = Bu^t; **51:** R¹ = R² = R³ = Oct^t;
52: R¹ = R² = R³ = H; **53:** R¹ = R² = H, R³ = Bu^t;
54: R¹ = R² = Oct^t, R³ = Bu^t; **55:** R¹ = R² = Prⁱ, R³ = Bu^t;
56: R¹ = R² = Ph, R³ = Bu^t; **57:** R¹ = R² = Oct^t, R³ = H;
58: R¹ = Bu^t, R² = R³ = H.

Two calixarene fragments connected by four ethylene spacers provide a rigid ensemble of eight electron-donating oxygen atoms for complexation with the metal. The calixarene fragments endow the structure with a filter restricting the size of the incoming cations, similar to the tyrosine filter which exists in the cell potassium channels.

Variation of substituents on the upper rim ensures fine adjustment of the rate of K⁺ capture by the calixarene fragment; this was evaluated using NMR data on the conformational changes during binding. The selectivity of complex formation by compounds **50–58** with K⁺ was demonstrated by NMR and electro-spray mass spectrometry. According to X-ray diffraction data (Fig. 30), the potassium ion in compound **50** is localised at the centre of a partially flattened cube formed by oxygen atoms, the K–O distances varying from 2.759(6) to 2.809(6) Å. The cone cavities contain two methanol molecules.

For elucidating the influence of the nature of the counter-ion on binding of the K⁺ cation, complexation of compound **50** with a number of potassium salts has been studied. Substantial differ-

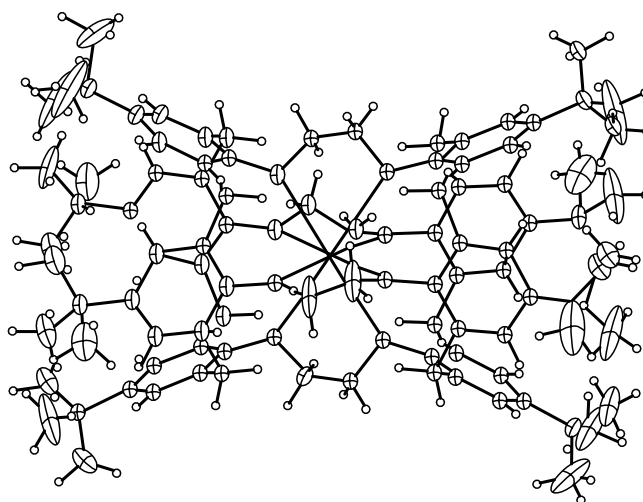


Figure 30. Structure of the crystalline complex of calix[4]arene **50** with K⁺.

ences in binding of the K⁺ cation were found. In particular, the complexation was most efficient with the iodide, hexafluorophosphate, benzoate and triflate anions present as counter-ions. The least pronounced or even zero binding was found for the nitrate, perchlorate and picrate anions. A competitive experiment for binding of the potassium cations by compound **50** and by [2.2.2]cryptand showed that the complex with the calix[4]arene tube **50** is exceptionally stable, whereas in the case of cryptand, 28% of potassium ions remain free after 15 h.

The selectivity of complexation of calix[4]arene tubes **50–58** with the potassium cation over other alkali metal cations and Ba²⁺ in a chloroform–methanol mixture (4 : 1) was determined at a 20-fold excess of Na⁺, Rb⁺, K⁺, Cs⁺, and Ba²⁺ iodides. Only K⁺ cations are bound by any of compounds **52–58**. Nanotube **50** binds less than 5% of Rb⁺, and tube **51** showed a 10% binding of Na⁺ cations after 48 h; over the same period of time, these compounds bind 100% of potassium. Thus, calix[4]arene tubes are highly selective for potassium cation and surpass in selectivity ionophores based on calix[4]crowns, which, despite the Na⁺/K⁺ selectivity, still capture substantial amounts of Rb⁺ cations.

Competitive complexation has also been studied by electro-spray mass spectrometry. All spectra of equimolar mixtures of compounds exhibited peaks only for the potassium complexes [M + K⁺] and [M + K⁺ + 2 H₂O]. Even in the case where the concentration of K⁺ decreased to 2.5 μmol litre^{−1} and the concentrations of competing ions were below 10 μmol litre^{−1}, the mass spectrum displayed the presence of only potassium-containing complexes, which proves substantial K⁺ selectivity of all of the calix[4]arene tubes.

In order to clarify how the K⁺ cation enters the calix[4]arene tube, molecular modelling of this process was performed. Two routes are possible for the potassium cations to flow through the tube, namely (i) the axial route where the cation passes the calixarene filter toward the polyether binding sites and (ii) the equatorial route where the cation is coordinated directly to groups of the cryptand-like binding sites. First, the influence of substituents occurring on the upper rim of the macrocycle (H, Bu^t, Oct^t, OH) was studied. It was found that the *tert*-butyl groups play an important role in the complexation through a change in the conformation of calix[4]arene tubes, which does not take place in the presence of sterically crowded *tert*-octyl groups, which block the *gggg*-conformation of the cone. The lack of alkyl groups on the upper rim (**52**, R¹ = R² = H) also deprives the cavity of any incentive to change the conformation.

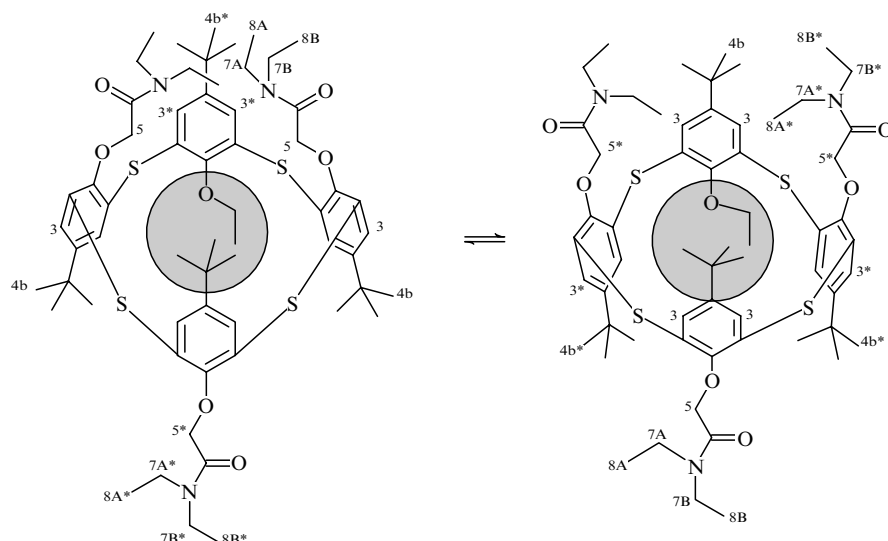


Figure 31. Passage of a potassium cation through the macrocyclic ring of compound **59** in the 1,3-*alternate* conformation.

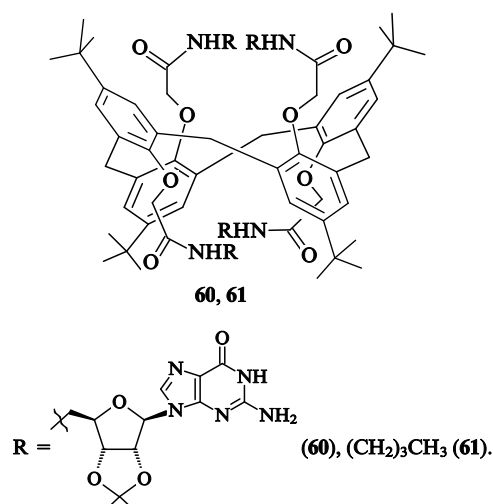
Data about the route travelled by the cation were obtained by molecular mechanics calculation of the energy of the cationic complex depending on the position of the potassium ion relative to the axis (along and across) of the calix[4]arene tube with a step of 0.5 Å. The flow of the cation through the *tert*-butyl groups of calix[4]arene with further movement along the axis toward the centre of the nanotube was found to be most favourable from the energy standpoint. Thus, the molecular modelling on the basis of crystallographic data confirmed that the potassium cation approaches the oxygen atoms along the axial plane of the calixarene dimer, passing through one of its lipophilic molecular cavities.

The possibility of passage of K^+ through the macrocyclic ring of thiacalix[4]arene has been confirmed experimentally by Solovieva *et al.*,¹⁰² who studied the 1:1 potassium complex (with chloride as the counter-ion) of the tetraamide derivative **59** in the 1,3-*alternate* conformation by 1D and 2D ^1H NMR spectroscopy in $CDCl_3$. They demonstrated the presence of chemical exchange between the amide fragments located on different sides of the macrocyclic plane, which are magnetically inequivalent in pairs (due to complexation with K^+). It is evident that such exchange is possible only in two cases: in the case of intramolecular migration of K^+ between the amide fragments located on different sides of the macrocyclic plane of 1,3-*alternate* **59** (Fig. 31) and upon dissociation of the complex formed on one side of the macrocycle and subsequent complexation on the other side of the macrocycle. The second route appears unlikely in nonpolar solvents ($CDCl_3$) due to the very low concentration of free ions in these solutions. Moreover, on heating in a nonpolar medium, this complex is destroyed and KCl precipitates.

3. Self-assembling nanotubes from combined calix[4]arene and guanosine fragments

It has been shown¹⁰³ that in the presence of sodium cations, calix[4]arene **60** containing guanosine fragments in the 1,3-*alternate* conformation forms self-assembling nanotubes.

It has been shown previously that telomeric DNA forms G-complexes with channels filled by the cations. The G-wires that reach 1000 nm in length can be visualised using atomic force



microscopy. This approach is based on the template self-assembly of guanosine on metal cations, in particular, in the presence of metal cations, guanosine forms a quartet with hydrogen bonds (Fig. 32 a). The cyclic G-quartet stabilised by the Na^+ or K^+ cation is capable of further self-assembly through stacking.

The Na^+ cations initiate one-dimensional association of G_4 -calix[4]arene **60** (Fig. 32 b). Calix[4]arene **60** in the 1,3-*alternate* conformation orients two orthogonal pairs of self-complementary G-nucleosides in such a way that they become capable of efficient intermolecular hydrogen bonding with neighbouring macrocycles. The process of assembling is fully reversible. The cation-template aggregation of calix[4]arene **60** can be controlled by varying the pH value and the temperature.

In the micrographs of compound **60** obtained by electron transmission microscopy, one can see extended structures about 1 μm long, which are arranged either as separate tubes or as 3 to 50 nm thick bundles of tubes. These structures are relatively straight and have no sharp turns. The thickness of separate tubes is close to the resolving power of the microscope, *i.e.*, it is about 3 nm.

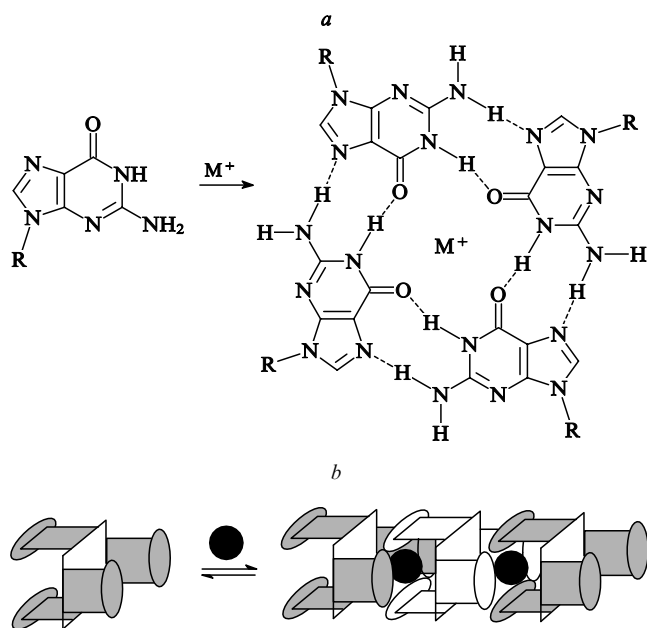


Figure 32. Template self-organisation of guanosine on metal cations (a) and cation-template self-assembly of calix[4]arene **60** to form a nanotube (b).

The squares stand for the calix[4]arene in the 1,3-*alternate* conformation, ellipses are the guanosine fragments and circles show the Na^+ cation.

4. The anionic channel based on aminocalix[4]arene

Sidorov *et al.*¹⁰⁴ have studied the transport activity of the tetrabutylamide derivative of calix[4]arene in the 1,3-*alternate* conformation (compound **61**) with respect to Cl^- and HSO_4^- anions in liposomes, planar bilayer lipid membranes and cells of the HEK-293 line.

The results of ionic conductance measurements, together with ^1H NMR and X-ray diffraction data indicate that compound **61**, first, forms ion channels in bilayer membranes; second, performs ion transport through a cell membrane with a positive holding potential; third, inverts the pH inside liposomes at a concentration gradient of chloride anions; fourth, demonstrates a substantial Cl^-/SO_4^{2-} selectivity. Calix[4]arene **61**, which binds HCl and forms an ion channel in a bilayer lipid membrane, is a rare example of a synthetic nonpeptide ion channel demonstrating anion selectivity. The ability to bind HCl and the transporting activity of this compound can be explained by the three-dimensional structure and hydrophobicity of calixarene and the presence of amide side chains in the molecule. The change of any of these parameters either shifts the selectivity from the anion to the cation or deprives the molecule of the transport activity. The transport of anions by compound **61** takes place through the H^+/Cl^- symport or Cl^-/OH^- antiport. Some crystal data indicate that calix[4]arene **61** forms self-assembling channels able to transmit Cl^- anions and water molecules. In addition, compound **61** performs the voltage-dependent selective transport of Cl^- anions through the membranes of the HEK-293 cells. This opens up broad prospects for investigating compound **61** as an antibiotic capable of selective interaction with the bacterial cell.

VIII. Conclusion

It is known that cell membranes have a common structural organisation. They are constructed as phospholipid bilayers with associated membrane proteins responsible for specific functions. Some proteins function as receptors responding to an external signal by activation of a number of intracellular signal cascades, some

others are involved in the transport of ions and molecules through the cell membrane. The design of models that mimic the ion transport in biological systems is needed for the understanding of very complex membrane processes that regulate the relationship of living organisms with the environment. The research into transmembrane ion channels is among the most vigorously progressing routes of modern biochemistry, nanotechnology and supramolecular chemistry. The design of ion-molecular devices that mimic the principles of transmembrane signal transfer opens up absolutely new opportunities for the development of natural science and technology. The use of simple artificial channel-like systems representing an alternative to natural peptides and proteins would result in the development of new nano-sized structures (nanotubes, ionic wires, *etc.*) with the properties of abiotic transmembrane channels ensuring the ionic permeability in natural systems (cells). The use of such systems in biosensors is a new engineering approach to the design of sensors for detection of various substrates both *in vitro* and *in vivo*.

During the last decade, significant progress has been attained in the study of properties of artificial ion channels and the key requirements of the design have been developed rather thoroughly. Any transmembrane ion channel has contacts with both the hydrophobic core of the lipid bilayer and aqueous solutions. In this connection, the channel-forming structures should be amphiphilic. The sites of a compound or an associate that are in contact with the aqueous medium surrounding the membrane should be enriched with polar and readily ionisable functional groups and the residues in contact with the lipid chains should contain long non-polar segments whose length must be sufficient to bridge the bilayer. Thus, when designing channel-forming structures, one should bear in mind that molecules incorporated in the lipid membrane should consist of a hydrophilic head in contact with the polar environment and the non-polar tail, which is incorporated in the membrane due to hydrophobic interactions. This follows from energy principles. In addition, for binding and transport of ions, charged or polar groups must be present inside the bilayer, *i.e.*, ion channels should be polar from the inside and hydrophobic from the outside.

Two key approaches to the design of channel-forming structures can be distinguished. One approach is the creation of molecules or various ion pairs that are able to form channel-like associates upon incorporation into a phospholipid membrane. The degree of aggregation of chemical species to form a half channel or a channel depends on a large number of factors; therefore aggregates of a variety of compositions can appear in the membrane.

Most artificial ion channels switch from the closed state to the open state as a result of random aggregation processes in the lipid bilayer. Self-assembling oligomeric associates immobilised on an electrode surface and mimicking the properties of biomolecules represent the first step in the creation of new ion-molecular devices used as sensors for various types of chemical species. This equipment is needed first of all for the diagnostics and analysis of the state of the environment.

The second approach is the design of a single pore-forming molecular structure, most often, containing a macrocyclic system which can be spontaneously incorporated into the membrane. However, in the case of these structures, two mechanisms of ion transport may compete (an ion channel or an ion carrier). The molecular structures whose length is sufficient to bridge the phospholipid membranes are nano-sized. This opens up broad prospects for using such structures for miniaturisation of electronic devices.

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